Original Article

Transcatheter versus surgical aortic valve replacement in aortic stenosis patients with advanced chronic kidney disease: a systematic review and meta-analysis

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Background: Transcatheter aortic valve replacement (TAVR) has been increasingly used in all levels of risk patients, which is less invasive and has fewer complications. However, the benefits of transcatheter and surgical methods of aortic valve replacement remain controversial for aortic stenosis (AS) patients with advanced chronic kidney disease (stage 3-5).

Methods: We comprehensively searched PubMed, Embase, the Cochrane Library, and the International Clinical Trials Registry Platform (ICTRP) from January 2000 to October 2020 and performed a systematic review to evaluate the two techniques. Two investigators independently conducted the literature searches, study eligibility assessment, and data extraction in duplicate.

Results: Compared to surgical aortic valve replacement (SAVR), TAVR had lower risk of in-hospital mortality [odds ratio (OR): 0.53; 95% confidence interval (CI): 0.36–0.78; P=0.001], lower stroke rate (OR: 0.68; 95% CI: 0.47–0.96; P=0.03), lower risk of acute kidney injury (AKI) (OR: 0.42; 95% CI: 0.34–0.52; P<0.00001) and AKI requiring dialysis (OR: 0.65; 95% CI: 0.58–0.73; P<0.00001), lower rate of bleeding (OR: 0.35; 95% CI: 0.31–0.38; P<0.00001) and blood transfusion (OR: 0.41; 95% CI: 0.32–0.52; P<0.00001), lower infection rate (OR: 0.23; 95% CI: 0.13–0.38; P<0.00001), lower risk of atrial fibrillation (AF) (OR: 0.37; 95% CI: 0.17–0.79; P=0.01) and cardiac tamponade (OR: 0.53; 95% CI: 0.37–0.75; P=0.0003), shorter ICU stay [weighted mean difference (WMD): −2.55; 95% CI: −4.13 to −0.98; P=0.002] and hospital stay (WMD: −7.06; 95% CI: −8.41 to −5.71; P<0.00001).

Discussion: TAVR is a safe, efficient, and feasible technique for AS patients with advanced CKD and probably a better solution for its advantage in reducing in-hospital mortality, postoperative complications, ICU, and hospital stay.

Keywords: Transcatheter aortic valve replacement (TAVR); chronic kidney disease (CKD); aortic stenosis (AS); meta-analysis

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Introduction

Aortic stenosis (AS) is one of the most common valvular heart diseases with an estimated prevalence of 12% in patients aged 75 or older and over 25% of them were severe (1). Chronic kidney disease (CKD) is closely related to AS, for patients with CKD lead to calcification of the aortic valve which aggravates AS (2), and low cardiac output caused by AS results in renal dysfunction. Over 19 million patients in the United States are estimated to suffer from CKD or end-stage renal disease (ESRD) (3). Although it is less clear the prevalence of CKD globally, with the rapid increase of hypertension and diabetes, the main causes of CKD (4), the number of CKD patients may be increased as well. And up to 75% of AS patients have some degree of chronic kidney disease before surgery (5). Therefore, AS patients with CKD is becoming a common problem for the cardiologist.

Symptomatic AS carries a grave prognosis without aortic valve replacement (6) and surgical aortic valve replacement (SAVR) used to be the golden standard treatment, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend valve replacement for patients with abnormal aortic valve which reduced systolic opening (7). However, patients with advanced CKD (stage 3-5) are associated with high mortality and complications (8,9) and were regarded as having a higher risk for cardiac surgery than patients without CKD. The first successful transcatheter aortic valve replacement (TAVR) in man has been reported in 2002 (10), and it has been widely used for it is less invasive and has fewer complications. Compared with the medical management of severe AS both SAVR and TAVR improved clinical outcomes by reducing postoperative mortality (11,12). Since patients with advanced CKD were excluded from large randomized controlled trials (RCT) (13-15), it's still less clear whether TAVR is as safe and effective for patients with advanced CKD (stage 3-5).

Since the U.S. Food and Drug Administration has approved TAVR for patients at high surgical risk in 2011, thousands of such devices have been implanted worldwide. The proportion of TAVR has increased significantly, whereas SAVR has decreased. According to the latest study, the volume of TAVR increased by approximately four-fold and SAVR increased by approximately 33% (16). In recent years, many studies compared outcomes between TAVR and SAVR in advanced CKD patients which were neglected and few studies have focused on. So, we performed a systematic review and meta-analysis on pooled data from eligible studies to compare the efficacy and safety between TAVR and SAVR. The study protocol complies with the PRISMA and MOOSE reporting checklists (available at https://dx.doi.org/10.21037/apm-21-758) (17,18).

Methods

Search strategy

We performed a comprehensive online search on PubMed, Embase, the Cochrane Library and the International Clinical Trials Registry Platform (ICTRP) from January 2000 to October 2020 with the following MeSH and EMTREE keywords: transcatheter aortic valve replacement, TAVR, transcatheter aortic valve implantation, surgical aortic valve replacement, SAVR, surgical aortic valve implantation, chronic kidney disease, chronic kidney disease stage 5, renal dysfunction, renal failure, renal insufficiency, end-stage renal disease, and dialysis. No language restrictions were applied.

Study selection

All published studies that included TAVR *vs.* SAVR in adults with advanced CKD were identified and included. And advanced CKD (stage 3-5) defined as glomerular filtration rate of ≤59 mL/min/1.73 m^2 (19). Review articles, animal studies, and non-comparative studies were excluded. When multiple articles for a single study had been published, we used the latest publication to avoid potential overlapping patients in the included studies. Two independent investigators (SL Wei and PB Zhang) conducted the literature searches, study eligibility assessment, and data extraction in duplicate. Discrepancies were resolved by consensus and consultation with experienced reviewers (D Liu and Y Li).

Outcomes

The primary outcomes included in-hospital mortality and postoperative stroke. Secondary clinical outcomes included 1-year mortality, bleeding, blood transfusion, new-onset AF, permanent pacemaker implantation (PPMI) requirement, acute kidney injury (AKI), cardiac tamponade, infection, AKI requiring dialysis, major vascular damage, intensive care unit (ICU) stay and length of stay (LOS). Postoperative stroke was defined as in the hospital or at 30-day follow-up focal deficit regardless of duration

time. PPMI requirement was defined as patients with atrioventricular block, bradycardia, sick sinus syndrome or any other situations need PPMI post-procedure. Cardiac tamponade was defined as pericardial effusion discovered by doppler echocardiography post-procedure. AKI was defined as an absolute increase in serum creatinine concentration of ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours post-procedure or a relative increase of >50% within 7 days from baseline. The definition of AKI requiring dialysis was an AKI necessitating dialysis during the index hospitalization. Major vascular damage was defined as requiring surgical or percutaneous treatment for any access site complication. Bleeding was defined using Valve Academic Research Consortium-2 criteria.

