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Mortality in low-risk patients with aortic stenosis undergoing transcatheter or surgical aortic valve replacement: a reconstructed individual patient data meta-analysis

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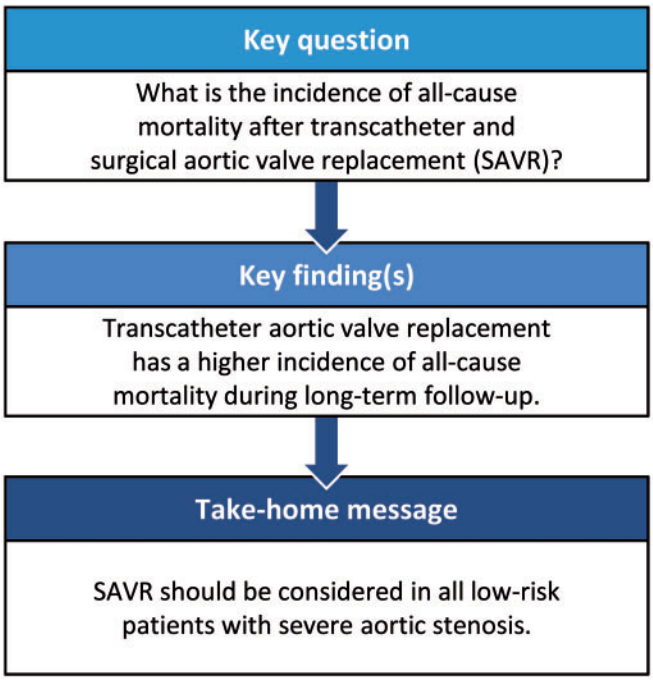

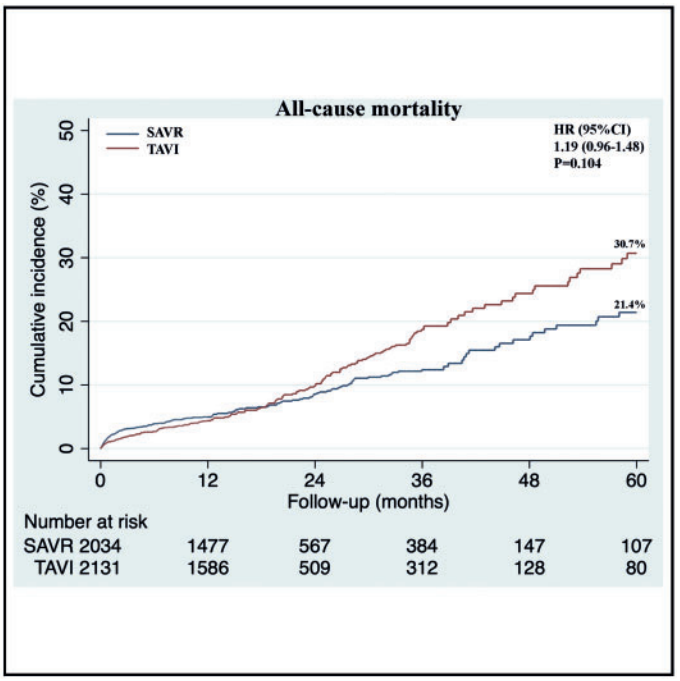

Abstract

OBJECTIVES: Although the standard of care for patients with severe aortic stenosis at low-surgical risk has included surgical aortic valve replacement (SAVR) since the mid-1960s, many clinical studies have investigated whether transcatheter aortic valve implantation (TAVI) can be a better approach in these patients. As no individual study has been performed to detect the difference in mortality between these 2 treatment strategies, we did a reconstructive individual patient data analysis to study the long-term difference in all-cause mortality.

METHODS: Randomized clinical trials and propensity score-matched studies that included low-risk adult patients with severe aortic stenosis undergoing either SAVR or TAVI and with reports on the mortality rates during the follow-up period were considered. The primary outcome was all-cause mortality of up to 5 years.

