Health-related quality of life following TAVI or cardiac surgery in patients at intermediate and low risk: a systematic review and meta-analysis

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ABSTRACT

Recent randomised trials have shown that clinical outcomes with transcatheter aortic valve implantation (TAVI) are non-inferior to surgical aortic valve replacement (SAVR) in patients with symptomatic aortic stenosis at intermediate to low risk. Health-related quality of life (HrQoL) outcomes in these patient groups remain uncertain. A systematic search of the literature was conducted that included nine trials and 11,295 patients. Kansas City Cardiomyopathy Questionnaire (KCCQ), a heart-failure-specific measure and EuroQol-5D (EQ-5D) (a generic health status tool) changes were the primary outcomes. New York Heart Association (NYHA) classification was the secondary outcome. Improvement in KCCQ scores was greater with TAVI (mean difference (MD)=13.56, 95% confidence interval (CI) 11.67–15.46, p<0.001) at 1 month, as was the improvement in EQ-5D (MD=0.07, 95% CI 0.05–0.08, p<0.001). There was no difference in KCCQ (MD=1.05, 95% CI –0.11 to 2.21, p=0.08) or EQ-5D (MD=–0.01, 95% CI –0.03 to 0.01), p=0.37) at 12 months. NYHA functional class 3/4 was lower in patients undergoing TAVI at 1 month (MD=0.51, 95% CI 0.34–0.78, p=0.002), but there was no difference at 12 months (MD=1.10; 95% CI 0.87–1.38, p=0.43). Overall, TAVI offers early benefit in HRQoL outcomes compared with SAVR, but they are equivalent at 12 months.

KEYWORDS: aortic stenosis, TAVI, SAVR, KCCQ, EQ-5D, NYHA

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Introduction

Aortic stenosis (AS) is one of the most common and prognostically significant heart valve diseases.[1] Its prevalence increases with age, and it is present in 2–7% of all patients over 65 years of age.[1] Symptomatic AS requires valve replacement either via transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR), and the choice has traditionally been made on surgical risk.[2] There are three categories of surgical risk (high risk >8%; intermediate risk 4–8%; low risk as <4%), based on a model developed to estimate the risk of death at 30 days following surgery.[2] The surgical risk score has been incorporated into trials comparing SAVR with TAVI through the heart multidisciplinary team (MDT).[2,3]

TAVI is preferable to surgical intervention in patients at high surgical risk[4] and is recommended by the current European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) guidelines (Fig 1).[5] The transfemoral (TF) TAVI 'minimalistic' approach is now the most used technique because it is associated with reduced complications and shorter hospital stay.[6] A recent meta-analysis showed that TAVI is associated with a reduction in all-cause mortality and stroke irrespective of the baseline surgical risk or the transcatheter heart valve system used.[7] Evaluation of changes in quality of life (QoL) might be a better outcome measure compared with survival in all-patient risk groups, and both outcomes can be combined in a cost-effectiveness analysis to measure the effect of a new intervention.[8,9] Ando *et al* evaluated health-related QoL (HRQoL) in patients at high risk with symptomatic aortic stenosis, demonstrating superiority of TAVI at 30 days after procedure.[10] Recent Cochrane systematic reviews and meta-analyses after TAVI or SAVR in patients at low[11] and intermediate[12] surgical risk included all-cause mortality, stroke and hospital readmission rate, displaying non-inferiority of TAVI in terms of survival; however, they did not include functional outcomes or QoL assessments.

Disease-specific HRQoL instruments provide crucial information because of their ability to detect small but important treatment effects and are often used to guide commissioning of new treatments and as part of cost-effectiveness evaluations.[9] HRQoL in patients undergoing TAVI or SAVR has been evaluated using various scoring

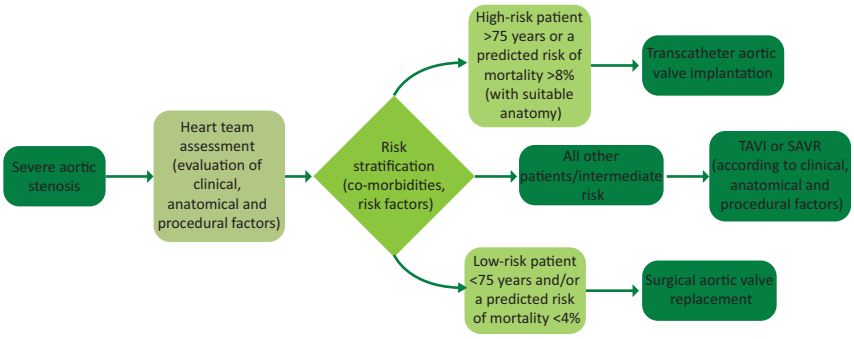

Fig 1. Current treatment approach for patients with severe aortic stenosis.[5] SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve intervention.

systems, including the Medical Outcomes Trust Short-Form 36-Item Health Survey (SF-36) and the Short-Form (SF-12), the Minnesota Living with Heart Failure questionnaire (MLHFQ), the EuroQoL-5D (EQ-5D), the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the MacNew tool.[13,14] Functional outcomes have been reported principally using the New York Heart Association (NYHA).[15]

In this review, we compare HRQoL and functional outcomes in patients at intermediate or low risk treated mainly by TF-TAVI because it is the most commonly used approach, or SAVR, because this area is yet uncovered as far as we know.

Methods

A systematic review and meta-analysis was conducted as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[16] registered with PROSPERO (CRD42022330632). Ethical approval was not required. A literature search was conducted via PubMed, EMBASE, OVID and the Cochrane Library to 5 June 2022. In addition, the World Health Organization International Clinical Trials Registry (http://apps.who.int/trial search/), ClinicalTrials.gov (http://clinical-trials.gov/) and ISRCTN Register (http://www.isrctn.com/) were searched for details of ongoing and unpublished studies. The bibliographic lists of articles of relevance were reviewed (Fig S1).

