



Trans-Catheter Aortic Valve Replacement and Surgical Aortic Valve Replacement Outcomes in Patients with Dialysis: Systematic Review and Meta-Analysis



Mohinder R. Vindhya^{a,*}, Paul Ndunda^a, Sinan Khayyat^a, Venkata Subbarao Boppana^{a,b}, Zaher Fanari^{a,b}

^a Internal Medicine, University of Kansas School of Medicine - Wichita, 1010 N Kansas, Wichita, 67214 KS, USA

^b Cardiology, Heartland Cardiology/Wesley Medical Center, 550 N Hillside, Wichita, 67214 KS, USA

ARTICLE INFO

Article history:

Received 14 November 2018

Accepted 6 December 2018

Keywords:

TAVR - transcatheter aortic valve replacement

SAVR - surgical aortic valve replacement

ESRD - end stage renal disease

ABSTRACT

Background: Dialysis is associated with higher rate of aortic valve calcification and higher cardiovascular mortality. Transcatheter aortic valve replacement (TAVR) is an established alternative for surgical aortic valve replacement (SAVR) in patients with higher and intermediate co-morbidities including dialysis.

Methods: Two independent investigators systematically searched Medline, Cochrane, and Web of Science. The ROBINS-I tool was used to analyze and assess the bias from the selected studies.

Results: The search resulted in 4 observational studies with a total of 966 patients. TAVR in dialysis patients was associated with no significant difference in in-hospital mortality [8.1% vs 10.3%; OR (95% CI) 0.74 (0.35, 1.60), I² = 50%, P = 0.45], risk-of-strokes at 30 days [2% vs 4.4%; OR (95% CI) 0.49 (0.22, 1.09), I² = 0%, P = 0.08], vascular complications [12.7% vs 13.2%; OR (95% CI) 0.96 (0.55, 1.67), I² = 0%, P = 0.89], need of blood transfusion [43.1% vs 66.4%; OR (95% CI) 0.27 (0.05, 1.39), I² = 89%, P = 0.12], or bleeding risk [5.6% vs 6.8%; OR (95% CI) 0.91 (0.18, 4.64), I² = 5%, P = 0.91] when compared to SAVR. TAVR was associated with significantly shorter length of stay [8.5 days vs 14.2 days; mean difference (95% CI) -5.89 (-9.13, -2.64), I² = 76%, P < 0.0001] and higher pacemaker implantation [11.4% vs 6.8%; OR (95% CI) 1.74 (1.07, 2.81), I² = 5%, P = 0.02].

Conclusion: TAVR outcomes were comparable to SAVR but had a significantly shorter length of stay and a higher pacemaker implantation rate in dialysis patients.

© 2018 Elsevier Inc. All rights reserved.

1. Introduction

Chronic kidney disease and end stage renal disease requiring dialysis is associated with increased mortality after cardiac surgery [1]. Calcified aortic stenosis is the most common valvular pathology in patients on dialysis [2]. Previously, surgical aortic valve replacement (SAVR) was the only available option for aortic valve replacement in severe aortic stenosis [3,4]. End-stage renal disease (ESRD) patients on dialysis are less likely to be offered SAVR due to the perceived increased morbidity and mortality associated with it [5–8]. Transcatheter aortic valve replacement (TAVR) procedure emerged as an alternative to SAVR in patients with intermediate and high-risk [9–13]. There are no randomized controlled trials (RCT) comparing TAVR and SAVR specifically in dialysis patients [14–18]. The available data is only from small retrospective studies comparing TAVR and SAVR in dialysis patients [14–18]. The goal of our meta-analysis is to evaluate the comparative outcomes of TAVR versus SAVR in patients with dialysis.

2. Methods

We searched three major electronic databases, Medline [PubMed], Web of Science, and the Cochrane Library Database, from January 2004 to May 2018 for all randomized controlled trials and observational studies comparing TAVR and SAVR in ESRD patients on dialysis. The search was conducted using the keywords: “transcatheter aortic valve replacement,” “transcatheter aortic valve implantation,” “surgical aortic valve replacement,” “surgical aortic valve implantation,” “end-stage renal disease,” “Chronic Kidney Disease,” “Chronic Kidney Disease stage 5” and “dialysis.” We also screened for significant cardiovascular conferences abstracts within the last two years for relevant studies.