RESULTS: In the reconstructed individual patient data analysis, there was no statistically significant difference in all-cause mortality between TAVI and SAVR at 5 years of follow-up [30.7% vs 21.4%, hazard ratio (HR) 1.19, 95% confidence interval (CI) 0.96–1.48; $P = 0.104$]. However, landmark analyses in patients surviving up to 1 year of follow-up showed significantly higher all-cause mortality at 5 years of follow-up (27.5% vs 17.3%, HR 1.77, 95% CI 1.29–2.43; $P < 0.001$) in patients undergoing TAVI compared to patients undergoing SAVR, respectively.

CONCLUSIONS: This reconstructed individual patient data analysis in low-risk patients with severe aortic stenosis demonstrates that the 5-year all-cause mortality rates are higher after TAVI than after SAVR, driven by markedly higher mortality rates between 1 and 5 years of follow-up in the TAVI group. The present results call for caution in expanding the TAVI procedure as the treatment of choice for the majority of all low-risk patients until long-term data from contemporary randomized clinical trials are available.

Keywords: Surgical aortic valve replacement • Transcatheter aortic valve replacement

ABBREVIATIONS

AS	Aortic stenosis
CI	Confidence interval
HR	Hazard ratio
PSM	Propensity score matched
RCT	Randomized controlled trial
SAVR	Surgical aortic valve replacement
STS	Society of Thoracic Surgery
TAVI	Transcatheter aortic valve implantation

INTRODUCTION

Since the mid-1960s, surgical aortic valve replacement (SAVR) has been the gold standard of care for the treatment of patients with severe symptomatic aortic stenosis (AS) who are at low risk for surgical mortality and have exhibited year-by-year improvements in both short- and long-term outcomes [1]. In 2002, the first successful transcatheter aortic valve implantation (TAVI) was performed in an inoperable patient with calcified AS presenting with cardiogenic shock [2]. Rapidly, the beneficial results of TAVI over medical therapy in inoperable patients [3] led to the expansion of the TAVI approach to high-risk patients [4, 5]. Comparable results from randomized controlled trials (RCTs) and prospective registries of those at high risk led to the further expansion of TAVI to patients at intermediate risk for surgical mortality [6, 7]. Moreover, this interventional approach is now widely indicated in the European and American guidelines for the management of symptomatic AS as class I for high-risk and class IIa for intermediate-risk patients [8, 9].

Recent studies including 2 large multicentre RCTs with 2 years of follow-up have initiated a debate about TAVI as the first-line treatment procedure in the majority of patients with severe AS irrespective of surgical risk [10, 11]. Controversy exists concerning whether the available data are robust enough to justify further TAVI expansion to the low-risk population, which represents the majority of all AS cases (75–80%) [12]. To date, the evidence is inconclusive on hard clinical outcomes, including all-cause mortality, because all published studies lacked statistical power to detect differences in individual outcomes between TAVI and SAVR. Therefore, we performed a reconstructed individual patient data meta-analysis of RCTs and propensity score-matched (PSM) studies to compare the risk of all-cause mortality of up to 5 years after TAVI and SAVR in low-risk symptomatic patients with severe AS.

METHODS

The reporting of this study complies with the Preferred Reporting Items for Systematic reviews and Meta-Analyses and Meta-analysis of Observational Studies in Epidemiology guidelines (Supplementary Material, Table S1) [13, 14].

Search strategy and study inclusion

The MEDLINE, Embase and Cochrane databases were searched from their inception to 13 March 2020 for full-length English-language RCTs or PSM cohort studies that reported on low-risk patients with severe AS who were treated with either SAVR or transfemoral TAVI. The search strategy is provided in Supplementary Material, Table S2. Because the data- sharing statements indicate confidentiality, the authors were not contacted for studies if data were unclear.

Two investigators (M.C. and A.P.D.) independently screened the search result in duplicate for eligibility. In case of a disagreement, a consensus was reached through discussion. First, the title and abstract were reviewed, after which the remaining articles were reviewed in depth. Relevant articles identified by cross-referencing were added manually to ensure that no relevant studies were missed.