Eligibility criteria

All articles were screened by two authors (AG and MA) using a two-stage strategy. Initially, articles were screened based on title or abstract relying on the inclusion and exclusion criteria. Full manuscripts were then reviewed for eligibility to be included in the main analysis. Any selection disagreements were resolved through discussion among the authors. We included all randomised controlled trials (RCTs) that compared HRQoL indices and functional status at 1 and 12 months between TAVI (mainly TF access route) and SAVR in patients at low and intermediate (surgical) risk.

Exclusion criteria included papers that evaluated non-TF TAVI, non-English, non-comparative and duplicate studies. Patients undergoing surgery using alternative access routes, such as transapical, transventricular or transaortic, were also excluded. Other exclusions were studies that only evaluated all-cause mortality, echocardiographic findings and procedural complications. Trials that evaluated cost-effectiveness (quality-adjusted life year) were excluded from the main analysis.

Primary outcome

Valve Academic Research Consortium-2 recommends that a comprehensive assessment of HRQoL for patients undergoing TAVI incorporates both a heart failure-specific measure and one or more generic measures.[17] The primary outcome in this meta-analysis was KCCQ as an instrument for heart failure-specific measurement and EQ-5D for generic health status measurement. Other outcomes, including SF-12, SF-36 and MLHFQ, were included in our extraction; however, they were excluded at a later stage because of the lack of homogeneity of data reporting at 1 and 12 months in some studies, as well as the lack of data reporting in other trials.

KCCQ overall score is a 23-item questionnaire that quantifies physical limitations, symptoms, self-efficacy, social interference and QoL. It has been recommended as a heart failure-specific performance measure for quantifying the HRQoL.[18] KCCQ can sensitively estimate the effect of heart failure on patients and is strongly associated with the clinical events over time; thus, it can improve patient-centred care.[18] Scores for the KCCQ summary and its subscales range from 0 to 100, with higher scores indicating better health status.[19] KCCQ overall scores were evaluated in six studies at baseline, 1 and 12 months.

EQ-5D is a generic (rather than heart-failure specific) self-administered questionnaire comprising health state description and evaluation. Health state description is assessed by five dimensions: mobility, self-care, usual activities, anxiety/depression and pain/discomfort. Similar to KCCQ, EQ-5D allows patient-centredness when assessing treatment effects in patients.[20] In the evaluation section, patients use a visual analogue scale to evaluate their overall health status on a scale of 0–100, with a higher score corresponding to better health status.[20] EQ-5D utility scores were evaluated in two studies at baseline, 1 and 12 months.

Secondary outcome

NYHA functional classification scores were evaluated at baseline, 1 and 12 months in six studies.[21] NYHA score is reported either as a proportion in each category or in categories 1/2 and 3/4.

Data analysis

All analysis was performed using R v4.1.2,[22] incorporating the meta, dmetar and altmeta packages,[23–25] to meta-analyse the extracted data. Publication bias was assessed for the primary and co-primary outcomes by inspection of funnel plots and by

Lin's hybrid test.[26] Different outcomes (including KCCQ, EQ-5D and NYHA) were analysed and their methods are detailed in the supplementary material.

Assessment of heterogeneity

Heterogeneity among the studies was assessed using the Cochran Q test ($\chi 2$). Inconsistency was quantified by calculating and interpreted using the following guide: 0–25%, low heterogeneity; 25–75%, moderate heterogeneity; and 75–100%, substantial heterogeneity.[27]

Methodological quality and risk of bias assessment

Studies eligible for inclusion were assessed for quality and risk of bias by two authors independently. Cochrane's tool was used to evaluate the risk of bias. The Agency for Healthcare Research and Quality (AHRQ) standard was used to provide an overall rating of good, fair or poor quality.[28]

Results

KCCQ overall

Baseline characteristics of the included studies are shown in Table 1. Improvement in KCCQ scores from baseline was higher with TAVI compared with SAVR (p<0.001) at 1 month (Fig 2). Heterogeneity was assessed by inspection of the statistic and its confidence interval (CI); an influence study was then undertaken because the 95% CI of effect of one study (Popma *et al*, 2019[34]) lay outside the 95% CI of the pooled size effect. Fig S2 displays the influence analysis for KCCQ change scores at 1 month, Baujat plot comparing influence on pooled effect with contribution to heterogeneity and the effect on the statistic of removing one study (Popma *et al*, 2019). There was a significant improvement in KCCQ scores at 1 month after removing (Popma *et al*, 2019[34]) (p<0.001; Fig S2). There was no significant difference in the improvement of KCCQ scores from baseline between TAVI and SAVR at 12 months (p=0.08; Fig 2). Publication bias was assessed at 1 and 12 months, using funnel plots (Fig S3).

EQ-5D utility scores

Change from baseline EQ-5D utility indices is shown in Table S2, with analyses involving three studies.[31,33,35] Heterogeneity was substantial when all three studies were included (85%, CI 61–95%), and the UK TAVI study[35] was classed as an outlier, because its 95% CI of effect lay outside the 95% CI of the pooled effect size. UK TAVI was not included in the main analysis but was reported quantitatively. Forrest plots for the two study comparisons are shown in Fig 3. There was a significant difference between TAVI and SAVR at 1 month (mean difference (MD)=0.07, 95% CI 0.05–0.08, p<0.001). EQ-5D difference at 12 month was reported in two studies. There was no significant difference between TAVI and SAVR at 12 months (MD=−0.01, 95% CI −0.03 to 0.01, p=0.37). Assessment of influence or publication bias was non-informative because there were only two studies included.