Two investigators independently (SK and MV) assessed and screened the published data including the abstracts submitted to cardiovascular conferences. No differences during the assessment and screening between that investigators were noted. Included studies had two arms comparing TAVR and SAVR in dialysis patients. Single arm TAVR and SAVR study data from observational studies were excluded. The same two independent authors performed data extraction which was cross-checked by the team of investigators.

* Corresponding author.

E-mail addresses: mvindhyal@hotmail.com (M.R. Vindhya), skhayyat@kumc.edu (S. Khayyat).

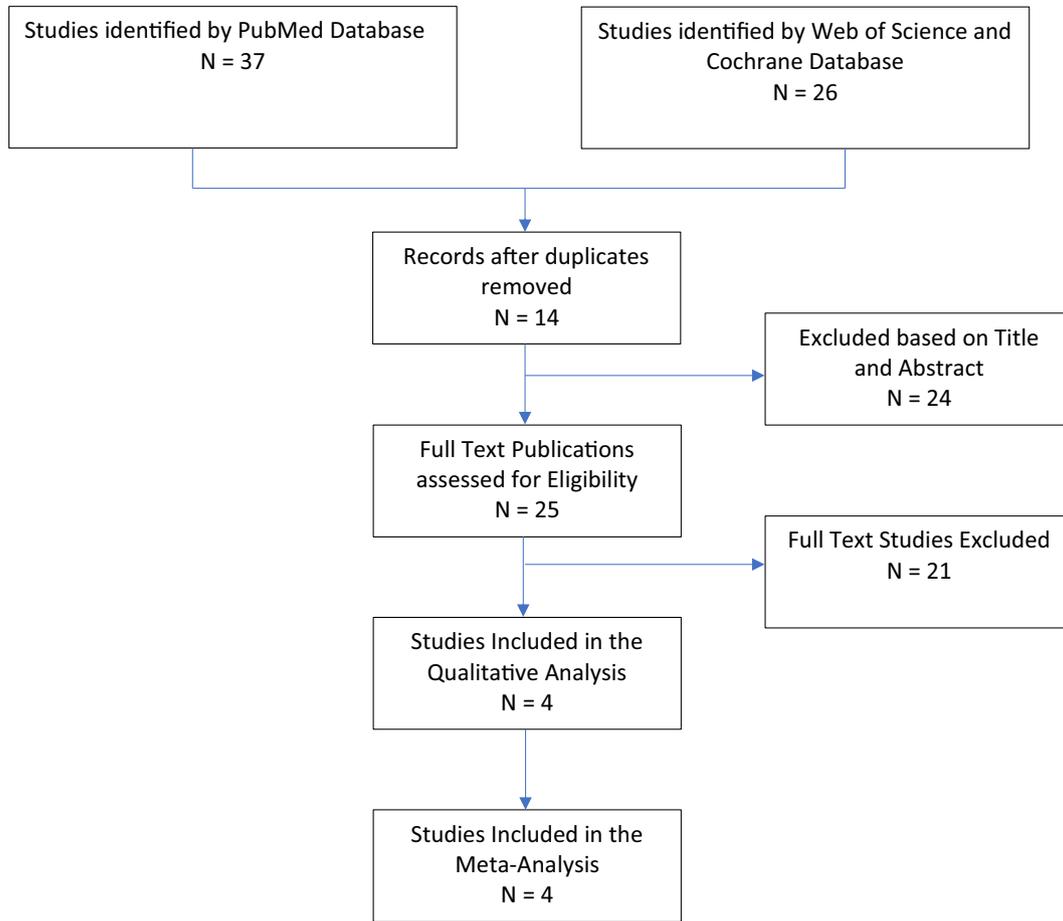


Fig. 1. Selection process of the included studies.

The quality of the identified studies was assessed with respect to control for confounders, measurement of exposure, completeness of follow-up, and blinding. We followed a scoring system based on a checklist derived from recommended criteria recommended by the QUOROM (The Quality of Reporting of Meta-analyses) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to assess the quality of the trials used in this meta-analysis [19,20].

The extracted data included information regarding the patient characteristics, study design, and outcomes. The primary outcomes of interest were in-hospital mortality and stroke in 30 days. The secondary outcomes were vascular complications, need for blood transfusions, bleeding risk, pacemaker implantation, and length of stay. Once the data were extracted, the Robbins-I tool was used to analyze and assess the bias from the selected studies. We performed a group analysis for all of the primary and secondary outcomes of interest. We calculated the percentages of various outcomes. We also assessed study heterogeneity. All authors assessed publication bias. We used the 95% confidence interval and a P value of <0.05 as statistically significant in all our analyses. All analysis was conducted using Rev-Man software version 5.3.