Data abstraction

Data abstraction was carried out by two independent investigators (S Wei and P Zhang) who used a predefined, standardized protocol and data collection tool. Disagreement will be settled through consensus and consultation with experienced reviewers (D Liu and Y Li). We collected basic information of each target study including first author, publication year, study type, sample size, country, study period, outcomes analyzed, type of the population, and proportion of patients. The following baseline characteristics of patients were also gathered, such as: age, gender, hypertension, previous myocardial infarction (MI), heart failure (HF)/New York Heart Association (NYHA) Class, stroke or cerebrovascular disease (CVD), diabetes, coronary artery disease (CAD), peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), AF, and chronic liver disease.

Quality assessment

The Newcastle-Ottawa Quality Assessment Scale (NOS), which consists of 9 questions with 9 possible points for the observational study was used to assess the quality of the included studies, a score ≥6 was considered as high-quality and a score lower than 6 was defined as poor quality. The details of the assessment process are available in the Table S1. The Jadad Scale which consisted of randomization (0–2 points), blinding (0–2 points) and withdrawals (0–1 point) for assessing the risk of bias was used for randomized studies. Studies scored ≥3 points were defined as high quality. Details in Table S2. The quality of all included studies was independently assessed by two investigators (S Wei and P Zhang) and discrepancies were resolved through discussion with experienced reviewers (D Liu and Y Li).

Statistical analysis

Continuous variables were reported as mean (± standard deviation) or median (interquartile range). To convert a median (interquartile range) to a mean (± standard deviation), we used the formulas accepted in the literature (20). Categorical variables were expressed as number and percentage (%). Statistical analysis was performed with RevMan 5.3 software (Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen) to calculate summary effects, which were presented with 95% confidence intervals (CIs). The odds ratio (OR) and mean difference (MD) were separately used as a summary statistic to assess dichotomous data and continuous data. The heterogeneity of the studies was evaluated by the Cochrane χ^2 test (Q) or I^2, and divided into three groups: as low (25%), moderate (50%), and high heterogeneity (75%). If P value less than 0.1 in the Cochran Q test or I^2 value greater than 50%, a random effects model was utilized otherwise a fixed effects model was applied. P values were two-tailed, and $P<0.05$ was considered statistically significant.

Results

Eligible studies

The literature search identified 1,264 potentially relevant studies, 664 of these were excluded by reviewing the title and abstract. The remaining 98 studies were excluded after full text evaluation, details in *Figure 1*. After a strict appraisal, 21 studies including 12 propensity score-matched, 8 observational cohort studies, and 1 randomized controlled study were included. Except for 10 studies included in the previous meta-analysis, 2 missed studies and 9 recently published studies were included, 38,989 patients with advanced CKD were incorporated into the data synthesis (16,21-40).

Baseline characteristics of the included studies

Summarized characteristics were displayed in *Table 1*. A total of 38,989 patients from 7 different countries were enrolled (19,678 TAVR *vs.* 19,311 SAVR). There were 12 propensity score-matched studies, 7 retrospective

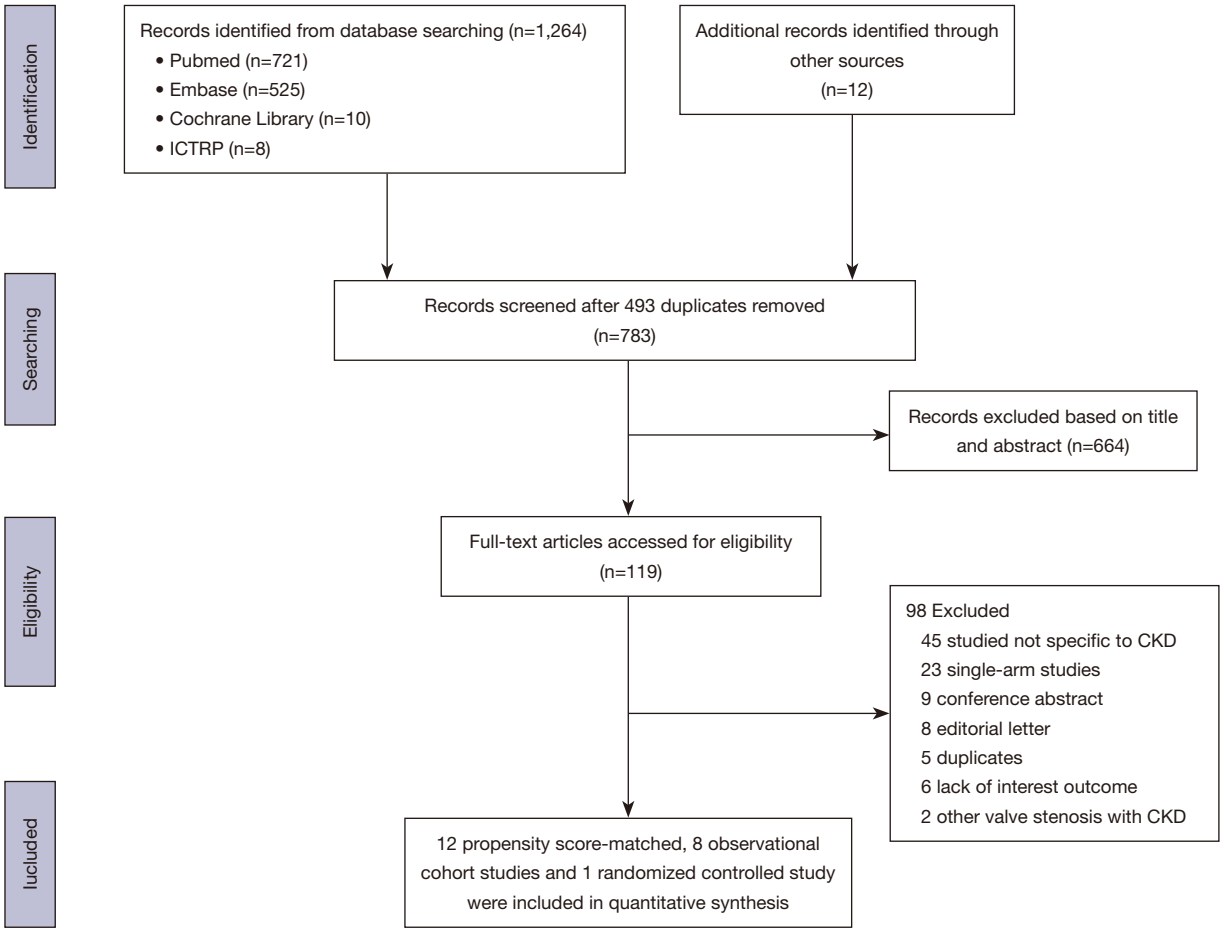

Figure 1 Flow diagram of the study selection process. ICTRP, the International Clinical Trials Registry Platform; CKD, chronic kidney disease.

observational studies, 1 prospective observational study, and 1 randomized controlled study, and all patients had advanced CKD including CKD stage 3 to 5, end stage renal disease and dialysis. Hypertension (89.8%), CAD (62.7%) and HF (51.8%) were the top three preoperative comorbidities in this population. Preprocedural dialysis patients were included exclusively in 11 studies. Patients in the TAVR group were more likely to be older and to have PVD, CAD, and MI (*Table 2*). Other characteristics were not statistical different between TAVR and SAVR.