NYHA

The proportion of NYHA class 3/4 patients was less at 1 month (Figs 4 and 5) following TAVI compared with SAVR. There was a larger reduction for TAVI, relative to SAVR, at both 1 and 12 months, although with a reduction in the difference after 12 months (0.435 reduction in TAVI and 0.382 reduction in SAVR at 1 month and 0.432 reduction in TAVI and 0.423 reduction in SAVR at 12 months, respectively) (Fig 5). These findings were consistent with the results displayed in Fig 6, where there was no significant difference at baseline (MD=1.01, 95% CI 0.93–1.10, p=0.80). At 1 month, there was a higher proportion of patients in NYHA classes 3 and 4 in the SAVR cohort compared with TAVI (MD=0.51, 95% CI 0.34–0.78, p=0.002), whereas there was no significant difference at 12 months (MD=1.10; 95% CI 0.87–1.38, p=0.43) (Fig 6).

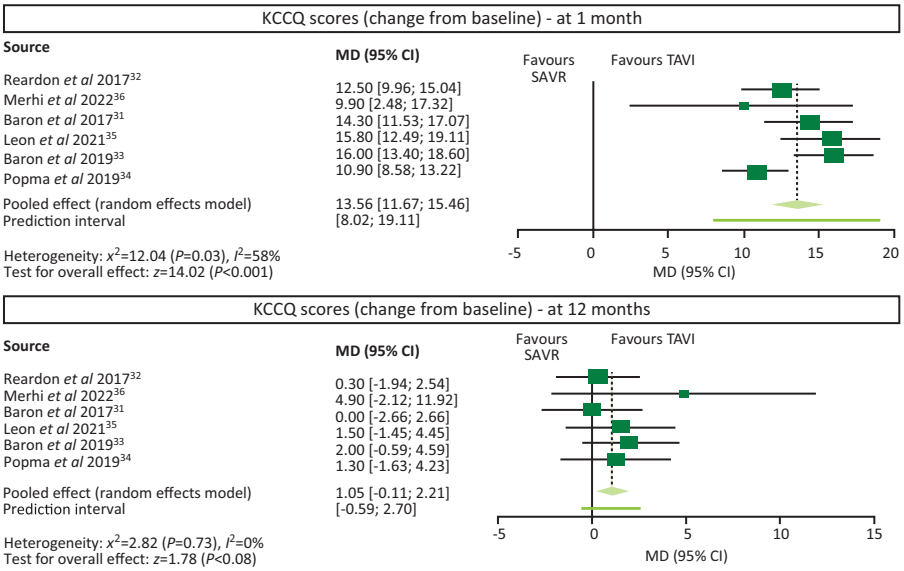

Fig 2. Difference in Kansas City Cardiomyopathy Questionnaire (KCCQ) overall scores after 1 and 12 months as reported in six studies. CI = confidence interval; MD = mean difference; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve intervention.

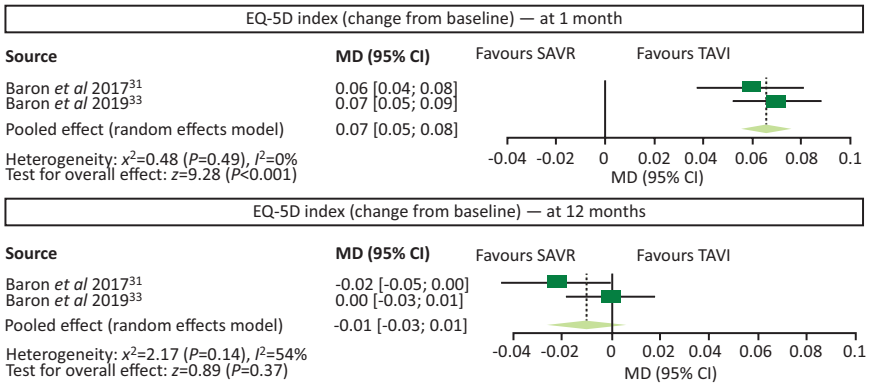

Fig 3. Difference in EuroQol-5D (EQ-5D) utility scores after 1 and 12 months as reported by two studies. CI = confidence interval; MD = mean difference; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve intervention.

The heterogeneity statistic, I^2, was moderately high at 1 month; influence analysis indicated that it was the study by Leon *et al*[30] that contributed significantly to the pooled effect size and this heterogeneity. Testing of the effect of one-at-a-time removal of each study showed that removal of Leon *et al*[30] reduced I^2 to 25% (Fig S4). However, the new pooled effect size still lies within the confidence interval of the 4-study analysis (Fig 6). Fig S4 also displays the influence analysis for NYHA change scores at 1-month post-operative, Baujat plot comparing influence on pooled effect with contribution to heterogeneity and the effect on heterogeneity I^2 statistic of removing one study (Leon *et al*[30]). There was still a significant difference at 1 month after removing Leon *et al*[30] ($p<0.001$) (Fig S4). Publication bias was assessed for at 1 and 12 months, using funnel plots (Fig S5).

There was a reduction in patients in NYHA classes 3 and 4 from baseline to after 1 and 12 months, and an increase in the number of patients in NYHA classes 1 and 2 (Fig 4). Visualisation of NYHA class in both TAVI and SAVR at different time points suggested that there was a legitimate decrease in the proportion of patients at NYHA class 3/4 at 1 and 12 months; this decrease outweighed the loss to follow-up, suggesting that the decrease is real and not an artefact of patient drop-out. There was a larger reduction in the pooled number of patients in NYHA class 3/4 undergoing TAVI, relative to SAVR, at both 1 and 12 months (Fig 5).

Methodological quality and risk of bias assessment

Selection bias, performance bias, detection bias, attrition bias and reporting bias were all assessed and categorised into low, some concern and high risk of bias (Fig 7).