3. Results

A total of 63 published manuscripts were identified, of which 14 were excluded as duplicates and 24 were excluded based on the title the abstract. Full texts of the remaining 25 studies were examined. Twenty-one studies were excluded after examination of the full text. Eventually, four observational studies were included in the qualitative analysis. Of the studies included for analysis, two were, and two had Cox proportional hazard model for matching the variables. Fig. 1 summarizes the selection process of the included studies. The overall risk of bias judgment for the propensity-matched studies was low; for the two Cox proportional hazard models' risk of bias was low to moderate due to confounding.

A total of 966 patient were included. Of these 444 underwent TAVR and 522 underwent SAVR. Table 1 summarizes the baseline characteristics of the included studies and Table 2 summarizes the demographic and clinical characteristics of the study cohort.

TAVR in dialysis patients was associated with no significant difference in in-hospital mortality [8.1% vs 10.3%; OR (95% CI) 0.74 (0.35, 1.60), I2 = 50%, P = 0.45, Fig. 2A], risk of strokes at 30 days [2% vs 4.4%; OR (95% CI) 0.49 (0.22, 1.09), I2 = 0%, P = 0.08, Fig. 2B], vascular complications [12.7%

Table 1
Characteristics of the studies included.

Author & year of publication	Alqahtani et al., 2017	Condado et al., 2017	Korbin et al., 2015	Nguyen et al., 2012
Study type	Observational	Observational	Observational	Observational
Study population	Dialysis	Dialysis	Dialysis	CKD and dialysis
TAVR arm (number)	197	30	194	101
SAVR arm (number)	197	30	194	23
Risk of bias (ROBINS-I)	Moderate	Moderate	Moderate	Moderate

Table 2
Demographic and clinical characteristics of the study population.

Study characteristic	Alqahtani et al. ^a		Condado et al. ^b		Korbin et al. ^a		Nguyen et al. ^b	
	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR
Age (mean)	73	72	71 ^c	63 ^c	77.7	78	79.6	60.7
Male (%)	65	64	70	63.3	58	56	60.9	52.5
Caucasian (%)	69	67	53.3	26.7	NA		82.6	45.5
African American (%)	17.8	20.8	NA		14	14	NA	
Hypertension (%)	86.8	87.3	90	100	NA		95.7	95.1
Diabetes (%)	45.7	45.2	63.3	43.3	69	66	52.2	46.5
Chronic pulmonary disease/COPD (%)	27.9	24.9	43.3	16.7	53	52	47.8	24.7
Atrial fibrillation/flutter (%)	42.6	40.1	43.3	50	NA		NA	
Peripheral vascular disease/PAD (%)	31.5	26.9	43.3	23.3	86	88	60.9	20.8
Coronary artery disease/CABG (%)	47.2	44.2	63.3	53.3	NA		39.1	16.8
Congestive heart failure (%)	11.7	12.7	93.3	76.7	97	95	NA	
Liver disease (%)	6.6	6.6	NA		11	12	NA	
Cerebrovascular accident (%)	NA		30	3.3	NA		34.8	6.9
Dyslipidemia (%)	NA		96.7	76.7	NA		100	49.5
Body mass index - kg/m ² (mean)	NA		26.3 ^c	28.3 ^c	NA		28	28.7

^a Propensity matched cohort.
^b Cox hazard matched cohort.
^c Median.

vs 13.2%; OR (95% CI) 0.96 (0.55, 1.67), I2 = 0%, P = 0.89 Fig. 3A], need of blood transfusion [43.1% vs 66.4%; OR (95% CI) 0.27 (0.05, 1.39), I2 = 89%, P = 0.12, Fig. 3B], or bleeding risk [5.6% vs 6.8%; OR (95% CI) 0.91 (0.18, 4.64), I2 = 5%, P = 0.91 Fig. 3C], when compared to SAVR. TAVR was associated with significantly shorter length of stay [8.5 days vs 14.2 days; mean difference (95% CI) -5.89 (-9.13, -2.64), I2 = 76%, P < 0.0001, Fig. 3D] and higher pacemaker implantation [11.4% vs 6.8%; OR (95% CI) 1.74 (1.07, 2.81), I2 = 5%, P = 0.02, Fig. 3E].