A study was included if it met the following criteria: (i) compared TAVI to SAVR; (ii) included adult patients with severe AS quantified by at least an aortic valve area of <1.0 cm^2 or an indexed aortic valve area <0.6 cm^2/m^2, a jet velocity of >4.0 m/s, or a mean gradient of >40 mmHg; (iii) included patients with low risk, defined as a mean Society of Thoracic Surgery (STS) score <4% or the logistic European System for Cardiac Operative Risk Evaluation <10%; and (iv) reported at least the event based on the valve replacement approach during follow-up.

Data extraction

After relevant articles were identified, 2 investigators (M.C. and A.P.D.) independently extracted clinically relevant data and data necessary for inclusion of the study in the present meta-analysis. The consensus was reached through discussion, in case of any disagreements. Study description data that were extracted included the location of the study, the design of the study, the number of included patients, the time span of patient inclusion, the transcatheter system used, the TAVI approach, whether the study used the Valve Academic Research Consortium-II definition and the primary objective of each study. Extracted baseline patient characteristic data included age, gender and left ventricular ejection fraction. Risk scores were used to assess the risk of surgical mortality. Further, we determined the number of patients with diabetes mellitus, coronary artery disease, previous cerebrovascular accidents, previous myocardial infarctions, peripheral vascular disease, atrial fibrillation, pre-existing pacemakers and the proportion of patients in New York Heart Association functional class III/IV. We extracted the total follow-up time, the mean or median follow-up time and the number of events that occurred during this follow-up period for our endpoint of interest. Furthermore, hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated from Kaplan–Meier survival curves. The risk of bias assessment was independently performed by 2 investigators (M.C. and M.M.M.). The consensus was reached through

discussion, in case of any disagreements. The Revised Cochrane Risk of Bias Tool for Randomized Controlled Trials version 2.0 was used to assess the bias in the randomized trials [15], and the ROBIN-1 Risk of Bias Tool for Non-Randomized Controlled Trials was used to assess the bias in the observational studies [16].

Statistical analyses

Descriptive statistics were summarized as mean ± standard deviation or crude numbers with percentages, where appropriate. The primary end point of this study was all-cause mortality at 5 years of follow-up. Since the 2 largest RCTs used a 'modified intention-to-treat' principle in their study design, which was virtually equal to the 'as-treated' principle, the analysis was performed on an 'as-treated' basis whenever possible.

All-cause mortality following TAVI versus SAVR was compared using aggregated reconstructed individual patient data. Kaplan–Meier survival data were extracted per study with DigitizeIt (http://digitizeit.de). The extracted data were then reconstructed and visually compared with the original published data. The estimated Kaplan–Meier curves did not demonstrate major graphical differences. If possible, reconstructed HRs were compared with the originally published estimates and their corresponding 95% CIs.

Data were then reconstructed from the published Kaplan–Meier curves as previously described [17, 18]. The reconstructed data were used to obtain pooled cumulative incidences of all-cause mortality and Cox regression HRs with the corresponding 95% CIs. Visual inspection of the Kaplan–Meier curves suggested a violation of the proportionality assumption. The proportional hazard assumption for the overall group was assessed using the scaled Schoenfeld residuals, which was violated ($P = 0.042$). Therefore, the landmark analyses were used to describe the occurrence of all-cause mortality over time, within 1 year and over 1–5 years. The hazard proportionality was further tested in the landmark subgroups within the first year ($P = 0.017$) and between 1 and 5 years (0.83). Further, a fully parametric model was used to obtain time-dependent HRs (Royston–Parmar model). In addition, a study-level meta-analysis was performed using a random-effects model. Data analyses were performed using Stata (version 16.1, StataCorp, College Station, TX, USA) and R software, version 3.5 (R Foundation, Vienna, Austria).