Discussion

SAVR remains the gold standard treatment of choice for patients with severe aortic stenosis at intermediate-to-low surgical risk, and current guidelines recommend TAVI for patients who have a high risk of surgery.[5] Recent trials, such as NOTION,[29] PARTNER 3[33] and EVOLUT,[36] showed that TAVI has superior HRQoL outcomes at 1 month compared with SAVR and is non-inferior at 12 months in patients at low risk. In this meta-analysis, KCCQ and EQ-5D HRQoL scores showed superiority for TAVI at 1 month but no significant difference compared with SAVR at 12 months. This was also the case for the improvement in NYHA classification. Assessment of HRQoL is influenced by factors that are uniquely perceived by each individual and are influenced by physical limitations (such as pain/discomfort) as well as emotional and

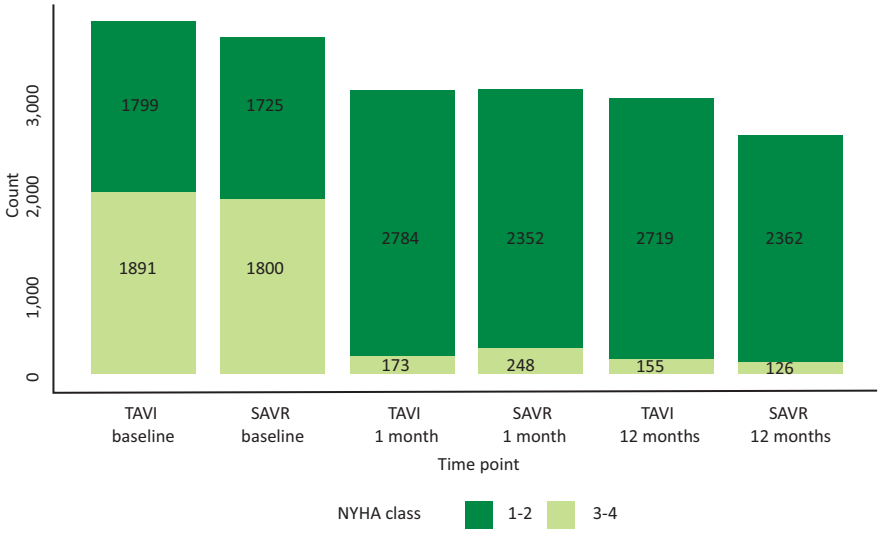

Fig 4. Number of patients in New York Heart Association (NYHA) classes aggregated across all studies at each time point (six studies at baseline and 12 months, four studies at 1 month). SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve intervention.

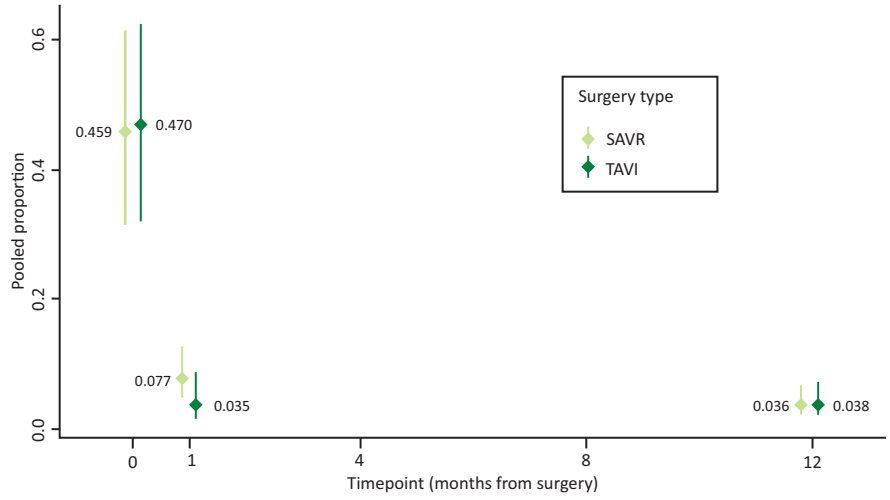

Fig 5. Pooled proportions of New York Heart Association (NYHA) class 3 and 4 at baseline, 1 and 12 months. Data points are the proportion of patients in NYHA class 3/4 out of total patients in each cohort (TAVI vs SAVR) across all studies at each time point. SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve intervention.

social factors, including self-care. These outcomes are important in promoting a patient-centred approach, which helps to facilitate shared decision-making and ensure that patient preferences are used to guide management.[38–40] HRQoL measures also provide a framework for clinical monitoring, in which reduced HRQoL outcomes were shown to be independent predictors of both further hospitalisation and mortality.[41,42] TAVI results in better mobility and performance of usual activities earlier than after SAVR.[19,20,38] Moreover, the incidence of anxiety and depression can be high early after cardiac surgery and can be associated with longer-term health outcomes for patients.[43,44] This could explain why KCCQ scores were lower in the surgical cohort because this includes social interference measures.[19] Anxiety and depression are assessed as one of the five dimensions in EQ-5D,[20] and the significant improvement in EQ-5D scores at 1 month following TAVI could reflect a reduced incidence of postoperative mental health problems compared with cardiac surgery.