Primary outcomes

In-hospital mortality

The in-hospital mortality was reported in 13 studies, and the overall in-hospital mortality was 8.3%. Although we did not find any statistical difference in non-dialysis patients, TAVR was associated with a lower risk of in-hospital mortality compared to SAVR (4.9% *vs.* 11.7%; OR: 0.53; 95% CI: 0.36–0.78; P=0.001; *Figure 2*). Subgroup analysis also showed that TAVR had a lower risk of in-hospital mortality than SAVR (4.5% *vs.* 12.7%; OR: 0.49; 95% CI: 0.29–0.84; P=0.01; *Figure 2*).

Stroke

The clinical outcome of stroke was reported in 17 studies, and the overall incidence of stroke was 2.6%. Compared with SAVR, our data indicated that TAVR significantly reduced the risk of stroke (2.1% *vs.* 3.2%; OR: 0.68; 95% CI: 0.47–0.96; P=0.03; *Figure 3*). In subgroup analysis, dialysis patients had a similar risk of stroke between TAVR and SAVR (*Figure 3*). However, TAVR was associated with a lower risk of stroke compared with SAVR in the non-dialysis group (*Figure 3*).

Table 1 Baseline characteristics of the included studies

Study	Nationality	Study type	Population	Study period	TAVR/SAVR, n	Outcomes analyzed	Study quality
Bagur *et al.*	Canada	Retrospective observational	CKD3-5	2005–2009	119/104	AKI, AKI requiring dialysis	NOS: 6
Rau *et al.*	Germany	Retrospective observational	Dialysis	2005–2010	15/24	LOS	NOS: 5
Nguyen *et al.*	United States	Retrospective observational	CKD3-5	2002–2012	162/421	In-hospital mortality, stroke, blood transfusion, AKI, AKI requiring dialysis, LOS, ICU stay, bleeding, AF	NOS: 6
Kobin *et al.*	United States	Retrospective propensity-matched	Dialysis	2011–2012	194/194	Stroke, LOS	NOS: 8
D'Errigo *et al.*	Italy	Prospective propensity-matched	CKD3b-5	2010–2012	170/170	Stroke, blood transfusion, AKI, AKI requiring dialysis, ICU stay, cardiac tamponade, major vascular damage, infection	NOS: 7
Alquhtani *et al.*	United States	Retrospective propensity-matched	Dialysis	2005–2014	197/197	stroke, in-hospital mortality, cardiac tamponade, blood transfusion, LOS, major vascular damage	NOS: 8
Bhise *et al.*	United States	Retrospective propensity-matched	Dialysis	2012–2013	119/244	In-hospital mortality, blood transfusion, LOS	NOS: 6
Condado *et al.*	United States	Retrospective observational	ESRD	2007–2015	30/30	stroke, 1-year mortality, PPMI, bleeding, major vascular damage, blood transfusion, ICU stay	NOS: 6
Doshi *et al.*	United States	Retrospective propensity-matched	CKD4-5, ESRD excluding dialysis	2012–2014	2,485/2,485	In-hospital mortality, stroke, blood transfusion, AKI, AKI requiring dialysis, LOS, AF, PPMI, cardiac tamponade, major vascular damage, infection	NOS: 8
Kumar *et al.*	United States	Retrospective propensity-matched	CKD3-4	2011–2014	1,001/1,001	In-hospital mortality, stroke, blood transfusion, PPMI, major vascular damage, AKI, AKI requiring dialysis	NOS: 8
Shavit *et al.*	Israel	Prospective observational	CKD3-4	1993–2015	58/111	In-hospital mortality, 1-year mortality, stroke, infection, AKI, LOS	NOS: 6
Alkhalil *et al.*	United States	Retrospective propensity-matched	Dialysis	2012–2014	175/175	In-hospital mortality, stroke, blood transfusion, LOS, PPMI, infection, bleeding, major vascular damage, cardiac tamponade	NOS: 8
Catalano *et al.*	United States	Retrospective propensity-matched	ESRD	2008–2017	399/402	In-hospital mortality, 1-year mortality, stroke, infection, AKI, LOS	NOS: 8
Pineda *et al.*	United States	Randomized controlled trill	CKD3-5 excluding dialysis	NR	244/216	1-year mortality, stroke, bleeding, AKI, major vascular damage, AKI requiring, dialysis, PPMI	Jadad score: 2
Reuillard *et al.*	France	Retrospective observational	CKD3b-5	2012–2015	73/54	In-hospital mortality, 1-year mortality, blood transfusion, stroke, PPMI, AKI, AKI requiring dialysis, LOS	NOS: 6

Table 1 (*continued*)

Table 1 (*continued*)

Study	Nationality	Study type	Population	Study period	TAVR/SAVR, n	Outcomes analyzed	Study quality
Sanaiha *et al.*	United States	Retrospective observational	CKD4-5, ESRD	2011–2014	2,323/2,993	In-hospital mortality, stroke, PPMI, LOS	NOS: 7
Ando *et al.*	United States	Retrospective observational	Dialysis	2013–2017	5,731/6,491	In-hospital mortality, stroke, bleeding, blood transfusion, LOS	NOS: 6
Färber *et al.*	Germany	Retrospective propensity-matched	Dialysis	2012–2015	661/457	1-year mortality, stroke, blood transfusion, LOS, PPMI, AF, cardiac tamponade, major vascular damage	NOS: 8
Khan *et al.*	United States	Retrospective propensity-matched	ESRD	2012–2017	1,065/654	In-hospital mortality, stroke, blood transfusion, LOS, PPMI, infections, AF, cardiac tamponade	NOS: 8
Lahoud *et al.*	England	Retrospective propensity-matched	CKD3-5 excluding dialysis	2007–2017	319/319	In-hospital mortality, stroke, blood transfusion, LOS, bleeding, AKI	NOS: 8
Mentias *et al.*	United States	Retrospective propensity-matched	Dialysis	2015–2017	4,130/2,565	In-hospital mortality, 1-year mortality, stroke, blood transfusion, LOS, PPMI, AF, major vascular damage, infection	NOS: 7

AKI, acute kidney injury; CKD, chronic kidney disease; ESRD, end-stage renal disease; NA, not available; LOS, length of stay; AF, atrial fibrillation; PPMI, permanent pacemaker implantation; NOS, New-castle-Ottawa Quality Assessment Scale; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement.

Secondary outcomes

1-year mortality

The clinical outcome of 1-year mortality was reported in 6 studies, and the overall 1-year mortality was 28.5%. Our study showed that TAVR could reduce the risk of 1-year mortality (27.7% *vs.* 29.7%; OR: 0.88; 95% CI: 0.80–0.97; P=0.007; *Figure 4*). There was no statistically significant difference in non-dialysis patients between the 2 groups. But for dialysis patients, TAVR had a lower risk of 1-year mortality than SAVR (28.8% *vs.* 31.7%; OR: 0.88; 95% CI: 0.80–0.97; P=0.009; *Figure 4*).

