openheart

Diabetes is associated with a higher incidence of short-term mortality risk and readmission in patients who undergo surgical but not transcatheter aortic valve replacement

Ahston D Souza,[1,2] Khalifa Bsheish,[1,3] Soha Dargham,[4,5] Amin Jayyousi,[6] Jassim Al Suwaidi,[7] Charbel Abi Khalil [1,7,8]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/openhrt-2024-003019).

To cite: D Souza A, Bsheish K, Dargham S, *et al*. Diabetes is associated with a higher incidence of short-term mortality risk and readmission in patients who undergo surgical but not transcatheter aortic valve replacement. *Open Heart* 2025;**12**:e003019. doi:10.1136/openhrt-2024-003019

Received 15 October 2024
Accepted 5 December 2024

For numbered affiliations see end of article.

Correspondence to
Professor Charbel Abi Khalil; cha2022@med.cornell.edu

ABSTRACT

Background Transcatheter aortic valve replacement (TAVR) is increasingly used for aortic valve replacement instead of surgical aortic valve replacement (sAVR). We aimed to examine the impact of diabetes on 30-day mortality, 30-day readmission and compare outcomes between TAVR and sAVR.

Methods Data were extracted from the Nationwide Readmissions Database from 2012 to 2017. The primary outcome was 30-day mortality, and the secondary outcome was 30-day readmission.

Results The study included 110 135 patients who underwent aortic valve replacement. Of these, 59 466 (54.0%) were hospitalised for TAVR, and 50 669 (46.0%) underwent sAVR. Diabetes was present in 36.4% of TAVR patients and 29.1% of sAVR patients. In TAVR patients, the adjusted risk of 30-day readmission and mortality was similar regardless of diabetes status (aHR=0.94 (0.86–1.03); 0.97 (0.84–1.12); respectively). However, sAVR patients with diabetes had a higher adjusted risk of 30-day mortality (aHR=1.13 (1.01–1.25)) but not readmission (aHR=0.92 (0.84–1.01)). When comparing outcomes between TAVR and sAVR in patients with diabetes, TAVR patients were older and had a higher prevalence of chronic kidney disease (CKD). Nevertheless, 30-day readmission and mortality were lower in patients who underwent TAVR (aHR=0.59 (0.53–0.67), aHR=0.29 (0.25–0.34), respectively) compared with sAVR. Coronary artery disease was the most significant predictor of readmission in patients with diabetes. CKD increased the risk of mortality by almost twofold in both techniques.

Conclusion Diabetes increases the risk of short-term mortality in sAVR but not TAVR. Moreover, the incidence of 30-day mortality and readmission is lower in TAVR compared with TAVR among patients with diabetes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Transcatheter aortic valve replacement (TAVR) is increasingly used for aortic valve replacement instead of surgical aortic valve replacement (sAVR).

⇒ Previous studies have demonstrated an increased prevalence of T2D in patients with aortic stenosis (AS) and a higher incidence of AS in diabetes patients, highlighting the bidirectional relationship between these conditions.

WHAT THIS STUDY ADDS

⇒ This study shows that diabetes significantly increases the 30-day mortality risk in sAVR but not TAVR.

⇒ Moreover, the incidence of 30-day mortality and readmission is higher in sAVR compared with TAVR among patients with diabetes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings suggest that TAVR may be a safer and more effective alternative to sAVR for patients with diabetes, reducing short-term mortality and morbidity.

⇒ This supports the use of minimally invasive techniques such as TAVR in clinical guidelines for diabetic patients with AS, potentially influencing decision-making in cardiology practice.

⇒ Future research should focus on long-term outcomes and the cost-effectiveness of TAVR in diabetes populations to further inform policy decisions.

INTRODUCTION

Aortic stenosis (AS) is a common aortic valve disorder characterised by progressive valve stiffening, which causes left ventricular outflow obstruction.[1] Severe AS is characterised by a significant limitation of blood flow through the valve and is observed in approximately 2%–9% of individuals aged 75 years and older.[2] This condition primarily affects older adults, progressing with advancing age. AS poses a significant burden on the healthcare system due to its progressive nature and the high mortality rate once symptomatic.[3]

Type 2 diabetes (T2D) is a common chronic medical condition that affects nearly 10.5% of the US population.[4] Cardiovascular disease,

Table 1 Comparison of readmitted versus non-readmitted patients undergoing transcatheter aortic valve replacement, according to the presence of diabetes

	No diabetes (%) N=36 457	Diabetes (%) N=20 922	P value
Mean (SD)	80.8 (8.3)	77.8 (8.1)	<0.001
Age (years)			
<55	366 (1.0)	180 (0.9)	
55–64	1260 (3.5)	1088 (5.2)	
65–74	5512 (15.1)	5331 (25.5)	
75–84	15 007 (41.2)	9578 (45.8)	
>84	14 312 (39.3)	4745 (22.7)	
Gender			
Male	19 414 (53.3)	12 000 (57.4)	<0.001
Female	17 043 (46.7)	8922 (42.6)	
Income			
Low	6173 (17.2)	4305 (20.8)	<0.001
Low-mid	9110 (25.3)	5606 (27.1)	
High-mid	10 214 (28.4)	5755 (27.8)	
High	10 484 (29.1)	5011 (24.2)	
Obesity	4807 (13.2)	6094 (29.1)	<0.001
Hypertension	30 822 (84.5)	19 616 (93.8)	<0.001
Smoking	12 578 (34.5)	7269 (34.7)	0.557
Dyslipidaemia	23 300 (63.9)	15 419 (73.7)	<0.001
Peripheral vascular disease	7834 (21.5)	3423 (16.4)	<0.001
Chronic kidney disease	9194 (25.2)	8522 (40.7)	<0.001
Coronary artery disease	1434 (3.9)	691 (3.3)	<0.001
Length of stay, median (IQR)	2 (1-3)	2 (1-4)	0.01

strongly associated with diabetes, remains the leading cause of death among diabetes patients.[5] Previous studies have demonstrated an increased prevalence of T2D in patients with AS[6] and an higher incidence of AS among individuals with diabetes.[7] Additionally, diabetes has been linked to a greater progression of AS from mild to severe.[8]