NYHA class 3/4 was significantly less with TAVI compared with SAVR at 1 month, likely reflecting earlier mobilisation and a reduction in length of hospital stay (average of 8 days for SAVR

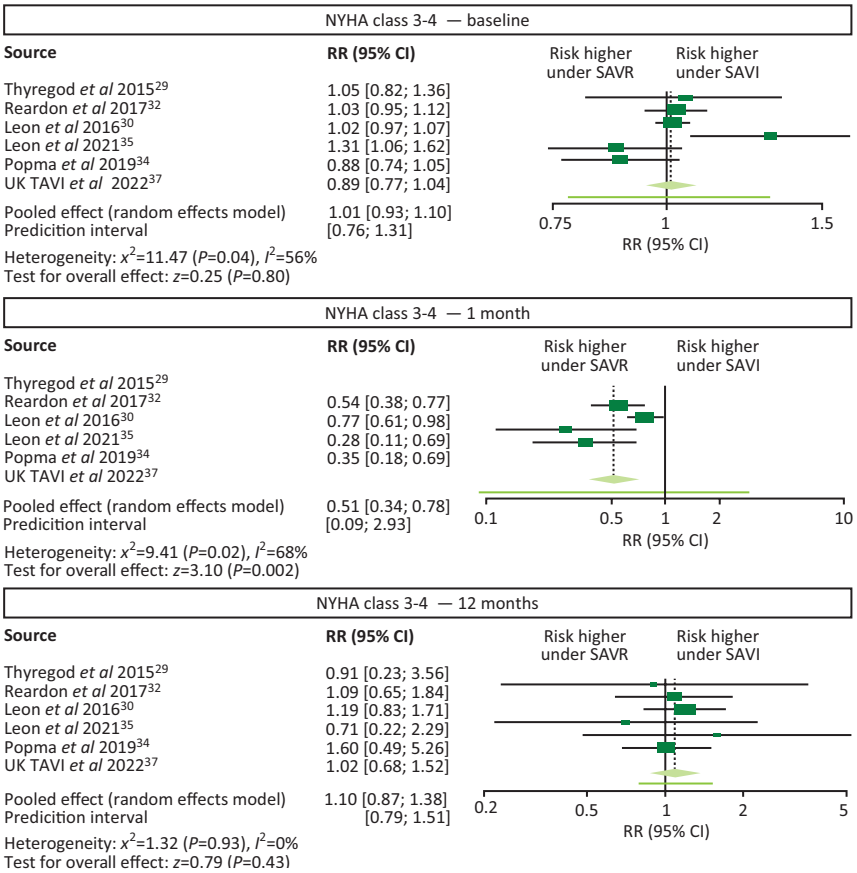

Fig 6. Risk of NYHA class 3 or 4 at baseline, 1 and 12 months. CI = confidence interval; RR = relative risk; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve intervention.

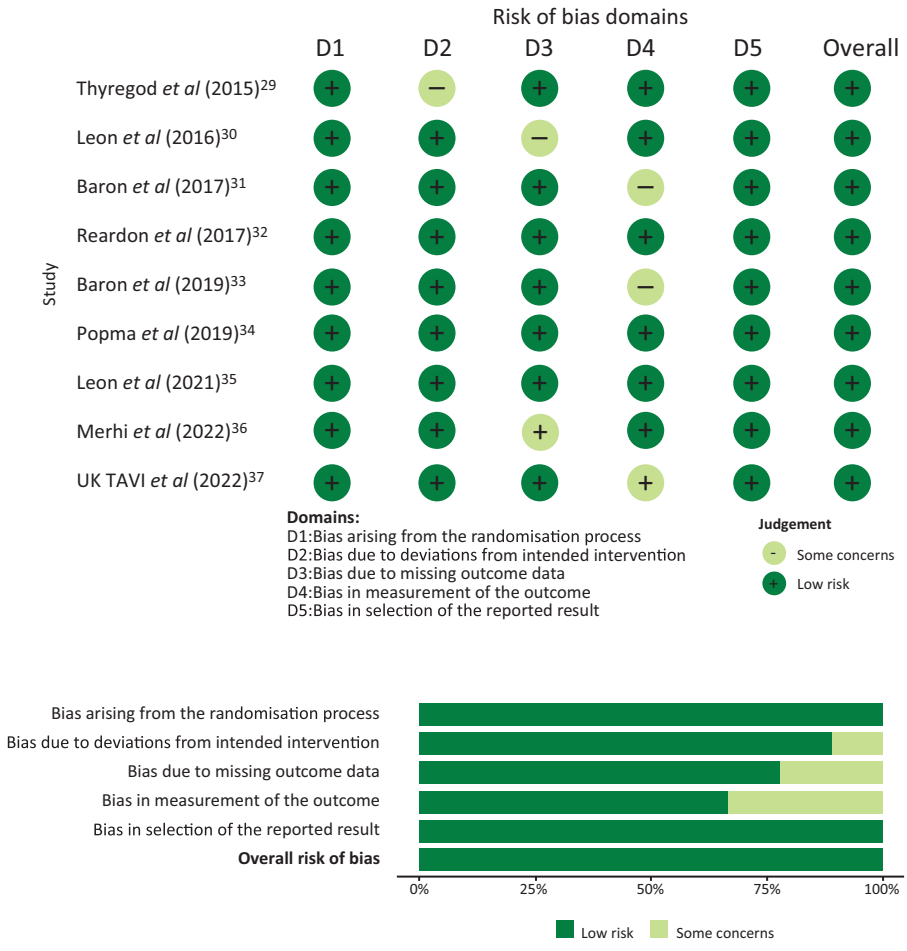

Fig 7. Risk of bias assessment utilising Cochrane RoB 2.0.

compared with 3 days for TAVI, as shown by the trials included in this analysis).[10,21,45,46] This improvement in functional status is consistent with the findings reported by Gavina *et al*,[47] which showed a greater improvement in functional class at 6 months after TAVI compared with cardiac surgery.[47] This functional improvement was attributed to higher effective prosthetic orifice area index (EAOI) following TAVI, potentially improving left ventricular remodeling.[47] Furthermore, TAVI resulted in an immediate haemodynamic response displayed as an immediate reduction in left ventricular ejection time (LVET) (suggesting rapid unloading of the ventricle) and a subsequent increase in HRQoL, which was evaluated by EQ-5D-5L 12 weeks after the intervention.[48] Some of the trials included in this analysis also showed that echocardiographic parameters remain superior following TAVI, including a larger mean valve area, effective orifice area and mean valve gradient[29,30,32,49] at 12 months. This again could explain the earlier improvement in the NYHA class.[49]