AKI and AKI requiring dialysis

Ten and eight studies reported the clinical outcome of AKI and AKI requiring dialysis, respectively. The overall incidence of postoperative AKI and AKI requiring dialysis was 32.9% and 14.8%. Pooled analysis showed that SAVR was more likely to have postoperative AKI and AKI requiring dialysis. However, TAVR could not only significantly reduce the incidence of postoperative AKI (40.0% *vs.* 25.3%; OR: 0.42; 95% CI: 0.34–0.52; P<0.00001; *Figure 5A*), but also AKI requiring dialysis (16.7% *vs.* 12.4%; OR: 0.65; 95% CI: 0.58–0.73; P<0.00001; *Figure 5B*).

Bleeding and blood transfusion

Six studies reported the incidence of bleeding and 14 studies of the blood transfusion rate. The overall incidence of bleeding and blood transfusion was 16.9% and 30.9%. Pooled data analysis indicated that SAVR significantly increased the risk of bleeding (22.6% *vs.* 10.4%; OR: 0.35; 95% CI: 0.31–0.38; P<0.00001; *Figure 6A*) and blood transfusion (39.2% *vs.* 23.0%; OR: 0.41; 95% CI: 0.32–0.52; P<0.00001; *Figure 6B*) compared with TAVR.

Infection, major vascular damage, and PPMI requirement

Seven, 9 and 14 studies reported the incidence of infection, major vascular damage, and PPMI requirement, and the overall incidence is 2.8%, 4.3% and 11.3%, respectively. Pooled data analysis indicated that TAVR had lower risk of postoperative infection than SAVR (1.0% *vs.* 4.9%; OR: 0.23; 95% CI: 0.13–0.38; P<0.00001; *Figure 7A*). However, SAVR significantly decreased the incidence of major vascular damage (5.1% *vs.* 3.4%; OR: 1.55; 95% CI: 1.08–2.22; P=0.02; *Figure 7B*) and PPMI requirement (15.4% *vs.* 6.7%; OR: 2.42; 95% CI: 1.82–3.21; P<0.00001; *Figure 7C*).

Table 2 Baseline Characteristics of the patients

Dichotomous	Study (N)	Sample size (N)	Prevalence [N]	Groups % (N)	P value	Continuous	Study (N)	MD 95% CI	Mean	Sample size (N)	P value
Male sex	21	38,989	63.0% [24,550]	TAVR: 61.9 (12,176/19,678); SAVR: 64.1 (12,374/19,311)	0.07						
Diabetes	20	38,626	45.6% [17,623]	TAVR: 48.3 (9,446/19,559); SAVR: 42.9 (8,177/19,067)	0.52						
PVD	19	37,988	29.9% [11,346]	TAVR: 32.9 (6,338/19,240); SAVR: 26.7 (5,008/18,748)	0.0004						
COPD	18	31,591	29.9% [9,432]	TAVR: 31.0 (4,737/15,259); SAVR: 28.7 (4,695/16,332)	0.17						
Hypertension	17	37,260	89.8% [33,472]	TAVR: 90.2 (17,024/18,876); SAVR: 89.5 (16,448/18,384)	0.56						
CVD	16	26,672	11.4% [3,049]	TAVR: 12.6 (1,598/12,732); SAVR: 10.4 (1,451/13,940)	0.07						
Heart failure	13	36,190	51.8% [18,760]	TAVR: 57.1 (10,500/18,390); SAVR: 46.4 (8,260/17,800)	0.05						
AF	11	29,255	40.0% [11,716]	TAVR: 40.0 (5,935/14,828); SAVR: 40.1 (5,781/14,427)	0.95						
CAD	10	13,050	62.7% [8,183]	TAVR: 63.6 (4,856/7,632); SAVR: 61.4 (3,327/5,418)	0.03						
MI	7	22,096	10.5% [2,312]	TAVR: 13.1 (1,367/10,449); SAVR: 8.1 (945/11,647)	0.01						
Chronic liver disease	7	16,864	6.6% [1,105]	TAVR: 6.9 (623/9,085); SAVR: 6.2 (482/7,779)	0.65						
						Age	18	3.48 (2.24–4.72)	TAVR: 72.6; SAVR: 68.2	TAVR: 16,235; SAVR: 15,073	<0.00001

PVD, peripheral vascular disease; COPD, chronic obstruction pulmonary disease; CVD, stroke or cerebrovascular disease; AF, atrial fibrillation; CAD, coronary artery disease; MI, myocardial infarction; MD, mean difference; CI, confidence interval; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement.

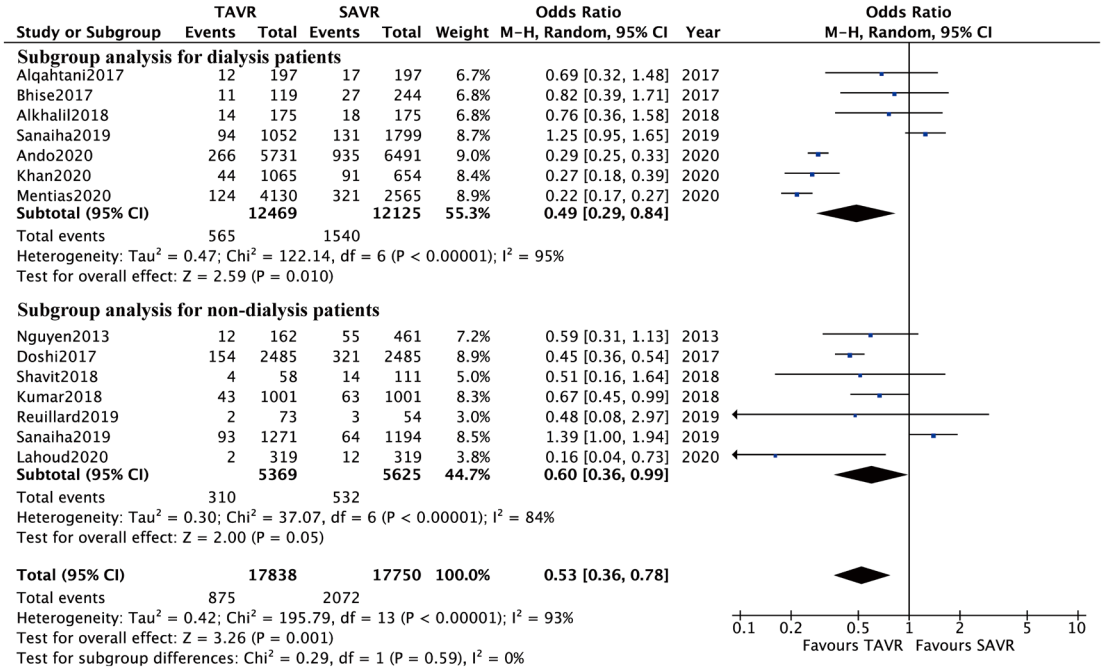

Figure 2 Comparison of in-hospital mortality between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