Our study aims to examine the impact of diabetes on short-term cardiovascular outcomes in patients with severe AS hospitalised for either surgical aortic valve replacement (sAVR) or transcatheter aortic valve replacement (TAVR). Using the Nationwide Readmissions Database (NRD), a large US cohort, we also aim to compare the outcomes of sAVR and TAVR in individuals with T2D.

METHODS

Data source

We extracted data from the NRD. This database was developed by the Agency for Healthcare Research and Quality as part of the Healthcare Cost and Utilization Project and contains data on all-payer hospital inpatient stays. The NRD includes comprehensive patient information, such as demographics, medical history, discharge status, readmission parameters and cardiovascular outcomes. To extract the data, we used the International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) codes to identify admissions of patients who underwent TAVR or sAVR from 2012 to 2017. The following codes were used to identify patients who underwent sAVR (ICD-9-CM 35.21, 35.22; ICD-10-CM 02RF07Z, 02RF08Z, 02RF0JZ, 02RF0KZ), while patients who underwent TAVR were identified by these codes (ICD-9-CM 35.05, 35.06; ICD-10-CM 02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, 02RF3KZ). Patients were excluded if they were under 18 years or had missing data regarding age, gender or outcomes.

Diagnosis and outcomes

We extracted patients hospitalised with a primary diagnosis of aortic valve replacement, either sAVR or TAVR (index group), and then followed them for up to 30 days. Patients were stratified based on the presence or absence of diabetes. The primary outcome was 30-day mortality, and the secondary outcome was 30-day readmission. We also explored the predictors of readmission and mortality, as well as the aetiology of readmission.

Table 2 HRs of 30-day outcomes in patients with TAVR and sAVR

	TAVR diabetes versus non-diabetes	P value	sAVR diabetes versus non-diabetes	P value	TAVR versus sAVR diabetes	P value
Readmission						
HR (95% CI)	0.93 (0.85 to 1.01)	0.093	0.93 (0.85 to 1.01)	0.1	0.59 (0.54 to 0.66)	<0.001
Adjusted HR (95% CI)	0.94 (0.86 to 1.03)	0.208	0.92 (0.84 to 1.01)	0.093	0.59 (0.53 to 0.67)	<0.001
Mortality						
HR (95% CI)	0.91 (0.80 to 1.05)	0.2	1.06 (0.96 to 1.18)	0.207	0.35 (0.30 to 0.40)	<0.001
Adjusted HR (95% CI)	0.97 (0.84 to 1.12)	0.712	1.13 (1.01 to 1.25)	0.02	0.29 (0.25 to 0.34)	<0.001

sAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

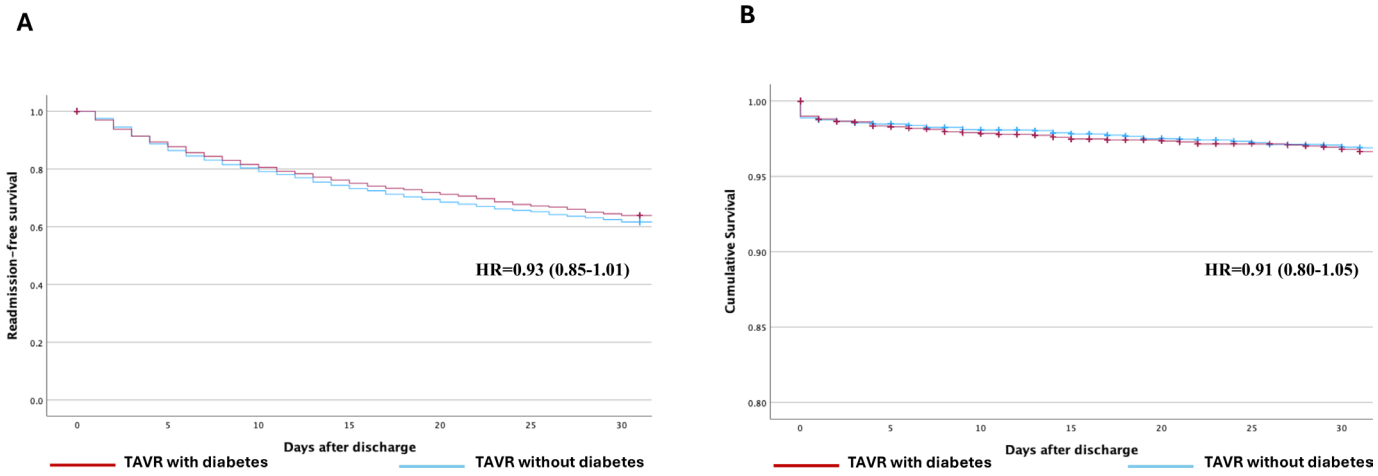

Figure 1 Kaplan-Meier curve comparing the probability of (A) readmission-free survival and cumulative survival (B) in patients with versus without diabetes undergoing TAVR. Patients were stratified into non-diabetes (blue line) and diabetes (red line). The x-axis represents days after discharge. The y-axis represents cumulative readmission-free survival in (A) and survival in (B). TAVR, transcatheter aortic valve replacement

Outcomes were identified by their ICD codes and chosen based on similar studies from the literature.