Potential explanations for higher HRQoL scores in TF-TAVI compared with SAVR at 1 month include early mobilisation, shorter coronary care unit stay, less pain/discomfort and less sedative use in TF-TAVI.[10] This might be the result of both EQ-5D and KCCQ including physical limitations and mobility domains, indicating that TAVI holds the advantage early on because of being less invasive. Better health outcomes can be attributed to a significantly lower incidence of acute kidney injury (AKI), new-onset or worsening atrial fibrillation, major bleeding events and cardiogenic shock at 30 days after TAVI.[29,30,32,44,49–51] This reduces the risk of postprocedural mortality and the risk of hospitalisation, which can worsen patient outcomes and, hence, result in poor health outcomes. Patients with severe aortic stenosis are characteristically older and have multiple health conditions, including a high prevalence of chronic renal insufficiency,[49] which could be precipitated by acute injury secondary to major bleeding events or cardiogenic shock, which are significantly higher in SAVR at 30 days.[28,29,31,46,49,50] Another likely contributor is that the mean in-hospital time or time spent in the intensive care unit (ICU) is shorter in patients that underwent TF-TAVI.[45]

However, TAVI was found to be inferior to SAVR in the rates of cardiac tamponade, permanent pacemaker (PPM) implantation, major vascular damage and paravalvular regurgitation.[49,52] The incidence of requiring a PPM was also higher in the TAVI cohort, although the mortality rate at 24 months did not increase in the population requiring a PPM in these studies.[29,32,52] There was also an increased risk of major vascular events, including femoral/radial artery dissection and thrombosis, in the TF-TAVI cohort in several studies.[29,30,52] These are likely the result of the access route taken during the procedure; however, TAVI still resulted in lower all-cause mortality 1 year post procedure[53] and is at least non-inferior at 2 years post procedure regardless of the pre-intervention surgical risk.[7,54] Complications associated with SAVR are usually more severe and lead to greater morbidity compared with those associated with TAVI, which could explain the significance of improvement of HRQoL displayed by TAVI at 1 month.

In terms of cost-effectiveness, TAVI was superior in patients at low-to-intermediate surgical risk compared with SAVR.[55–57] Cost per

Table 1. Baseline characteristics of the included studies[29–37]

Characteristics	Study								
	Thyregod *et al* (2015)[29]	**Leon *et al* (2016)[30]**	**Baron *et al* (2017)[31]**	**Reardon *et al* (2017)[32]**	**Baron *et al* (2019)[33]**	**Popma *et al* (2019)[34]**	**Leon *et al* (2021)[35]**	**Merhi *et al* (2022)[36]**	**UK TAVI *et al* (2022)[37]**
Year	**2015**	**2016**	**2017**	**2017**	**2019**	**2019**	**2021**	**2022**	**2022**
Type	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT	Multi-centre RCT
Outcome(s)	NYHA follow-up for 12 months	NYHA follow-up for 24 months	KCCQ and EQ-5D for 24 months	KCCQ and NYHA for 24 months	KCCQ and EQ-5D for 12 months	KCCQ for 24 months	KCCQ and NYHA for 24 months	KCCQ for 12 months	EQ-5D and NYHA for 12 months
Total (TAVI), n	145	1,011	950	864	494	734	496	76	458
Total (SAVR), n	135	1,020	883	796	449	734	454	62	455
Age years (TAVI), mean±SD	79.2±4.9	81.5±6.7	81.6±6.7	79.9±6.2	73.3±5.8	74.0±5.9	73.3±5.8	75.0±5.0	81
Age years (SAVR), mean±SD	79.0±4.7	81.7±6.7	81.8±6.8	79.7±6.1	73.6 ±6.1 (p=0.467)	73.8±6.0	73.6±6.1	73.3±6.5 (p=0.08)	81
Male (TAVI), %	53.8	54.2	55	57.6	67.4	63.8	67.5	68	53.9
Male (SAVR), %	52.6	54.8	56.6	55	71.3 (p=0.204)	66.5	71.1	79 (p=0.16)	53.2
BMI (TAVI), n	N/A	28.6±6.2	N/A	2.3 <21 kg/m^2	N/A	N/A	30.7±5.5	N/A	27.1
BMI (SAVR), n	N/A	28.3±6.2	N/A	2.6 <21 kg/m^2	N/A	N/A	30.3±5.1	N/A	27.7
STS risk (TAVI), mean±SD	2.9±1.6	5.8±2.1	5.8±2.1	4.4±1.5	1.9±0.7	1.9±0.7	1.9±0.7	1.8±0.6	2.6
STS risk (SAVR), mean±SD	3.1 ±1.7	5.8±1.9	5.6±1.7	4.5±1.6	1.9±0.6 (p=0.225)	1.9±0.7	1.9±0.6	1.6±0.6 (p=0.10)	2.7
NYHA class (TAVI), %	Baseline class 1: 4.9; class 2: 46.5; class 3: 46.5; class 4: 2.1	Class 3 or 4=77.3 %	Class 3 (correlates to KCCQ 53.3±21.9)	Baseline class 2: 39.8; class 3: 54.6; class 4: 5.6	N/A	Baseline class 1: 10.5; class 2: 64.9; class 3: 24.5; class 4: 0.1	Class 3 or 4=31.3 %	N/A	Class 3 or 4=40.3 %
NYHA class (SAVR), %	Baseline class 1: 2.2; class 2: 52.2; class 3: 42.5; class 4: 3.0	Class 3 or 4=76.1 %	Class 3 (correlates to KCCQ 53.1±21.1)	Baseline class 2: 41.8; class 3: 51.6; class 4: 6.5	N/A	Baseline class 1: 9.9; class 2: 62.1; class 3: 27.5; class 4: 0.4	Class 3 or 4=23.8	N/A	Class 3 or 4=45.2 %
Coronary artery disease (TAVI), %	N/A	69.2	N/A	62.6	27.6	N/A	27.7	N/A	30