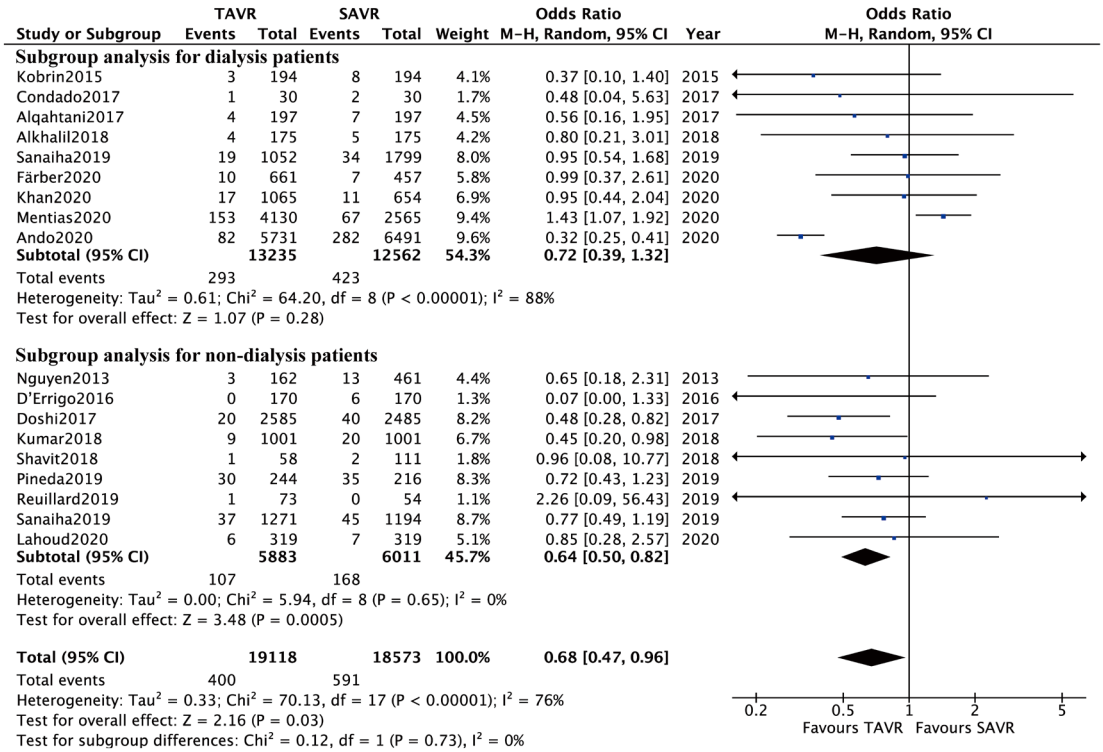

Figure 3 Compare the risk of stroke between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

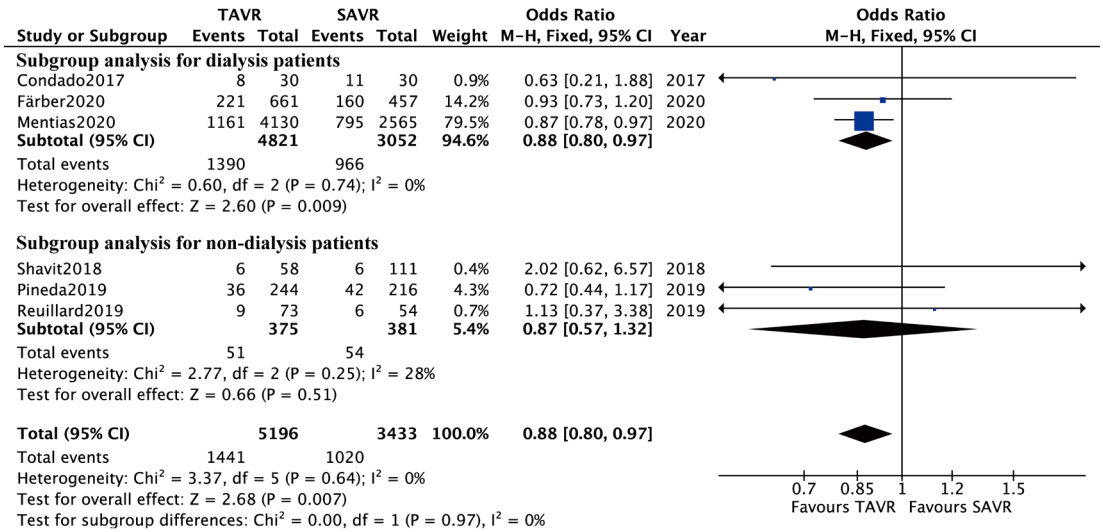

Figure 4 Comparison of 1-year mortality between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

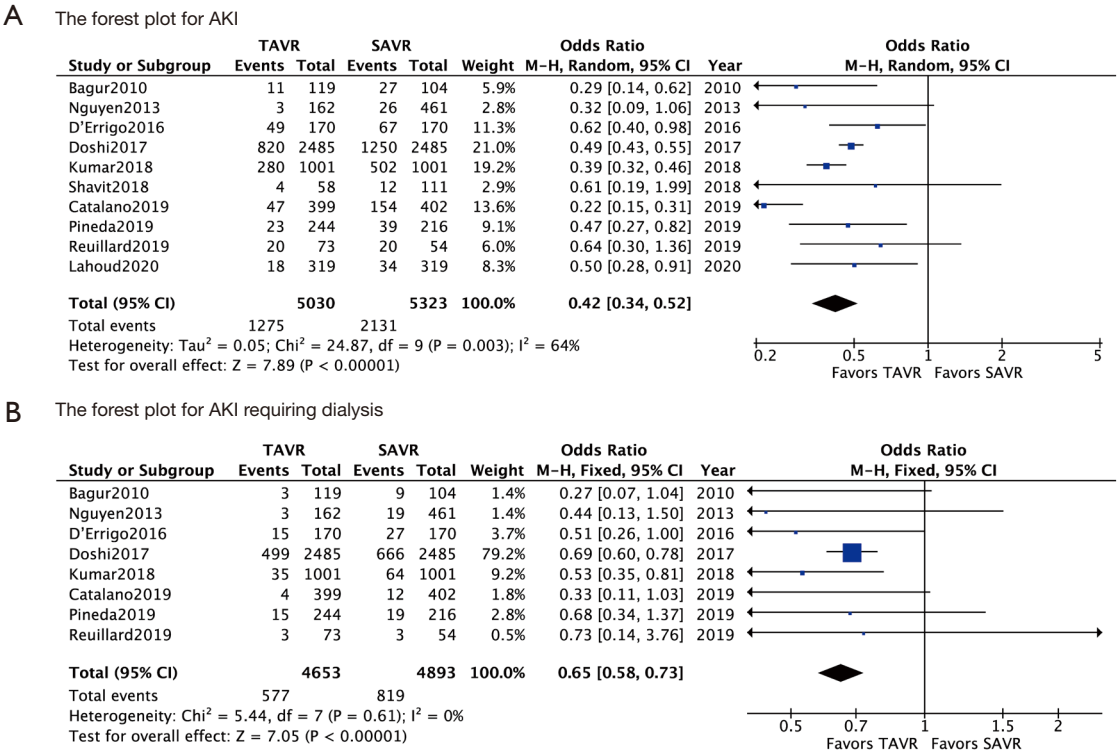

Figure 5 Compare the risk of acute kidney injury (AKI) (A) and AKI requiring dialysis (B) between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