Statistical analysis

We compared TAVR patients who were readmitted with those who were not, within both diabetes and non-diabetes groups. Further, we compared readmitted patients according to the presence of diabetes. A similar comparison was made for sAVR patients. Finally, we compared outcomes between diabetes patients who underwent sAVR and those treated with TAVR. Baseline characteristics within each group are shown as mean (SD), median (IQR) or n (%). Differences in baseline characteristics were analysed using the Pearson χ^2 test for categorical variables and the independent t-test for continuous variables. The Kaplan-Meier curve and log-rank test were used to compare the incidence of 30-day readmission and mortality. Cox regression analysis was performed to obtain adjusted HRs after accounting for significant comorbidities and demographic differences between the groups. Variables included age, gender, income, obesity, hypertension, smoking, dyslipidaemia, peripheral vascular disease, chronic kidney disease (CKD) and coronary artery disease (CAD). All statistical analysis was performed with SPSS software, and the significance threshold was set at p<0.05.

RESULTS

Study group

The study included 110 135 patients who underwent aortic valve replacement. Of these, 59 466 (54%) were hospitalised for TAVR and 50 669 (46%) for sAVR. Among TAVR patients, 36.4% had diabetes, while diabetes prevalence was 29.1% among sAVR patients.

Transcatheter aortic valve replacement (TAVR)

Among non-diabetes patients, 1339 (3.52%) who underwent TAVR were admitted. Readmitted patients were older relative to non-readmitted patients (81.9 (7.9) vs 80.8 (8.3) years, respectively; p<0.001) (online supplemental table 1). CKD and CAD were more common among readmitted patients. Cardiometabolic risk factors and comorbidities were significantly less prevalent in non-readmitted patients. The length of stay (LoS) during initial hospitalisation was considerably longer in readmitted patients (3 (4) vs 2 (3)), p<0.001. Among diabetes patients who underwent TAVR, 748 (3.45%) were readmitted. Readmitted patients were older and had a higher prevalence of CAD, as well as twofold longer LoS (p<0.001 for both comparisons) (online supplemental table 2).

When comparing readmitted patients with TAVR according to the presence of diabetes, those with diabetes were younger and more likely to be men (table 1). Obesity, hypertension, dyslipidaemia and CKD were more prevalent in the presence of diabetes, while CAD prevalence did not differ significantly. The incidence of 30-day readmission and mortality were not different according to the presence of diabetes (adjusted HR=0.94 (0.86–1.03); 0.97 (0.84–1.12), respectively) (table 2 and figure 1).

Surgical aortic valve replacement (sAVR)

Among patients who underwent sAVR, 4.7% of non-diabetes patients and 4.9% of diabetes patients were readmitted. Online supplemental tables 3 and 4 compare the demographics and comorbidities of readmitted patients to non-readmitted ones. In both diabetes and non-diabetes groups, readmitted patients were older and more likely to have CAD and CKD (p<0.05 for all comparisons). No significant difference in the gender distribution was observed. Interestingly, all readmitted patients initially had a shorter LoS.

When we compared readmitted sAVR patients, those with diabetes were, on average, 3 years older (69 (10) vs 66 [(13), diabetes vs non-diabetes, p<0.001), more likely to have a lower income, and had a high

Table 3 Comparison of readmitted versus non-readmitted patients undergoing sAVR, according to the presence of diabetes

	No diabetes (%) N=1706	Diabetes (%) N=729	P value
Mean (SD)	66.9 (13.9)	69.1 (10.1)	<0.001
Age (years)			
<55	294 (17.2)	59 (8.1)	<0.001
55–64	312 (18.3)	146 (20.0)	
65–74	528 (30.9)	283 (38.8)	
75–84	478 (28.0)	218 (29.9)	
>84	94 (5.5)	23 (3.2)	
Gender			
Male	1155 (67.7)	478 (65.6)	0.305
Female	551 (32.3)	251 (34.4)	
Income			
Low	422 (25.2)	195 (26.9)	0.016
Low-mid	423 (25.2)	192 (26.5)	
High-mid	407 (24.3)	197 (27.2)	
High	424 (25.3)	140 (19.3)	
Obesity	177 (10.4)	197 (27.0)	<0.001
Hypertension	1038 (60.8)	637 (87.5)	<0.001
Smoking	514 (30.1)	194 (26.6)	0.080
Dyslipidaemia	855 (50.1)	480 (65.8)	<0.001
Peripheral vascular disease	186 (10.9)	100 (13.7)	0.048
Chronic kidney disease	271 (15.9)	221 (30.3)	<0.001
Coronary artery disease	224 (13.1)	47 (6.4)	<0.001
Length of stay, median (IQR)	4 (2-7)	5 (3-9)	<0.001

prevalence of obesity, dyslipidaemia, hypertension and CKD (p<0.05 for all comparisons) (table 3). sAVR patients with diabetes were not at increased risk of readmission within 30 days (HR=0.92 (0.84–1.01)) but had a higher adjusted risk of mortality (aHR=1.13 (1.01–1.25)) (table 1 and figure 2).