RESULTS

Description of included studies

We screened 2029 studies, of which 14 were judged potentially eligible during the screening of titles and abstracts (Fig. 1). The search strategy is available in Supplementary Material, Table S2. Six studies met our inclusion criteria [10, 11, 19–22], including 3 RCTs and 3 PSM cohort studies (Table 1). One study was evaluated as an intention-to-treat study [21], whereas the other 5 studies were analysed as as-treated studies [10, 11, 19, 20, 22]. An overview of quality assessment is presented in Supplementary Material, Tables S2 and S3. Most patients were men (60.5%) and were aged >70 years (Table 2). Transfemoral access was the most frequently used approach for TAVI. All RCTs reported perioperative procedural risk of mortality using the Society of Thoracic Surgeons (STS) Predicted Risk of Mortality score at 30 days. In addition, 2 studies reported the logistic European System for Cardiac Operative Risk Evaluation. The mean STS scores ranged from 1.9% to 3.0%.

Mortality

Our secondary pooled Kaplan–Meier analyses for all-cause mortality showed a significant difference in the rate of all-cause mortality at 30 days (1.1% vs 1.8%, HR 0.59, 95% CI 0.35–0.99; $P = 0.048$) in favour of TAVI. However, no significant differences in the rate of all-cause mortality between TAVI and SAVR were noted at 1 year of follow-up (4.4% vs 5.0%, HR 0.85, 95% CI 0.64–1.14; $P = 0.28$), at 3 years of follow-up (18.7% vs 12.4%, HR 1.17 95% CI 0.91–1.43; $P = 0.26$) and 5 years of follow-up (30.7% vs 21.4%, HR 1.19, 95% CI 0.96–1.48; $P = 0.10$), respectively (Fig. 2). At landmark analyses with patients surviving up to 1 year, the 5-year mortality was significantly higher after TAVI than after SAVR (HR 1.77, 95% CI 1.29–2.43; $P < 0.001$) (Fig. 2). The early hazard was in favour of TAVI, whereas over time this favour diminished and mortality was higher with TAVI. The crossover started at approximately the first half-year, significantly favouring SAVR after 24 months (Fig. 3). In addition, a study-level meta-analysis of all-cause mortality was performed (Supplementary Material, Fig. S1). Early mortality showed a trend in favour of TAVI (HR 0.73, 95% CI 0.37–1.44), whereas there was a trend in favour of SAVR at 5 years of follow-up (HR 1.53, 95% CI 0.89–2.62). Further, a comparison between extracted HR and reported HR for the PARTNER 3 trial did show no significant difference (Supplementary Material, Fig. S2).

DISCUSSION

These reconstructed individual patient data analyses from 3 RCTs and 3 PSM cohort studies were used to estimate the long-term all-cause mortality following TAVI and SAVR in low-risk patients. The main findings of this study are as follows: (i) all-cause mortality at 30 days tended to be lower in patients treated with TAVI compared to those treated with SAVR; (ii) comparable outcomes were seen at 1 year; and (iii) at the 5-year follow-up, the incidence of mortality was markedly higher after TAVI than after SAVR.

The initial comparable outcomes between TAVI and SAVR in patients at intermediate-to-high surgical risks led to further expansion of the TAVI approach across the risk spectrum of the patient population. The U.S. Food and Drug Administration approved certain TAVI devices to be used in low-risk patients in November 2019. It is expected that this approval will increase the use of TAVI worldwide, irrespective of surgical risk, given the fact that 10% of European TAVI centres were already performing routine TAVI in low-risk patients even before the Food and Drug Administration announcement [23].

Our results confirm the benefit of TAVI over SAVR in the early post-procedural phase. Whereas the in-hospital outcomes after SAVR are linked to the need for more invasive treatment with cardiopulmonary bypass and general anaesthesia, SAVR has a naturally occurring higher likelihood of early interventional hazard compared with TAVI itself [24, 25]. On the other hand, the less invasive character of TAVI and the continuous improvements such as treatment under analgosedation only and with shorter hospital stays, certainly lower the complication rates and subsequent early mortality [26]. With increasing operator [27], hospital