Table 1. Baseline characteristics of the included studies[29–37] (Continued)

Characteristics	Study								
	Thyregod *et al* (2015)[29]	Leon *et al* (2016)[30]	Baron *et al* (2017)[31]	Reardon *et al* (2017)[32]	Baron *et al* (2019)[33]	Popma *et al* (2019)[34]	Leon *et al* (2021)[35]	Merhi *et al* (2022)[36]	UK TAVI *et al* (2022)[37]
Year	**2015**	**2016**	**2017**	**2017**	**2019**	**2019**	**2021**	**2022**	**2022**
Coronary artery disease (SAVR), %	N/A	66.5	N/A	64.2	27.6 (p=0.999)	N/A	28	N/A	33.3
Previous myocardial infarction (TAVI), %	5.5	18.3	17.4	14.5	5.7	6.7	N/A	5	N/A
Previous myocardial infarction (SAVR), %	4.4	17.5	16.4 (p=0.62)	13.9	5.8 (p=0.999)	5.3	N/A	5 (p>0.99)	N/A
Previous CABG (TAVI), %	N/A	23.6	23.1	16	N/A	2.5	3	N/A	N/A
Previous CABG (SAVR), %	N/A	25.6	22.4 (p=0.75)	17.2	N/A	2.3	1.8	N/A	N/A
Previous PCI (TAVI), %	7.6	27.1	25.7	21.3	N/A	13.9	N/A	9	N/A
Previous PCI (SAVR), %	8.9	27.6	24.8 (p=0.68)	21.2	N/A	12.7	N/A	10 (p=0.93)	N/A
Peripheral vascular disease (TAVI), %	4.1	27.9	22	30.8	6.9	7.6	6.9	5	N/A
Peripheral vascular disease (SAVR), %	6.7	32.9	25.7 (p=0.11)	29.9	7.4 (p=0.801)	8.5	7.3	2 (p=0.38)	N/A
Diabetes mellitus (TAVI), %	17.9	37.7	36.8	34.1	31.4	31.1	31.3	25	N/A
Diabetes mellitus (SAVR), %	20.7	34.2	33.9 (p=0.26)	34.8	30.1 (p=0.724)	30.5	30.2	27 (p=0.75)	N/A
COPD any (TAVI), %	11.7	31.8	2.8	None: 64.6; mild: 22.0; moderate: 10.3; severe: 3.0	5.1	15.1	5.1	Chronic lung disease: 16	N/A
COPD any (SAVR), %	11.9	30.0	2.2 (p=0.53)	None: 66.5; mild: 20.2; moderate: 9.7; severe: 3.6	6 (p=0.569)	17.2	6.2	3 (P=0.02)	N/A
Atrial fibrillation (TAVI), %	27.8	31.0	32	28.1	15.6	15.5	15.7	9	N/A
Atrial fibrillation (SAVR), %	25.6	35.2	36.3 (p=0.09)	26.5	18.8 (p=0.225)	14.9	18.8	7 (p=0.75)	N/A

Table 1. Baseline characteristics of the included studies[29–37] (Continued)

Characteristics	Study								
	Thyregod *et al* (2015)[29]	Leon *et al* (2016)[30]	Baron *et al* (2017)[31]	Reardon *et al* (2017)[32]	Baron *et al* (2019)[33]	Popma *et al* (2019)[34]	Leon *et al* (2021)[35]	Merhi *et al* (2022)[36]	UK TAVI *et al* (2022)[37]
Year	2015	2016	2017	2017	2019	2019	2021	2022	2022
Permanent pacemaker (TAVI), %	3.4	11.7	N/A	9.7	N/A	3.4	2.4	N/A	N/A
Permanent pacemaker (SAVR), %	4.4	12.0	N/A	9	N/A	3.8	2.9	N/A	N/A
Frailty (TAVI), %	N/A	5-m walk test time >7 s: 44.4; serum albumin <3.5g/dL: 15.2	45.5	Falls in past 6 months: 11.8, Five meter gait speed > 6 seconds: 51.8, six minute walk (meters): 254.1±115.8	N/A	N/A	0	N/A	CSHA Clinical Frailty Scale score ≥5: 12.8%
Frailty (SAVR), %	N/A	5-m walk test time >7 s: 46.4; serum albumin <3.5 g/dL: 14.7	46.4 (p=0.76)	Falls in past 6 months: 12.7; 5 m gait speed >6 s: 52.9; 6-min walk (m): 260.9±117.9	N/A	N/A	0	N/A	CSHA Clinical Frailty Scale score ≥5: 13.4%
Aortic-valve area (TAVI), cm^2	N/A	0.7± 0.2	0.7±0.2	N/A	0.8±0.2	0.8±0.2	N/A	N/A	0.7
Aortic-valve area (SAVR), cm^2	N/A	0.7± 0.2	0.7±0.2 (p=0.32)	N/A	0.8±0.2 (p=0.780)	0.8±0.2	N/A	N/A	0.7
Aortic-valve gradient (TAVI), mmHg	N/A	44.9± 13.4	44.8±13.8	N/A	49.4±12.7	47.2±12.3	N/A	N/A	73
Aortic-valve gradient (SAVR), mmHg	N/A	44.6± 12.5	44.8±12.4 (p=0.93)	N/A	48.4±11.8 (p=0.203)	46.7±12.2	N/A	N/A	74
Left ventricular ejection fraction (TAVI), %	N/A	56.2± 10.8	56.5±10.4	N/A	65.7±9.0	61.7±7.9	N/A	N/A	57
Left ventricular ejection fraction (SAVR), %	N/A	55.3± 11.9	55.3±11.9 (p=0.11)	N/A	66.2± 8.6 (p=0.431)	61.9±7.7	N/A	N/A	57