Comparison of TAVR to sAVR in patients with diabetes

We further compared both aortic replacement techniques in diabetes patients. TAVR patients were, on average, 9 years older than sAVR patients (78 (8) vs 69 (10), respectively, p<0.001), more likely to have a higher income, and had a higher prevalence of CKD (44.3% vs 30.3%, TAVR vs sAVR, p<0.001) (table 4). Fewer women underwent sAVR compared with TAVR (34.4 vs 40.4%, respectively; p=0.018). Figure 3 shows the Kaplan-Meier curves of readmission and mortality. The incidence of 30-day readmission and mortality was lower in TAVR patients (adjusted HR=0.59 (0.53–0.67); 0.29 (0.25–0.34), respectively) (table 2).

Predictors of the 30-day outcome

Age was associated with a higher risk of readmission in diabetes patients undergoing aortic valve replacement (table 5). However, gender distribution did not significantly impact outcomes in either technique. CAD increased the risk of readmission by nearly twofold in TAVR patients (OR=2.01 (1.48–2.72)) and by 3.5-fold in sAVR patients (OR=3.52 (2.56–4.85)). Interestingly, risk factors such as obesity, hypertension and dyslipidaemia were associated with a lower risk of readmission.

Age and female gender increased the risk of mortality in sAVR (OR=1.01 (1.009–1.02), 1.46 (1.23–1.74), respectively), but not in TAVR (table 6). CKD increased the risk of mortality by nearly twofold in both groups (OR=2.02 (1.60–2.53)), 2.33 (1.96–2.69), TAVR and sAVR, respectively). CAD was also associated with a higher risk in sAVR patients (OR=1.70 (1.07–2.69)) but not in TAVR ones.

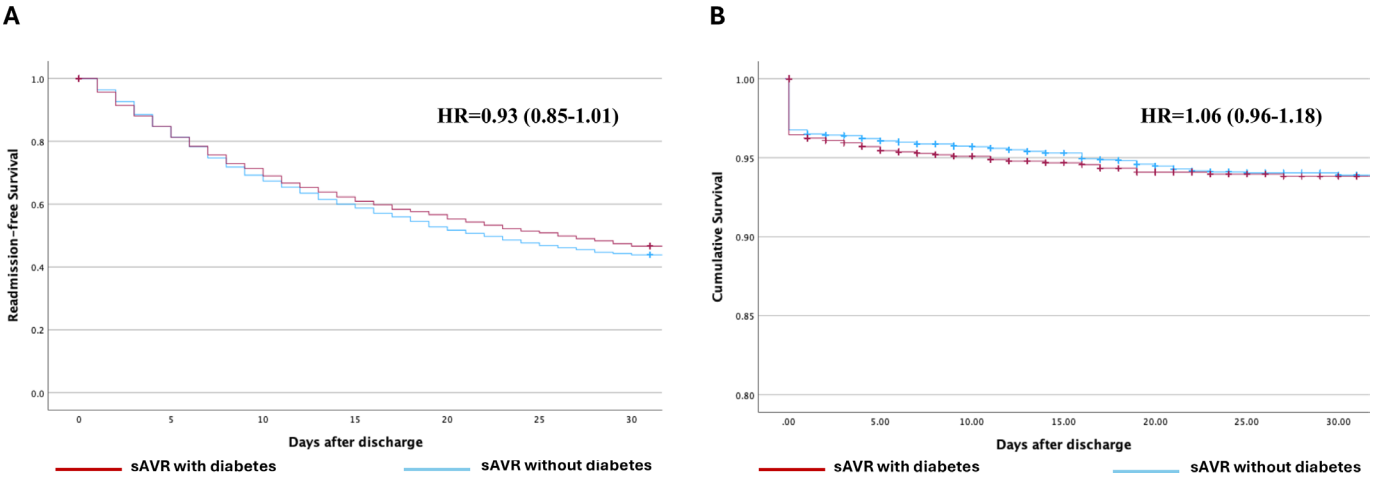

Figure 2 Kaplan-Meier curve comparing the probability of (A) readmission-free survival and cumulative survival (B) in patients with versus without diabetes undergoing sAVR. Patients were stratified into non-diabetes (blue line) and diabetes (red line). The x-axis represents days after discharge. The y-axis represents cumulative readmission-free survival in (A) and survival in (B). sAVR, surgical aortic valve replacement.

D Souza A, *et al*. *Open Heart* 2025;**12**:e003019. doi:10.1136/openhrt-2024-003019

Table 4 Comparison of readmitted patients with diabetes undergoing TAVR versus sAVR

	TAVR (%) N=748	sAVR (%) N=729	P value
Mean (SD)	78.6 (8.2)	69.1 (10.1)	<0.001
Age (years)			
<55	7 (0.9)	59 (8.1)	<0.001
55–64	36 (4.8)	146 (20.0)	
65–74	167 (22.3)	283 (38.8)	
75–84	337 (45.1)	218 (29.9)	
>84	201 (26.9)	23 (3.2)	
Gender			
Male	446 (59.6)	478 (65.6)	0.018
Female	302 (40.4)	251 (34.4)	
Income			
Low	148 (20.1)	195 (26.9)	<0.001
Low-mid	177 (24.0)	192 (26.5)	
High-mid	208 (28.2)	197 (27.2)	
High	205 (27.8)	140 (19.3)	
Obesity	149 (19.9)	197 (27.0)	0.001
Hypertension	663 (88.6)	637 (87.5)	0.507
Smoking	234 (31.3)	194 (26.6)	0.048
Dyslipidaemia	506 (67.6)	480 (65.8)	0.462
Peripheral vascular disease	110 (14.7)	100 (13.7)	0.587
Chronic kidney disease	331 (44.3)	221 (30.3)	<0.001
Coronary artery disease	48 (6.4)	47 (6.4)	0.981
Length of stay, median (IQR)	4 (4)	5 (6)	<0.001

sAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

DISCUSSION

We have previously demonstrated that TAVR is increasingly being done in patients with diabetes, whereas the proportion of sAVR is decreasing.[9] Further, we showed a temporal decrease in mortality declined in both procedures. This study reports that diabetes increases the 30-day mortality risk in sAVR but not TAVR. Moreover, the incidence of 30-day mortality and readmission is higher in sAVR compared with TAVR among patients with diabetes.

Traditionally, sAVR has been the standard treatment for severe AS. However, TAVR has provided an alternative treatment option over the past two decades, particularly for high-risk patients unsuitable for sAVR.[10] With the advancement of TAVR techniques and prostheses and increased physician experience, outcomes for TAVR have improved significantly.[11] Initially, clinical trials showed that TAVR is non-inferior or superior to sAVR in mortality and other cardiovascular endpoints in high-risk surgical candidates.[12–16] Recent trials have also demonstrated TAVR's non-inferiority in intermediate-risk and superiority in low-risk surgical candidates.[17–19] A meta-analysis combining data from clinical trials indicates that TAVR is associated with lower short-term cardiovascular events than sAVR, regardless of the surgical risk. However, long-term data remain unclear.[19 20]

Our results align with previous studies, which demonstrated that diabetes is an independent predictor of long-term mortality post-sAVR,[21] increasing mortality rates and reducing quality of life (10). Diabetes was also an independent predictor of 30-day readmission after sAVR in the USA.[22] Our results in TAVR patients align with an analysis of the Transcatheter Valve Therapy Registry, which reported that diabetes was not associated with an increased risk of 30-day mortality.[23] This finding was confirmed in two meta-analyses of more than 15 000 patients each.

To our knowledge, we are the first to compare the short-term outcome of aortic valve replacement in diabetes patients in sAVR and TAVR. Large randomised controlled

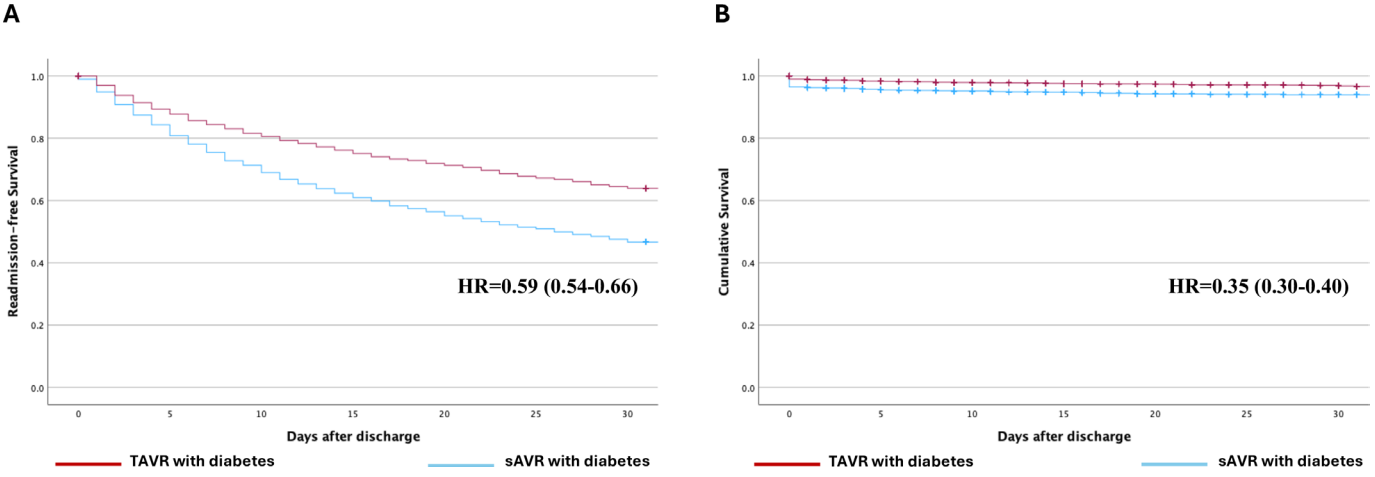

Figure 3 Kaplan-Meier curve comparing the probability of (A) readmission-free survival and (B) cumulative survival in patients with diabetes undergoing TAVR versus sAVR. Patients were stratified into sAVR diabetes (blue line) and TAVR with diabetes (red line). The x-axis represents days after discharge. The y-axis represents readmission-free survival in (A) and cumulative survival in (B). sAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement

Table 5 Predictors of readmission in patients with diabetes undergoing TAVR versus sAVR