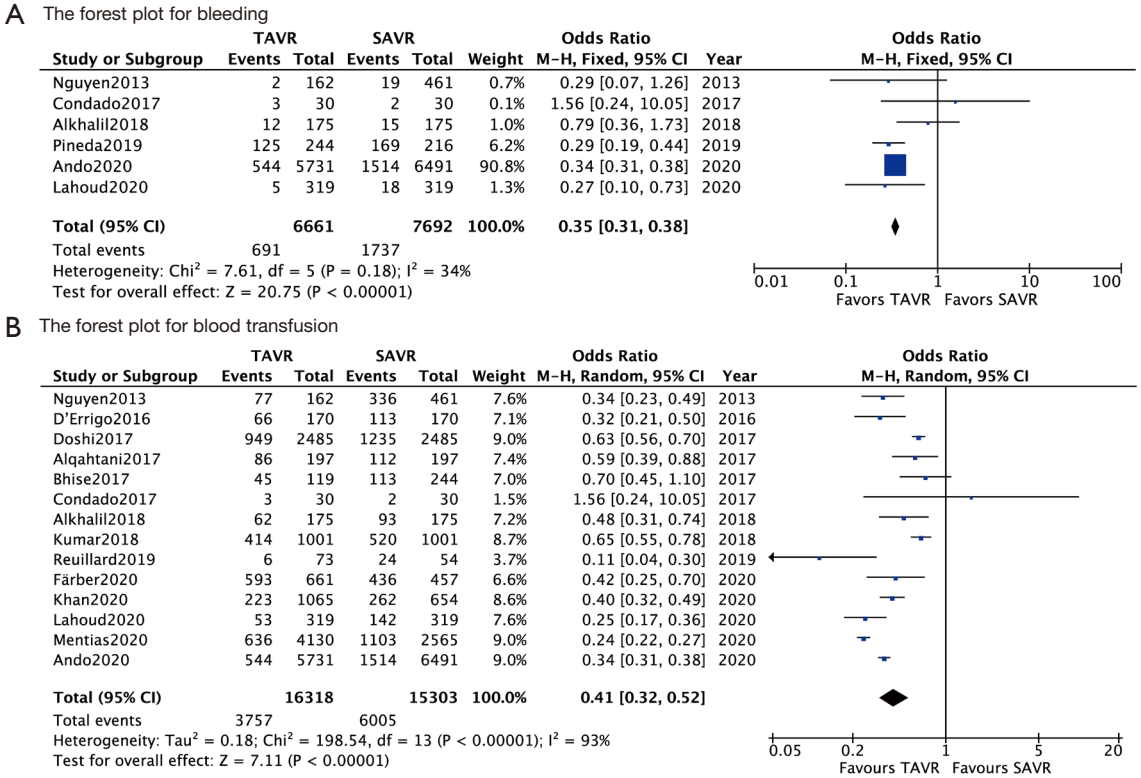

Figure 6 Compare the incidence of bleeding (A) and blood transfusion (B) between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

New-onset AF and cardiac tamponade

Five studies reported the incidence of AF and 6 studies the cardiac tamponade. The overall incidence is 25.9% and 1.5% respectively. Pooled analysis showed that TAVR could significantly lower the risk of AF (18.6% *vs.* 35.2%; OR: 0.37; 95% CI: 0.17–0.79; P=0.01; *Figure 8A*) and cardiac tamponade (1.1% *vs.* 2.1%; OR: 0.53; 95% CI: 0.37–0.75; P=0.0003; *Figure 8B*).

Duration of ICU stay and LOS

Four and 15 studies reported the length of ICU stay and hospital stay. Compared with SAVR, TAVR significantly shortened the time in ICU [weighted mean difference (WMD): −2.55; 95% CI: −4.13 to −0.98; P=0.002; *Figure 9A*] and hospital (WMD: −7.06; 95% CI: −8.41 to −5.71; P<0.00001; *Figure 9B*).

Discussion

This meta-analysis incorporated some latest studies which compared the clinical outcomes between TAVR and SAVR in advanced CKD patients. The remarkable findings of this study were even through the patients of TAVR group were older and more likely to have preoperative comorbidities, it reduced the incidence of postoperative in-hospital mortality, stroke and other complications, such as AKI, AKI requiring dialysis, bleeding, blood transfusion, infection, major vascular damage, new-onset AF and cardiac tamponade. Moreover, it shortened the length of ICU stay and hospital stay.

Since the first commercially available transcatheter was implanted (41), TAVR has been widely used for AS patients and randomized clinical trials showed that TAVR to be equal or superior to SAVR in high-risk patients (14,42). However, patients with severe CKD were excluded from these studies, it remains unclear whether TAVR is comparable to SAVR for patients with advanced CKD. In this latest study, the overall in-hospital mortality is much higher with TAVR (3.4% *vs.* 4.9%) and SAVR (6.5% *vs.* 11.7%) than the previous study (14). This could be explained by our study focused on severe CKD or dialysis patients, which is associated with a much higher risk of