Table 1. Baseline characteristics of the included studies[29–37] (Continued)

Characteristics	Study								
	Thyregod *et al* (2015)[29]	Leon *et al* (2016)[30]	Baron *et al* (2017)[31]	Reardon *et al* (2017)[32]	Baron *et al* (2019)[33]	Popma *et al* (2019)[34]	Leon *et al* (2021)[35]	Merhi *et al* (2022)[36]	UK TAVI *et al* (2022)[37]
Year	**2015**	**2016**	**2017**	**2017**	**2019**	**2019**	**2021**	**2022**	**2022**
Mitral regurgitation (TAVI), %	N/A	16.8	16.6	N/A	N/A	N/A	N/A	N/A	10.7
Mitral regurgitation (SAVR), %	N/A	19.1	19.4 (p=0.19)	N/A	N/A	N/A	N/A	N/A	13.3
Serum creatinine >2 mg/dL (TAVI), %	1.4	5.0	5.1	1.6	0.2	0.4	N/A	N/A	N/A
Serum creatinine (SAVR), %	0.7	5.2	4.9 (p=0.87)	2.1	0.2 (p=0.999)	0.1	N/A	–	N/A
History of hypertension (TAVI), %	71	N/A	N/A	92.7	N/A	84.9	N/A	79	N/A
History of hypertension (SAVR), %	76.3	N/A	N/A	90.3	N/A	82.9	N/A	77 (p=0.83)	N/A
Stroke (TAVI), %	16.6	32.1	8.9	6.6	3.4	N/A	3.4	N/A	N/A
Stroke (SAVR), %	16.3	31.0	9.3 (p=0.79)	7.2	5.1 (p=0.257)	N/A	5.1	N/A	N/A

CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CSHA = Canadian Study of Health and Aging; EQ-5D = EuroQol 5D; KCCQ = Kansas City Cardiomyopathy Questionnaire; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RCT = randomised controlled trial; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

quality-adjusted life years (QALY) was lower in patients who underwent TF-TAVI, yielding a higher incremental cost-effectiveness ratio per QALY saved. This could result from the more significant improvement in HRQoL early on after the intervention, as shown by our analysis of the trials.[29–37] It could also be because of the shorter hospital stays, as discussed above, as well as improved cardiac clinical outcomes[29,30,32,46] and HRQoL measures[29–37] leading to reduced lifetime costs of TAVI versus SAVR. However, more research is needed into why the early HRQoL benefit from TAVI is lost. HRQoL outcomes to 5 years utilising multiple measures, such as SF-36, SF-12, MLHFQ and EQ-5D, is now required.

According to the 2021 European Society of Cardiology (ESC)/ European Association for Cardio-Thoracic Surgery (EACTS) Guidelines for the management of valvular heart disease, new information from randomised studies comparing TAVI with SAVR in patients at intermediate-to-low surgical risk has led to a need to clarify whether TAVI should be used in patients at lower risk.[5] At 12 months, TAVI showed non-inferiority in clinical outcomes, including re-intervention and rehospitalisation.[52] Additionally, studies found that there was no increase in the overall 5-year mortality and all-cause mortality in the TF-TAVI cohorts, thereby displaying non-inferiority of TAVI.[29,30] Our analysis showed that TAVI had better HRQoL for patients at intermediate and lower risk in the short term, but was similar to SAVR at 12 months; hence, TAVI could be considered as an alternative gold standard for aortic stenosis in the absence of coronary artery disease requiring surgical revascularisation, severe primary mitral or tricuspid valve disease, significant dilatation/aneurysm of the aortic root and/or ascending aorta, or other anatomical/procedural factors that would indicate the need for SAVR.[5] The availability of more robust evidence for longer HRQoL benefit and data on the cost-effectiveness of TAVI could make this possible.

Limitations

Limitations of our meta-analysis include the lack of homogenous HRQoL data, which resulted in the exclusion of some studies from some meta-analyses. This led to us only being able to use data that were used in consensus in most of the studies. Differing times of follow-up only allowed comparisons across two consistent time points (1 and 12 months). Additionally, HRQoL measures are subjectively reported and are not standardised, which can result in less accurate results. Moreover, the inconsistent reporting of data and lack of homogenous data at different time intervals did not allow the inclusion of other HRQoL measures, such as the subcategories of KCCQ, SF-12, SF-36 and MLHFQ. Furthermore, other functional outcomes, such as the 6-min walking test, were not reported by the trials. The recent 'low-risk' studies principally assessed the KCCQ overall summary and not KCCQ categorical breakdowns, making analysis of the specific reasons for KCCQ being superior at 1 month but not 12 months difficult. Moreover, some baseline characteristics that affect quality of life (such as frailty, heart failure and other multiple health conditions) were not reported by some studies. Our meta-analysis is a study rather than patient-level analysis and, therefore, might be subject to biases. Nonetheless, the selected studies featured low levels of bias across all the Cochrane domains (Fig 7). In addition, our study did not address those patients who were excluded from the selected randomised trials.

Conclusion

In conclusion, TAVI offers early benefit in HRQoL outcomes in patients at intermediate to low risk compared with SAVR. However, further robust trials are required to better analyse its benefit to patients in the long term. Implementation of TAVI as a gold standard therapy for patients at lower risk could have a better impact on patient recovery and, hence, QoL, because it is less invasive, potentially supporting the superiority of TAVI in terms of cost-effectiveness. ■

Supplementary material

Supplemental information

Additional supplementary material may be found in the online version of this article at www.rcpjournals.org/content/clinmedicine

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