	TAVR			sAVR		
	OR	95% CI	P value	OR	95% CI	P value
Mean (SD)	1.01	1.00 to 1.02	0.01	1.01	1.00 to 1.02	0.008
Age (years)						
<55	Ref	Ref	–	Ref	Ref	–
55–64	0.85	0.37 to 1.94	0.701	0.85	0.62 to 1.16	0.297
65–74	0.81	0.37 to 1.74	0.582	0.88	0.66 to 1.17	0.376
75–84	0.90	0.42 to 1.94	0.797	1.20	0.90 to 1.62	0.219
>84	1.09	0.50 to 2.35	0.827	2.05	1.24 to 3.39	0.005
Gender						
Male	Ref	Ref	–	Ref	Ref	–
Female	0.91	0.78 to 1.06	0.217	1.17	1.00 to 1.37	0.052
Income						
Low	Ref	Ref	–	Ref	Ref	–
Low-mid	0.92	0.74 to 1.15	0.452	0.79	0.64 to 0.96	0.021
High-mid	1.05	0.85 to 1.30	0.647	0.87	0.71 to 1.07	0.185
High	1.19	0.96 to 1.48	0.113	0.80	0.64 to 1.00	0.054
Obesity						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.60	0.50 to 0.73	<0.001	0.58	0.49 to 0.69	<0.001
Hypertension						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.52	0.41 to 0.66	<0.001	0.79	0.63 to 0.99	0.041
Smoking						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.86	0.73 to 1.00	0.051	0.76	0.64 to 0.90	0.001
Dyslipidaemia						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.75	0.64 to 0.87	<0.001	0.76	0.65 to 0.90	<0.001
Peripheral vascular disease						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.88	0.72 to 1.08	0.229	0.63	0.51 to 0.78	<0.001
Chronic kidney disease						
No	Ref	Ref	–	Ref	Ref	–
Yes	1.16	1.00 to 1.34	0.055	1.38	1.17 to 1.62	<0.001
Coronary artery disease						
No	Ref	Ref	–	Ref	Ref	–
Yes	2.01	1.48 to 2.72	<0.001	3.52	2.56 to 4.85	<0.001

sAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

trials that compared TAVR with sAVR for severe AS in the diabetes population are lacking. The procedural choice often depends more on other factors, such as age, frailty and the presence of comorbidities, rather than diabetes alone. TAVR has been associated with better valve haemodynamics and a lower risk of structural valve deterioration over time compared with sAVR.[24] This benefit may be particularly relevant for diabetes patients who face higher risks of vascular complications. A post hoc stratified analysis of the PARTNER trial showed that among patients with diabetes, TAVR was associated with a survival benefit at 1 year compared with sAVR.[25] However, it should be noted that this study only included high-risk patients with severe symptoms. Another meta-analysis of

Table 6 Predictors of mortality in patients with diabetes undergoing TAVR versus sAVR

	TAVR			sAVR		
	OR	95% CI	P value	OR	95% CI	P value
Mean (SD)	1.01	0.99 to 1.02	0.313	1.01	1.009 to 1.02	0.022
Age (years)						
<55	Ref	Ref	–	Ref	Ref	–
55–64	0.46	0.18 to 1.19	0.111	0.79	0.56 to 1.10	0.159
65–74	0.42	0.18 to 0.97	0.043	0.78	0.57 to 1.06	0.118
75–84	0.38	0.17 to 0.88	0.024	1.06	0.77 to 1.46	0.729
>84	0.54	0.23 to 1.25	0.151	1.94	1.12 to 3.34	0.018
Gender						
Male	Ref	Ref	–	Ref	Ref	–
Female	1.10	0.88 to 1.38	0.387	1.46	1.23 to 1.74	<0.001
Income						
Low	Ref	Ref	–	Ref	Ref	–
Low-mid	1.18	0.85 to 1.62	0.319	0.95	0.76 to 1.20	0.683
High-mid	0.94	0.67 to 1.31	0.696	1.12	0.89 to 1.41	0.33
High	0.94	0.66 to 1.32	0.702	0.66	0.50 to 0.88	0.004
Obesity						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.57	0.42 to 0.76	<0.001	0.83	0.70 to 0.99	0.043
Hypertension						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.55	0.38 to 0.79	0.001	0.82	0.64 to 1.07	0.142
Smoking						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.60	0.46 to 0.78	<0.001	0.65	0.54 to 0.79	<0.001
Dyslipidaemia						
No	Ref	Ref	–	Ref	Ref	–
Yes	0.43	0.34 to 0.54	<0.001	0.55	0.46 to 0.65	<0.001
Peripheral vascular disease						
No	Ref	Ref	–	Ref	Ref	–
Yes	1.81	1.40 to 2.34	<0.001	1.56	1.30 to 1.89	<0.001
Chronic kidney disease						
No	Ref	Ref	–	Ref	Ref	–
Yes	2.02	1.60 to 2.53	<0.001	2.33	1.96 to 2.76	<0.001
Coronary artery disease						
No	Ref	Ref	–	Ref	Ref	–
Yes	1.25	0.71 to 2.18	0.439	1.70	1.07 to 2.69	0.024

low-to-intermediate-risk cohorts found that mortality or major stroke at 1 year was significantly lower in TAVR compared with sAVR. Still, this outcome was not modulated by diabetes.[26] The PARTNER-3 trial concluded that among patients with severe, symptomatic AS who were at low surgical risk, 1-year and 3-year cardiovascular events were lower with TAVR than with sAVR.[18 27] However, the recent analysis of the 5-year follow-up showed the loss of survival benefit of TAVR over sAVR.[28]

Nevertheless, this study did not compare diabetes to non-diabetes patients. Further, the proportion of diabetes patients was balanced between both (around 30%), and a subgroup analysis was not performed. Similarly, the 10-year follow-up of the NOTION trial did not report a difference in the risk of major clinical outcomes between sAVR and TAVR.[29]