4. Discussion

Dialysis in ESRD patients is associated with an increased risk cardiovascular disease including valvular disorders [21–23]. The improvement of the care of ESRD patients led to declining mortality rates in this complex population which in turn reflected in increased the number of patients living with complex comorbid conditions and the procedures that they may be subjected to giving they are living longer [24]. While TAVR showed an

improved outcome in patients with high surgical risk and comparable results in those with intermediate risk [9–13], it is unclear whether TAVR offers a comparable outcome in ESRD on dialysis as these patients were not studied well in randomized controlled trials (RCT).

Data comparing TAVR in dialysis patients to patients with a normal renal function would show similar improvement in New York Heart Association class if there were no significant peri-procedural complications in dialysis group [25]. Data are less clear when there is a complication related to TAVR.

Our study is trying to pool existing non-randomized data available to offer a potential answer in the light of the current lack of data derived from RCT. As compared to dialysis patients who underwent SAVR, TAVR patients had a significantly shorter length of stay at the expense of a higher pacemaker implantation rate. The bleeding risk need for transfusion, vascular complications, in-house mortality, and 30-day stroke outcomes were similar in the TAVR and SAVR arms.

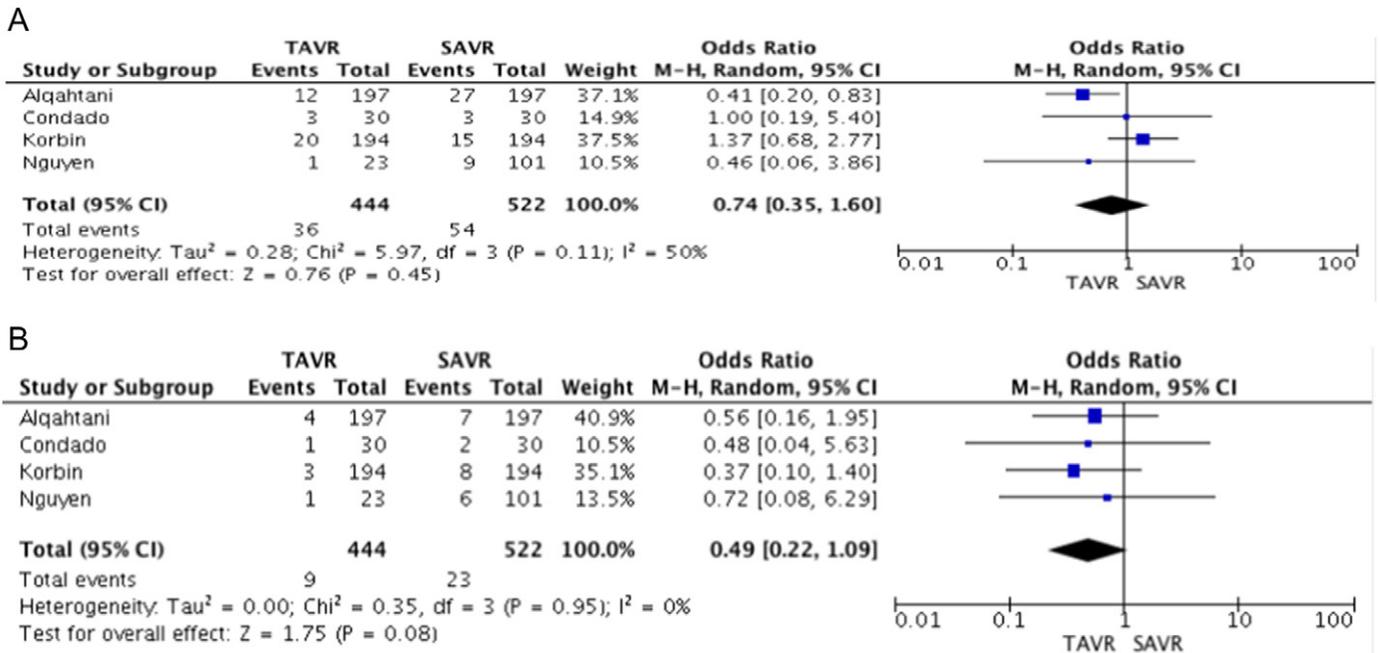
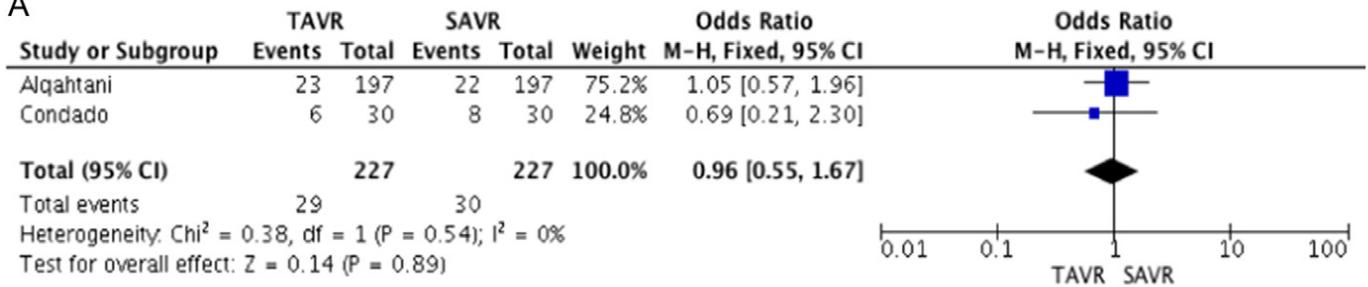
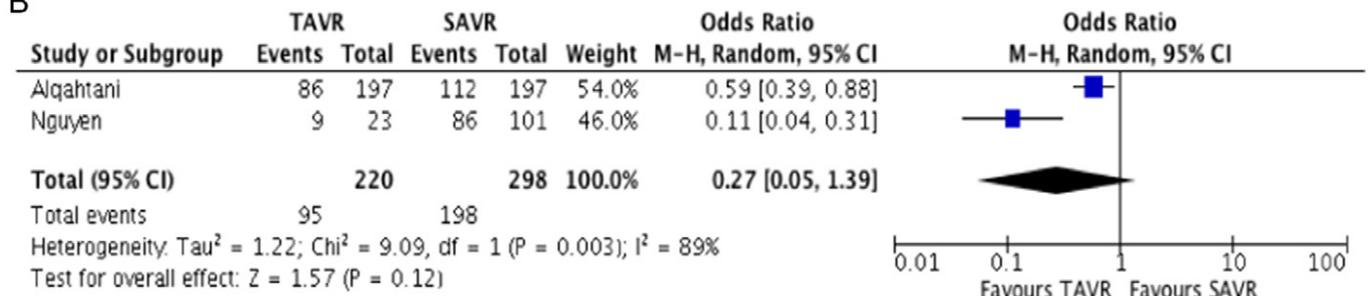