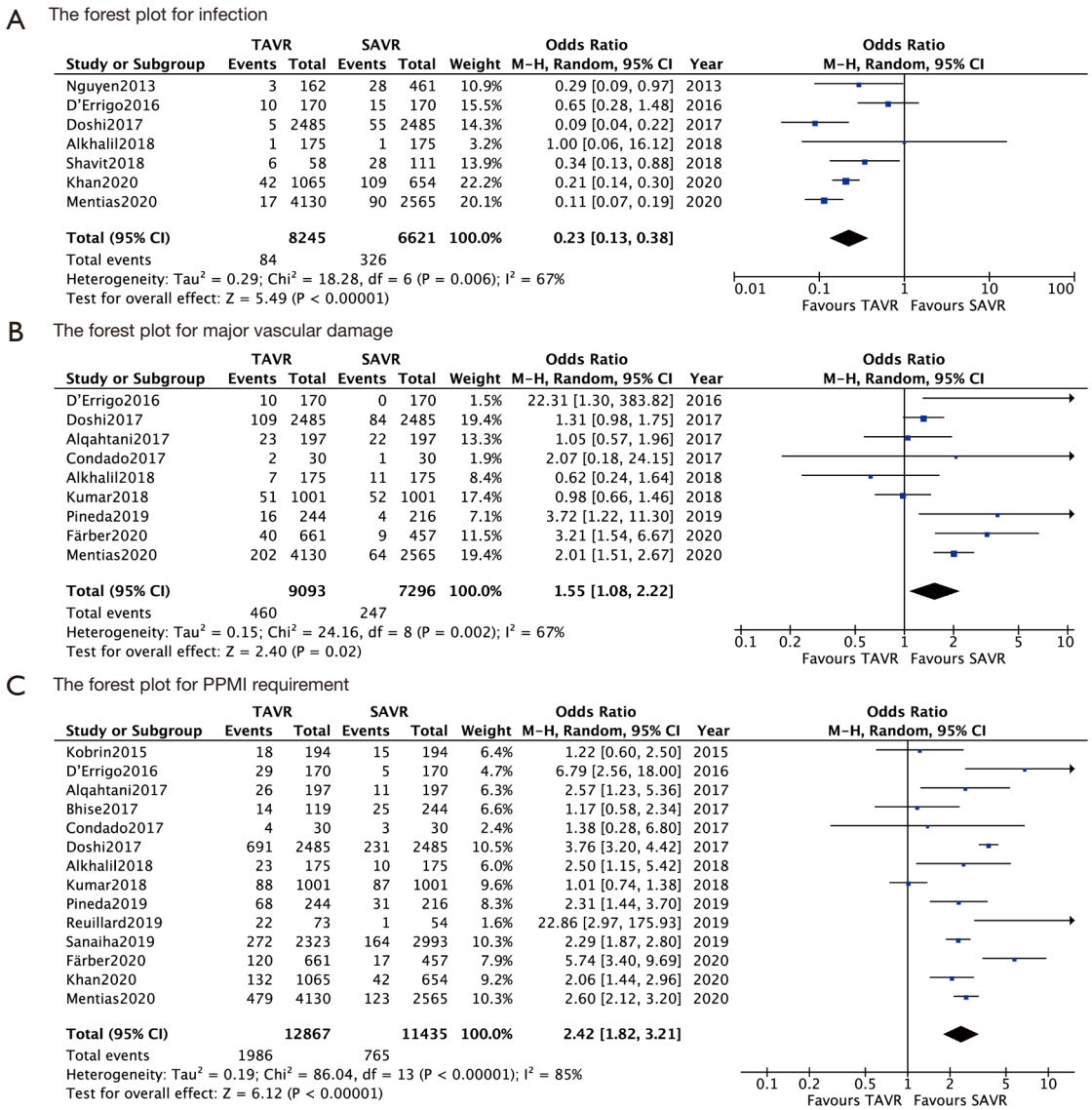

Figure 7 Comparison of Infection (A) major vascular damage (B) and permanent pacemaker implantation (PPMI) requirement (C) between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

mortality (43). However, TAVR is associated with a much lower in-hospital mortality than SAVR (4.9% *vs.* 11.7%). The less invasive nature and fewer complications of TAVR might be the main reason. Another explanation could be a higher risk of postoperative AKI in SAVR group. Since Elhmidi *et al.* reported that a higher postoperative AKI rate could increase the in-hospital mortality (44). In subgroup analysis we found TAVR could decrease in-hospital mortality in dialysis patients. But such difference disappeared in non-dialysis patients which is consistent with previous studies excluded patients with severe CKD. Our study indicated that SAVR is of significant risk for dialysis patients. Nevertheless, we did not have enough data to do a longer follow-up analysis, although some studies showed that there is no difference in long-term mortality (27,30), we still need more studies to confirm these findings.

The postoperative stroke was closely related to long-term mortality. In this meta-analysis, the risk of stroke was much lower in TAVR group, which is contradicted with the previous study. Possible reasons for this phenomenon could be explained as follows: (I) with the advancement in transcatheter heart valves and the improved operator

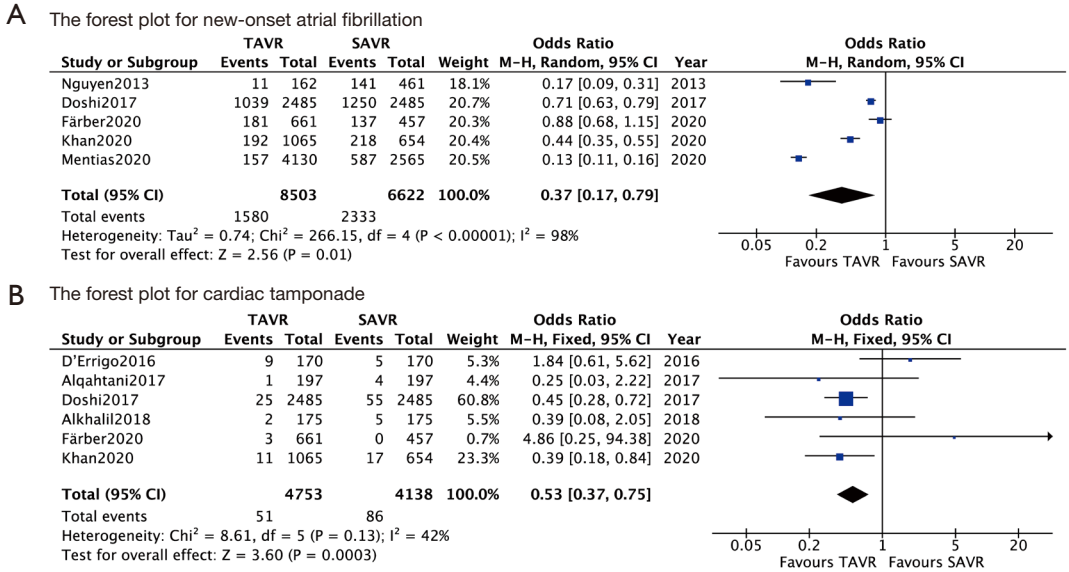

Figure 8 Comparison of new-onset atrial fibrillation (A) and cardiac tamponade (B) between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