Diabetes is associated with accelerated progression of valvular disease and decreased left ventricular systolic and diastolic function in patients with AS.[30–32] This may

be explained by the increased macrovascular disease risk seen with diabetes, which can worsen ventricular hypertrophic remodelling caused by AS due to altered myocyte structure and increased fibrosis[5 30]—the accelerated progression to AS results from the increased development of atherosclerosis in diabetes.[33] Proposed mechanisms of the underlying pathophysiology include activation of the renin–angiotensin–aldosterone axis, production of free radicals, elevation of inflammatory interleukins and glycosylation of proteins leading to increased calcific and profibrotic processes causing calcification of the aortic valve.[33 34] Unlike the transcatheter approach, there is increased reperfusion and ischaemic injury induced by cardioplegia and cardiopulmonary bypass in sAVR, which could explain the worse outcome associated with surgery in all patients, including the ones with diabetes.[25] Further, TAVR patients have a higher postprocedural indexed effective orifice area and a lower prosthesis-patient mismatch than sAVR.[35]

Among the limitations we acknowledge in our study is its retrospective design, which allows us to infer only association but not causation. The NRD is an administrative claim-based database lacking clinical and laboratory variables, subject to reporting and coding errors. Causes of readmission are identified using the primary discharge diagnosis codes, and deaths outside of the hospital are not captured in the NRD. Outcomes might be influenced by confounding factors not included in our study, such as medications, surgical risk scores, glycaemic control, duration of diabetes and echocardiographic parameters. One notable limitation of this study is the interpretation of p values, especially in the context of our large sample size. Even small effect sizes in studies with large samples can produce statistically significant p values,[36] which may not necessarily translate into meaningful or clinically relevant findings. Consequently, the p value in such cases should be interpreted cautiously, as it is more indicative of hypothesis generation rather than definitive evidence of an effect.[37] Further research is warranted to confirm and contextualise these results in diverse populations and settings. Despite these limitations, our multivariable analysis provides insights into the impact of diabetes on short-term cardiovascular outcomes in patients hospitalised for aortic valve replacement.

CONCLUSION

As the overall lifespan of people in the USA and worldwide has increased, more people are living longer lives and, hence, are more susceptible to developing AS. Trials in the past ten years indicated that TAVR is safe and equally effective as surgical replacement in severe AS, regardless of the risk. Our data, among others, show that patients with diabetes could benefit from this minimally invasive technique without incurring additional mortality and morbidity in the short-term.

Author affiliations
[1]Research Department, Weill Cornell Medicine—Qatar, Doha, Qatar
[2]Department of Medicine, Rochester General Hospital, Rochester, NY, USA
[3]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
[4]Department of Medical Education, Weill Cornell Medicine – Qatar, Doha, Qatar
[5]Biostatistics core, Weill Cornell Medicine – Qatar, Doha, Qatar
[6]Department of Endocrinology, Hamad Medical Corporation, Doha, Qatar
[7]Heart hospital, Hamad Medical Corporation, Doha, Qatar
[8]Sanford and I. Weill Department of Medicine, Weill Cornell Medicine, New York, NY, USA

Contributors CAK was involved in the design of the study. ADS, KB and SD conducted the data analysis. ADS, AJ, JAS and CAK interpreted the data. ADS completed the first draft of the manuscript. All authors were involved in the critical revision of the manuscript. All authors read and approved the final manuscript. CAK is the guarantor of this work and, as such, has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The study was exempted from full institutional review board approval by Weill Cornell Medicine Qatar (determination letter 21-00021).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The NIS is a publicly available database. Data presented in this article are available on reasonable request from the correspondent author.

ORCID iD
Charbel Abi Khalil http://orcid.org/0000-0002-1428-6324

REFERENCES

1 Pujari SH, Agasthi P. Aortic stenosis. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, 2024.
2 Osnabrugge RLJ, Mylotte D, Head SJ, *et al*. Aortic stenosis in the elderly: disease prevalence and number of candidates for transcatheter aortic valve replacement: a meta-analysis and modeling study. *J Am Coll Cardiol* 2013;62:1002–12.
3 Zilberszac R, Gabriel H, Schemper M, *et al*. Asymptomatic Severe Aortic Stenosis in the Elderly. *JACC Cardiovasc Imaging* 2017;10:43–50.
4 CDC. National diabetes statistics report | diabetes. 2023.
5 Huang D, Refaat M, Mohammedi K, *et al*. Macrovascular Complications in Patients with Diabetes and Prediabetes. *Biomed Res Int* 2017;2017:7839101.
6 Lu Q, Lv J, Ye Y, *et al*. Prevalence and impact of diabetes in patients with valvular heart disease. *i Sci* 2024;27:109084.