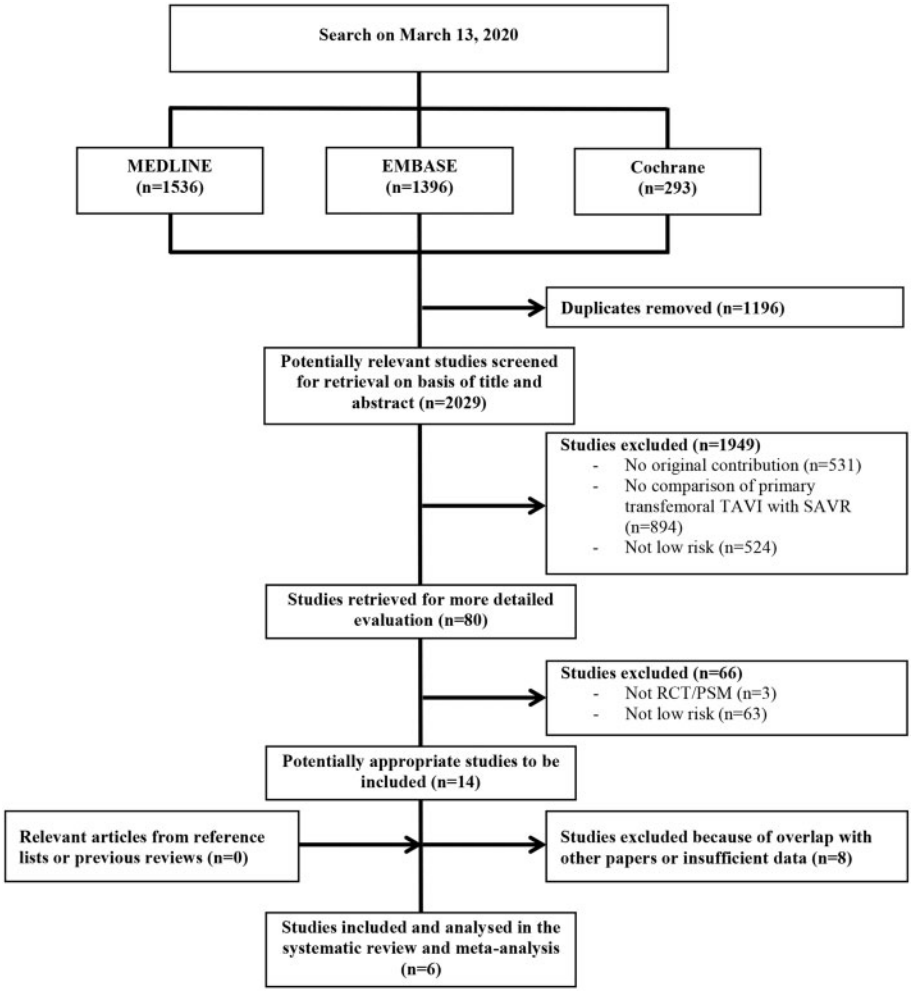

Figure 1: Flow chart of systematic literature search and study inclusion. A total of 2029 potentially relevant articles were screened, 6 of which were finally eligible for this study. PSM: propensity score matched; RCTs: randomized controlled trials; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

[28] and international experience, low hospital mortality rates have been achieved [29, 30]. Moreover, the newer generation devices used in contemporary practice show in-hospital mortality at historically low levels [31, 32].

The early favourable nature of TAVI is reflected by low post-procedural mortality rates, although this outcome might not fully reflect the difference of treatment effects in the long-term. Again, SAVR is linked to a naturally occurring higher likelihood of early interventional hazard compared to TAVI due to its nature. To avoid this early bias, due to the violation of the proportional hazards assumption, patients surviving up to 1 year were selected in a landmark approach. However, using an additional landmark approach might inherently (i) lead to the omission of events that could be important and occur early on and (ii) loss of power [33]. However, choosing an early point for landmarking minimizes these risks.

Recently published results of a meta-analysis that summarized the mortality rates of available RCTs irrespective of surgical risk for up to 2 years show a significant reduction of all-cause mortality with TAVI over SAVR [34]. However, additional analyses accounting for the non-proportionality across the studies nullify this assumption. A divergence in all-cause mortality favouring SAVR during the long-term follow-up is noted. There is an earlier onset of this divergence as one moves down the risk ladder. The 5-year results in high-risk patients show similar survival rates with nearly equal or even a crossover of survival rates after 60 months favouring SAVR in the long-term [35], whereas this crossover is expected with earlier onset in the intermediate-risk patients [7].