Fig. 2. A. In-hospital mortality, TAVR & SAVR in dialysis. B. Risk of stroke at 30 days, TAVR & SAVR in dialysis.

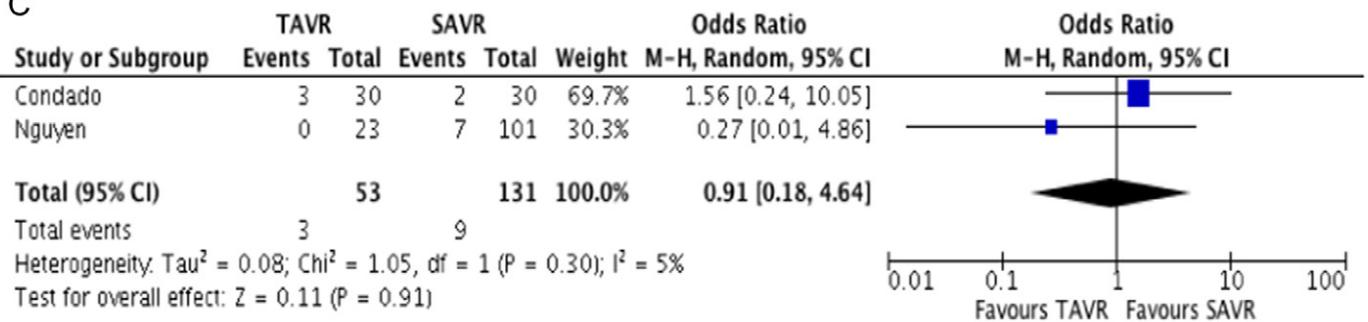
A



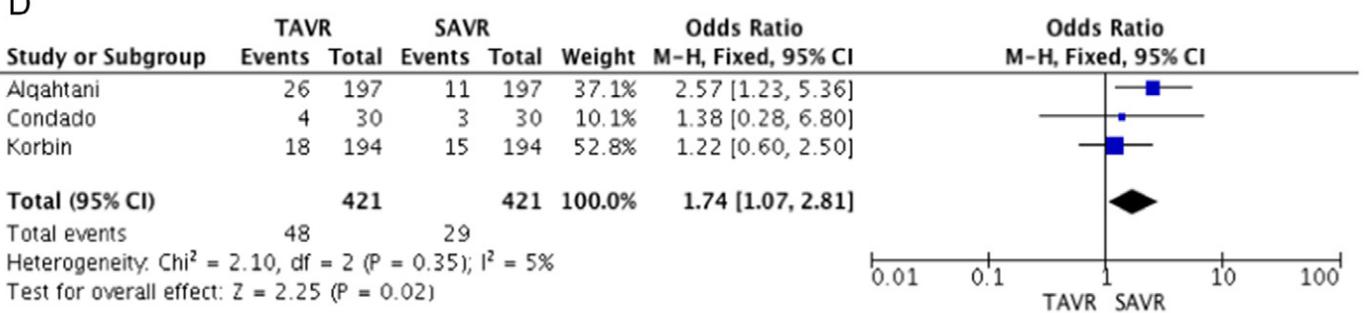
B



C



D



E

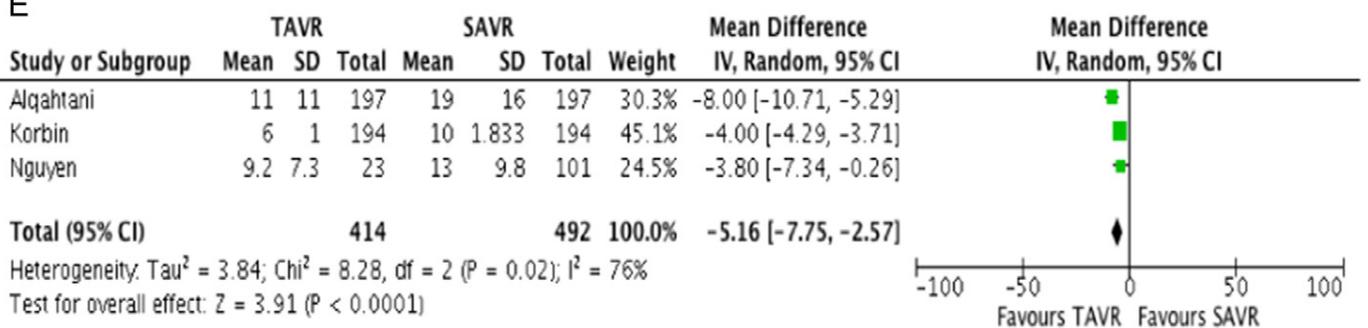


Fig. 3. A. Vascular complications, TAVR & SAVR in dialysis. B. Need for blood transfusion, TAVR & SAVR in dialysis. C. Bleeding risk, TAVR & SAVR in dialysis. D. Pacemaker implantation rate, TAVR & SAVR in dialysis. E. Length of stay, TAVR & SAVR in dialysis.

Several other studies assessed the outcomes of TAVR in dialysis patients but were not propensity-matched nor compared to SAVR outcomes. Alqahtani et al. [16] study included the data from the National Inpatient Sample database which collected the data from 2005 to 2014. Bhise V et al. [26] and Alkhalil et al. [27] studies were excluded from the analysis to avoid duplication as the data for that study came from the same National Inpatient Sample from years 2012 to 2014. Thourani et al. reported that SAVR was associated with increased in-hospital mortality in end-stage renal disease patients with dialysis compared with patients who do not have a renal disease (15.8% vs 2.9%; $P < 0.01$) [7]. Similarly, Dumonteil et al. also reported that all-cause high 30-day mortality rate after the TAVR procedure in end-stage renal disease patients with dialysis when compared to patients who do not have a renal disease (15.2% vs 1.8%; $P < 0.007$) [28].