7 Roderburg C, Loosen SH, Luedde T, *et al*. Diabetes mellitus is associated with an increased incidence of aortic valve stenosis. *Diab Vasc Dis Res* 2021;18:14791641211033819.
8 Mourino-Alvarez L, Corbacho-Alonso N, Sastre-Oliva T, *et al*. Diabetes Mellitus and Its Implications in Aortic Stenosis Patients. *Int J Mol Sci* 2021;22:6212.
9 Khan S, Dargham S, Al Suwaidi J, *et al*. Trends and Outcomes of Aortic Valve Replacement in Patients With Diabetes in the US. *Front Cardiovasc Med* 2022;9:844068.
10 Vahanian A, Beyersdorf F, Praz F, *et al*. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2022;43:561–632.
11 Winter M-P, Bartko P, Hofer F, *et al*. Evolution of outcome and complications in TAVR: a meta-analysis of observational and randomized studies. *Sci Rep* 2020;10:15568.
12 Adams DH, Popma JJ, Reardon MJ, *et al*. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790–8.
13 Deeb GM, Reardon MJ, Chetcuti S, *et al*. 3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol* 2016;67:2565–74.
14 Kapadia SR, Leon MB, Makkar RR, *et al*. 5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomised controlled trial. *The Lancet* 2015;385:2485–91.
15 Yakubov SJ, Adams DH, Watson DR, *et al*. 2-Year Outcomes After Iliofemoral Self-Expanding Transcatheter Aortic Valve Replacement in Patients With Severe Aortic Stenosis Deemed Extreme Risk for Surgery. *J Am Coll Cardiol* 2015;66:1327–34.
16 Smith CR, Leon MB, Mack MJ, *et al*. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–98.
17 Reardon MJ, Van Mieghem NM, Popma JJ, *et al*. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med* 2017;376:1321–31.
18 Mack MJ, Leon MB, Thourani VH, *et al*. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med* 2019;380:1695–705.
19 Blankenberg S, Seiffert M, Vonthein R, *et al*. Transcatheter or Surgical Treatment of Aortic-Valve Stenosis. *N Engl J Med* 2024;390:1572–83.
20 Siontis GCM, Overtchouk P, Cahill TJ, *et al*. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis. *Eur Heart J* 2019;40:3143–53.
21 Ram E, Kogan A, Levin S, *et al*. Type 2 diabetes mellitus increases long-term mortality risk after isolated surgical aortic valve replacement. *Cardiovasc Diabetol* 2019;18:31.
22 Khoury H, Ragalie W, Sanaiha Y, *et al*. Readmission After Surgical Aortic Valve Replacement in the United States. *Ann Thorac Surg* 2020;110:849–55.
23 Abramowitz Y, Vemulapalli S, Chakravarty T, *et al*. Clinical Impact of Diabetes Mellitus on Outcomes After Transcatheter Aortic Valve Replacement: Insights From the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *Circ Cardiovasc Interv* 2017;10:e005417.
24 Ternacle J, Hecht S, Eltchaninoff H, *et al*. Durability of transcatheter aortic valve implantation. *EuroIntervention* 2024;20:e845–64.
25 Lindman BR, Pibarot P, Arnold SV, *et al*. Transcatheter versus surgical aortic valve replacement in patients with diabetes and severe aortic stenosis at high risk for surgery: an analysis of the PARTNER Trial (Placement of Aortic Transcatheter Valve). *J Am Coll Cardiol* 2014;63:1090–9.
26 Ando T, Ashraf S, Villablanca P, *et al*. Meta-Analysis of Effectiveness and Safety of Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement in Low-to-Intermediate Surgical Risk Cohort. *Am J Cardiol* 2019;124:580–5.
27 Forrest JK, Deeb GM, Yakubov SJ, *et al*. 3-Year Outcomes After Transcatheter or Surgical Aortic Valve Replacement in Low-Risk Patients With Aortic Stenosis. *J Am Coll Cardiol* 2023;81:1663–74.
28 Mack MJ, Leon MB, Thourani VH, *et al*. Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years. *N Engl J Med* 2023;389:1949–60.
29 Thyregod HGH, Jørgensen TH, Ihlemann N, *et al*. Transcatheter or surgical aortic valve implantation: 10-year outcomes of the NOTION trial. *Eur Heart J* 2024;45:1116–24.
30 Falcão-Pires I, Hamdani N, Borbély A, *et al*. Diabetes mellitus worsens diastolic left ventricular dysfunction in aortic stenosis through altered myocardial structure and cardiomyocyte stiffness. *Circulation* 2011;124:1151–9.
31 Lindman BR, Arnold SV, Madrazo JA, *et al*. The adverse impact of diabetes mellitus on left ventricular remodeling and function in patients with severe aortic stenosis. *Circ Heart Fail* 2011;4:286–92.
32 Kamalesh M, Ng C, El Masry H, *et al*. Does diabetes accelerate progression of calcific aortic stenosis? *Eur J Echocardiogr* 2009;10:723–5.
33 Testuz A, Nguyen V, Mathieu T, *et al*. Influence of metabolic syndrome and diabetes on progression of calcific aortic valve stenosis. *Int J Cardiol* 2017;244:248–53.
34 Le Quang K, Bouchareb R, Lachance D, *et al*. Early development of calcific aortic valve disease and left ventricular hypertrophy in a mouse model of combined dyslipidemia and type 2 diabetes mellitus. *Arterioscler Thromb Vasc Biol* 2014;34:2283–91.
35 Hahn RT, Pibarot P, Stewart WJ, *et al*. Comparison of transcatheter and surgical aortic valve replacement in severe aortic stenosis: a longitudinal study of echocardiography parameters in cohort A of the PARTNER trial (placement of aortic transcatheter valves). *J Am Coll Cardiol* 2013;61:2514–21.
36 Sullivan GM, Feinn R. Using Effect Size-or Why the P Value Is Not Enough. *J Grad Med Educ* 2012;4:279–82.
37 Boscardin CK, Sewell JL, Tolsgaard MG, *et al*. How to Use and Report on p-values. *Perspect Med Educ* 2024;13:250–4.