A number of concerns arise when one tries to extrapolate the favourable TAVI results to the younger population. First, the global average life expectancy increased by 5.5 years between 2000 and 2016 and continues to increase markedly, leading to a substantially higher risk for reintervention over the life span. Second, low risk does not automatically mean 'younger', because the mean age of our patients was 76 years of age. Because younger age is associated with lower mortality [36], one expects a multiplier effect for TAVI in the young low-risk patients because of its non-invasive character. Third, a high need for pacemaker implantation is likely to impair the quality of life of active patients. Finally, given the unknown long-term effects on mortality and the durability of these valves, it is necessary to exercise caution when offering TAVI to the younger, low-risk patients with a life expectancy exceeding 10 years, especially after noting an earlier onset of crossover and divergence of mortality in favour of SAVR while descending the risk ladder. We, therefore, look forward to the long-term data from the younger population with bicuspid morphology (NCT02701283: Medtronic Evolut

Table 1: Characteristics of included studies

Study, year	Number of patients	Period	Age (years), mean ± SD	STS risk score, mean ± SD	Design	Follow-up (months)	Transcatheter system used	Type of approach for TAVI	VARC-II definition used	Primary objectives
Schaefer *et al.* [20], 2019	218	2009–2014	75.2 ± 8.0	2.0 ± 0.8[a]	PSM	60	N/A	Transfemoral 100%	Yes	All-cause mortality; 30 days
Virtanen *et al.* [22], 2019	608	2008–2017	78 ± 5.4	2.1 ± 0.7	PSM	36	Third generation	Transfemoral 100%	No	All-cause mortality; 30 days and 3 years
PARTNER 3, 2019	950	2016–2017	73.4 ± 5.9	1.9 ± 0.7	RCT	12	SAPIEN 3	Transfemoral 100%	Yes	Composite of all-cause mortality, stroke or rehospitalization; 1 year
EVOLUT, 2019	1403	2016–2018	73.9 ± 6.0	1.9 ± 0.7	RCT	24	CoreValve, Evolut R, Evolut PRO	Transfemoral 99.0%; direct aortic 0.4%; subclavian 0.6%	Yes	Composite of all-cause mortality or stroke; 2 years
NOTION, 2019	280	2009–2013	79.1 ± 4.8	3.0 ± 1.7	RCT	60	CoreValve	Transfemoral 96.5%; subclavian 3.5%	Yes	Composite of all-cause mortality, stroke or MI; 1 year
Rosato *et al.* [19], 2016	710	2010–2012	80.1 ± 5.8	<4%[a]	PSM	36	SAPIEN XT, CoreValve	Transfemoral 91.1%; transapical 8.9%	No	All-cause mortality; 3 years

[a]EuroSCORE II.

EuroSCORE: European System for Cardiac Operative Risk Evaluation; N/A: not assessed; PSM: propensity score matched; RCT: randomized controlled trial; SD: standard deviation; TAVI: transcatheter aortic valve implant; VARC: valve academic research consortium.

Table 2: Baseline patient characteristics[a]