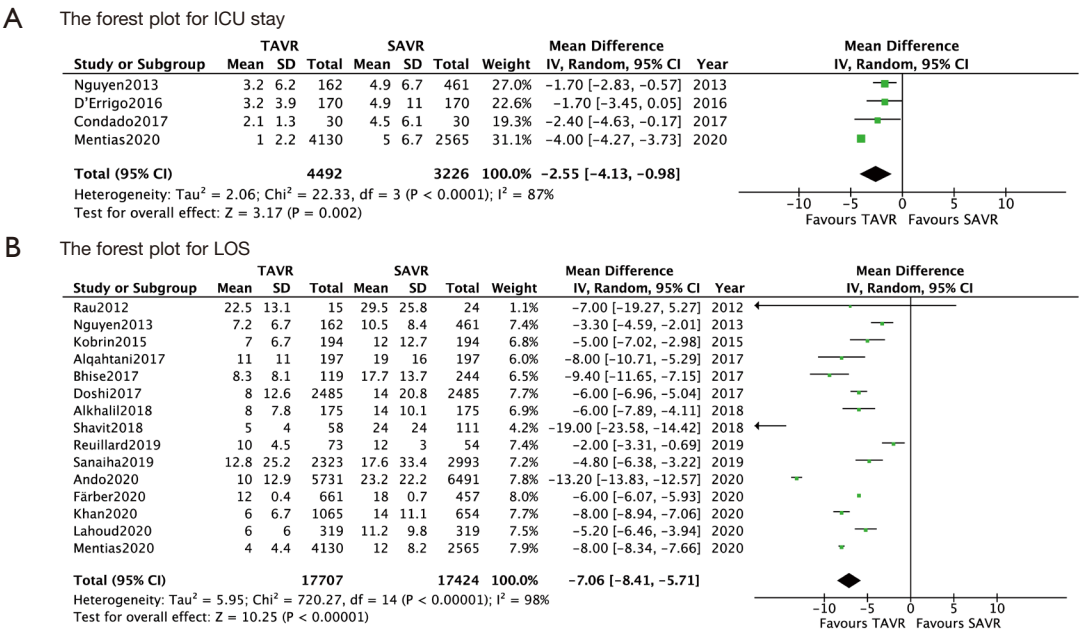

Figure 9 Comparison of intensive care unit (ICU) stay (A) and length of stay (LOS) (B) between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

experience, the risk of stroke with TAVR has declined in the general population (45). (II) Our study showed that TAVR had a lower risk of postoperative AF, and it is well known that new-onset AF is associated with a higher risk of stroke (46). In subgroup analysis, pooled analysis found TAVR could lower the risk of stroke in non-dialysis patients, however there was no statistical difference between two groups in dialysis patients. This discrepancy could be

explained by those patients on dialysis were associated with platelet dysfunction, hemostatic abnormalities and dialysis patients need frequent anticoagulation therapy during dialysis which result in higher incidences of hemorrhagic stroke than non-dialysis patients (47).

Although both surgical and interventional treatment have a negative impact on renal function, our study demonstrated that the incidence of postoperative AKI and AKI requiring dialysis is much higher in SAVR group, which is consistent with previous studies. There are some possible explains for this phenomenon: (I) bleeding and blood transfusion is more common in SAVR, bleeding could associated hypotension which decreased flow of kidney, and blood transfusion is associated with 3-fold risk of AKI (48); (II) the impact of contrast agent on kidney might be overestimated (49,50); (III) the avoidance of CPB may contribute to lower risk of AKI in TAVR. As far as the author concerned, kidney injury should be minimized during operation since AKI places patients at a 5-fold increased mortality during hospitalization (51). And by minimizing volume of contrast media or reducing the incidence of bleeding and blood transfusion, the risk of postoperative AKI could be decreased further.

Although the risk of PPMI requirement is higher in TAVR group, we found there is a decline in overall PPMI requirement and major vascular damage compared with a previous meta-analysis, this can be explained by advancements in delivery-system, procedural experience, multidisciplinary engagement, and valvular design (52,53). Both bleeding and blood transfusion rate are high which have been reported before (54,55). Since our study focused on severe CKD and dialysis patients, which appears to be associated with platelet dysfunction and hemostatic abnormalities leading to a higher risk for hemorrhagic events (56), and the need for dual antiplatelet therapy after TAVI and SAVR may aggravate the rate of bleeding. The pooled data showed TAVR significantly shortened the stay in ICU and hospital, which is consistent with previous study. TAVR group has fewer complications, which could be the main reason decreased LOS and ICU stay. With the significantly reduce on LOS, it may minimize the potential negative effect on elderly patients. Therefore, TAVR is as safe and efficient as SAVR for patients with advanced CKD.

Limitations

Our meta-analysis has several limitations. First, most of the studies were retrospective observational studies, only one randomized controlled trial included. Although 12 of them did a propensity score-matched manner to get comparable baseline characteristics, eight studies were not matched, potential selection bias could not be ruled out. Moreover, sicker and older patients were more likely to be denied for SAVR, and selection bias may exist at beginning. And there may be a minor overlap in patients included for some studies used the same database. However, excluding these studies would also have excluded patients without any overlap and result in a selection bias. Although we included 21 studies in our meta-analysis, some outcomes scarcely reported may not have enough power to reach a credible conclusion. Second, TAVR is a new technique and with a rapid development, different counties and centers used different delivery-system and different valve design. Moreover, diverse experience for different surgeons is closely related to complications. Therefore, outcomes were inevitably affected by these confounding factors. Third, the specific information on radiation-dose exposure, type of contrast media and volume, valve type, peri and postoperative medication use, severity of stenosis, and concomitant procedures were not available. So, some potential confounders still exist. Forth, there is only one RCT in our meta-analysis, more RCTs will be needed to test the conclusion. And only few studies reported long-term outcomes, we need more evidence in the future to testify long-term efficiency of TAVR for patients with advanced CKD.

Conclusions

Our study demonstrated that TAVR was associated with lower risk of in-hospital and 1-year mortality than SAVR in patients with advanced CKD, especially in dialysis patients. Although TAVR increased the risk of PPMI and major vascular damage, it decreased the risk of stroke, AKI, bleeding, blood transfusion, AKI requiring dialysis, infection, major vascular damage, new-onset AF, cardiac tamponade, ICU stay and LOS. TAVR might be a better selection over SAVR for severe CKD and dialysis patients. More large, prospective, randomized controlled trials are needed to confirm these discoveries.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Assessment of study quality by NOS

Study/(Ref. #)	Quality indicators from NOS									
	Selection			Comparability			Exposure/outcome			Score
Bagur *et al.*	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	6
Rau *et al.*	Yes	Yes	No	Yes	No	No	Yes	No	Yes	5
Nguyen *et al.*	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	6
Kobrin *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
D'Errigo *et al.*	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7
Alqahtani *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Bhise *et al.*	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	6
Condado *et al.*	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	6
Doshi *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Kumar *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Shavit *et al.*	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Alkhalil *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Catalano *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Reuillard *et al.*	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Sanaiha *et al.*	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	7
Ando *et al.*	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Färber *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Khan *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Lahoud *et al.*	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Mentias *et al.*	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7

NOS: Newcastle-Ottawa quality assessment Scale. For case-control studies: (1) represents cases with independent validation; (2) cases are consecutive or representative; (3) controls are community; (4) controls have no history of prior cardiac surgery; (5) study controls are comparable for age and sex; (6) study controls for any additional factor(s); (7) cases and controls have the same method of ascertainment; (8) was follow-up long enough for outcomes to occur; and (9) cases and controls have complete follow-up.

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Table S2 Quality assessment of RCT with Jadad Score

Items	Score Standard			Study
	0	1	2	Pineda *et al.*
Randomization	Not randomized or inappropriate method of randomization	The study was described as randomized	The method of randomization was described appropriately	1
Double blinding	No blind or inappropriate method of blinding	The study was described as double blinding	The method of double blinding was described appropriately	0
Withdrawals and dropouts	Not describe the follow-up	A description of withdrawals and dropouts		1
Score summaries				2

The full mark for Jadad Score was 5-point. Scores≥3 was considered with high-quality.

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