There is an abundant amount of TAVR and SAVR outcomes data from the different registries such as German Aortic Valve Registry, Nordic Aortic Valve Intervention Trial, and the Placement of Aortic Transcatheter Valves trial registry but there are very few studies comparing TAVR and SAVR outcomes in End Stage Renal Disease patients with dialysis [5–8,14–18,21,22]. Dialysis patients often coexist with other cardiovascular risk factors such as dyslipidemia, smoking, psychosocial stressors, diabetes, hypertension and obesity which increases the cardiovascular mortality risk [29]. Dialysis is also associated with markers of inflammation such as TNF-alpha, which may play a role in cardiovascular (myocardial infarction, stroke, etc.) and non-cardiovascular mortality causation (septicemia and bacteremia) [30,31]. It should be noted that dialysis is also associated with an increased risk of peripheral vascular disease and vascular calcification which may lead to an increased risk of vascular complications as well as bleeding. Interestingly we did not see this potential impact affecting the outcomes of TAVR patients in this meta-analysis [32–34].

In this day and age of health care reform and resource utilization, when the TAVR and SAVR have almost similar outcomes, the gravity to reduce the cost of hospitalization and post-hospital care has been of utmost importance. SAVR patients are more likely to need skilled nursing care and long-term care post-surgery before they return home. The length of stay has been significantly shorter in the TAVR group when compared to the SAVR patients from our meta-analysis, which may play a role in the near future especially in a certain patient population who are lacking resources. It should also be noticed that most of the patients included in our cohort were between 2002 and 2014. TAVR valves improved significantly since then with smaller sheaths sizes leading to lower vascular complications, improved pacemaker rate and length of stay with the newer generations of TAVR. These improvements lead to significant improvement in the cost-effectiveness of TAVR in patients at higher risk profile.

This meta-analysis has some limitations. First, single arm observational reporting data only in TAVR and SAVR outcomes without any comparison arms were excluded from the study. Second, even though we merged the propensity-matched and Cox hazard group data in our analysis, there were multiple possible confounding factors. Third, not all the studies included in the analysis have the same variables used for propensity matching or with Cox hazard grouping. Fourth, there were limited observational data in both TAVR and SAVR groups to find outcomes that are predicted with a high degree of sensitivity and specificity.

5. Conclusions

TAVR, when compared to SAVR, had a significantly lower length of stay but also had higher pacemaker implantation rates. More robust data is needed in dialysis patients undergoing TAVR and SAVR procedures for further delineation. More long-term outcomes should be followed in future studies as the data are scarce in both TAVR and SAVR groups.

References

- [1] Mooney JF, Ranasinghe I, Chow CK. Preoperative estimates of glomerular filtration rate as predictors of outcome after surgery: a systematic review and meta-analysis. *Anesthesiology* 2013;4:809–24.
- [2] Ohara T, Hashimoto Y, Matsumura A, Suzuki M, Isobe M. Accelerated progression and morbidity in patients with aortic stenosis on chronic dialysis. *Circ J* 2005;12:1535–9.
- [3] 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;11:1336–41.
- [4] Kaplon RJ, Cosgrove 3rd DM, Gillinov AM, Lytle BW, Blackstone EH, Smedira NG. Cardiac valve replacement in patients on dialysis: influence of prosthesis on survival. *Ann Thorac Surg* 2000;2:438–41.
- [5] Horst M, Mehlhorn U, Hoerstrup SP, Suedkamp M, de Vivie ER. Cardiac surgery in patients with end-stage renal disease: 10-year experience. *Ann Thorac Surg* 2000;1:96–101.
- [6] Brinkman WT, Williams WH, Guyton RA, Jones EL, Craver JM. Valve replacement in patients on chronic renal dialysis: implications for valve prosthesis selection. *Ann Thorac Surg* 2002;1:37–42.
- [7] Thourani VH, Keeling WB, Sarin EL. Impact of preoperative renal dysfunction on long-term survival for patients undergoing aortic valve replacement. *Ann Thorac Surg* 2011;6(1798–1806) [1806–1797].
- [8] Thourani VH, Sarin EL, Keeling WB. Long-term survival for patients with preoperative renal failure undergoing bioprosthetic or mechanical valve replacement. *Ann Thorac Surg* 2011;4:1127–34.
- [9] Leon MB, Smith CR, Mack M. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;17:1597–607.
- [10] Smith CR, Leon MB, Mack MJ. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;23:2187–98.
- [11] Adams DH, Popma JJ, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;19:1790–8.
- [12] Leon MB, Smith CR, Mack MJ. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;17:1609–20.
- [13] Reardon MJ, Mieghem NMV, Popma JJ. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;14:1321–31.
- [14] Kobrin DM, McCarthy FH, Herrmann HC. Transcatheter and surgical aortic valve replacement in dialysis patients: a propensity-matched comparison. *Ann Thorac Surg* 2015;4(1230–1236):1236–7.
- [15] Ailawadi G, LaPar DJ, Speir AM. Contemporary costs associated with transcatheter aortic valve replacement: a propensity-matched cost analysis. *Ann Thorac Surg* 2016;1:154–60.
- [16] Alqahtani F, Aljohani S, Boobes K. Outcomes of transcatheter and surgical aortic valve replacement in patients on maintenance dialysis. *Am J Med* 2017;1464 [1461–1464, 1411].
- [17] Nguyen TC, Babaliaros VC, Razavi SA. Impact of varying degrees of renal dysfunction on transcatheter and surgical aortic valve replacement. *J Thorac Cardiovasc Surg* 2013;6(1399–1406):13406–7.
- [18] Condado JF, Maini A, Leshnowar B. End-stage renal disease and severe aortic stenosis: does valve replacement improve one-year outcomes? *Catheter Cardiovasc Interv* 2017;6:1109–15.
- [19] Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of reporting of meta-analyses. *Lancet* 1999.
- [20] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;4:264–9 [264].
- [21] Szerlip M, Kim RJ, Adeniyi T. The outcomes of transcatheter aortic valve replacement in a cohort of patients with end-stage renal disease. *Catheter Cardiovasc Interv* 2016;7:1314–21.
- [22] Buttner S, Weiler H, Zoller C. Aortic valve stenosis in a dialysis patient waitlisted for kidney transplantation. *Ann Thorac Surg* 2016;102.
- [23] Kim D, Shim CY, Hong GR. Effect of end-stage renal disease on rate of progression of aortic stenosis. *Am J Cardiol* 2016;12:1972–7.
- [24] R. Saran, B. Robinson, K. C. Abbott, Renal Data System 2017 Annual Data Report: epidemiology of kidney disease in the United States, *Am J Kidney Dis*.
- [25] Allende R, Webb JG, Munoz-Garcia AJ. Advanced chronic kidney disease in patients undergoing transcatheter aortic valve implantation: insights on clinical outcomes and prognostic markers from a large cohort of patients. *Eur Heart J* 2014;38:2685–96.
- [26] Bhise V, Kanade P, Shantha GP. Transcatheter and surgical aortic valve replacement in patients with end-stage renal disease. *J Am Coll Cardiol* 2017;14:1875–6.
- [27] Alkhalil A, Golbari S, Song D. In-hospital outcomes of transcatheter versus surgical aortic valve replacement in end stage renal disease. *Catheter Cardiovasc Interv* 2018;4:757–65.
- [28] Dumonteil N, Boon RM, Tchetché D. Impact of preoperative chronic kidney disease on short- and long-term outcomes after transcatheter aortic valve implantation: a Pooled-Rotterdam-Milano-Toulouse In Collaboration Plus (PRAGMATIC-Plus) initiative substudy. *Am Heart J* 2013;5:752–60.
- [29] Shlipak MG, Fried LF, Cushman M. Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. *JAMA* 2005;14:1737–45.
- [30] Stenvinkel P, Ketteler M, Johnson RJ. IL-6, and TNF-alpha: central factors in the altered cytokine network of uremia—the good, the bad, and the ugly. *Kidney Int* 2005;4:1216–33.
- [31] Ishani AJ, Collins, Herzog CA, Foley RN. Septicemia, access and cardiovascular disease in dialysis patients: the USRDS Wave 2 study. *Kidney Int* 2005;1:311–8.

- [32] Fanari Z, Weintraub WS. Cost-effectiveness of transcatheter versus surgical management of structural heart disease. *Cardiovasc Revasc Med* 2016 Jan-Feb;17(1):44–7.
- [33] Cohen D, PARTNER 2 Investigators. Cost-effectiveness of transcatheter vs. surgical aortic valve replacement in intermediate risk patients. Results from the PARTNER 2A and Sapien3 Intermediate Risk Trials, presented at TCT 17. Available from: https://www.acc.org/-/media/Clinical/PDF-Files/Approved_PDFs/2017/10/24/TCT17_Presentation_Slides/Tue_Oct31/PARTNER-2A-SAPIEN-3-Cost-Effectiveness-TCT-2017.pdf, Accessed date: 14 April 2018.
- [34] Reynolds MR, Lei Y, Wang K. Cost-effectiveness of transcatheter aortic valve replacement with a self-expanding prosthesis versus surgical aortic valve replacement. *J Am Coll Cardiol* 2016;1:29–38.