Study, year		Number of patients	Mean age	Male (%), *n* (%)	STS	Diabetes (%)	Left ventricular ejection fraction	Coronary disease, *n* (%)	Previous CVA, *n* (%)	Previous MI, *n* (%)	Peripheral vascular disease, *n* (%)	Atrial fibrillation, *n* (%)	Pre-existing pacemaker (*n*, %)	NYHA functional class III or IV, *n* (%)
Schaefer *et al.* [20], 2019	SAVR	109	74.4 ± 7.5	46 (50)	2.0 ± 0.8	22 (24)	N/A	29 (32)	9 (10)	5 (5)	N/A	N/A	N/A	57 (62)
	TAVI	109	75.9 ± 8.4	46 (50)	2.0 ± 0.8	16 (17)	N/A	30 (33)	12 (13)	4 (4)	N/A	N/A	N/A	68 (74)
Virtanen *et al.* [22], 2019	SAVR	304	78.1 ± 4.8	151 (49.7)	2.1 ± 0.5	68 (22.4)	N/A	57 (18.8)	24 (7.9)	N/A	N/A	105 (34.5)	15 (4.9)	N/A
	TAVI	304	77.9 ± 6.0	143 (47.0)	2.1 ± 0.9	68 (22.4)	N/A	57 (18.8)	26 (8.6)	N/A	N/A	107 (35.2)	21 (6.9)	N/A
PARTNER 3, 2019	SAVR	454	73.6 ± 6.1	323 (71.1)	1.9 ± 0.6	137/453 (30.2)	66.2 ± 8.6	127 (28.0)	23/453 (5.1)	26/452 (5.8)	33/453 (7.3)	85/453 (18.8)	13 (2.9)	108 (23.8)
	TAVI	496	73.3 ± 5.8	335 (67.5)	1.9 ± 0.7	155 (31.2)	65.7 ± 9.0	137/494 (27.7)	17 (3.4)	28/495 (5.7)	34/494 (6.9)	78 (15.7)	12 (2.4)	155 (31.2)
EVOLUT, 2019	SAVR	678	73.6 ± 5.9	449 (66.2)	1.9 ± 0.7	207 (30.5)	61.9 ± 7.7	N/A	80 (11.8)	33 (4.9)	56 (8.3)	N/A	26 (3.8)	193 (28.4)
	TAVI	725	74.1 ± 5.8	464 (64.0)	1.9 ± 0.7	228 (31.4)	61.7 ± 7.9	N/A	74 (10.2)	48 (6.6)	54/718 (7.5)	N/A	23 (3.2)	182 (25.1)
NOTION, 2019	SAVR	135	79.0 ± 4.7	71 (52.6)	3.1 ± 1.7	28 (20.7)	N/A	N/A	22 (16.3)	6 (4.4)	9 (6.7)	N/A	6 (4.4)	61/134 (45.5)
	TAVI	145	79.2 ± 4.9	78 (53.8)	2.9 ± 1.6	26 (17.9)	N/A	N/A	24 (16.6)	8 (5.5)	6 (4.1)	N/A	5 (3.4)	70/144 (48.6)
Rosato *et al.* [19], 2016	SAVR	355	80.0 ± 5.1	209 (58.9)	N/A	57 (16.1)	304 (85.6)[b]	45 (12.7)	N/A	29 (8.2)	31 (8.7)	N/A	N/A	182 (51.3)
	TAVI	355	80.1 ± 6.4	206 (58.0)	N/A	53 (14.9)	304 (85.6)[b]	56 (15.8)	N/A	26 (7.3)	36 (10.1)	N/A	N/A	180 (50.7)
Pooled	SAVR	2035	75.8 ± 5.7	1249 (61.4)	2.1 ± 0.8	519 (25.5)	63.6 ± 8.1	258 (21.1)	158 (9.4)	99 (5.7)	129 (8.0)	190 (25.1)	60 (3.8)	601 (34.7)
	TAVI	2134	75.9 ± 6.0	1272 (59.6)	2.0 ± 0.8	546 (25.6)	63.3 ± 8.4	280 (22.2)	153 (8.6)	114 (6.2)	130 (7.6)	185 (23.1)	61 (3.7)	655 (35.8)

[a]Plus–minus values are means ± SD.

[b]≥50%, *n* (%).

CVA: cerebrovascular accident; MI: myocardial infarction; N/A: not applicable; NYHA: New York Heart Association; SAVR: surgical aortic valve replacement; SD: standard deviation; STS: Society of Thoracic Surgeons; TAVI: transcatheter aortic valve implantation.

Transcatheter Aortic Valve Replacement in Low-Risk Patients) and the 3 RCTs (PARTNER 3, Evolut Low Risk and the NOTION 2 trials) in younger low-risk patients. These trials were recently completed and will provide follow-up data for up to 10 years [10, 11].

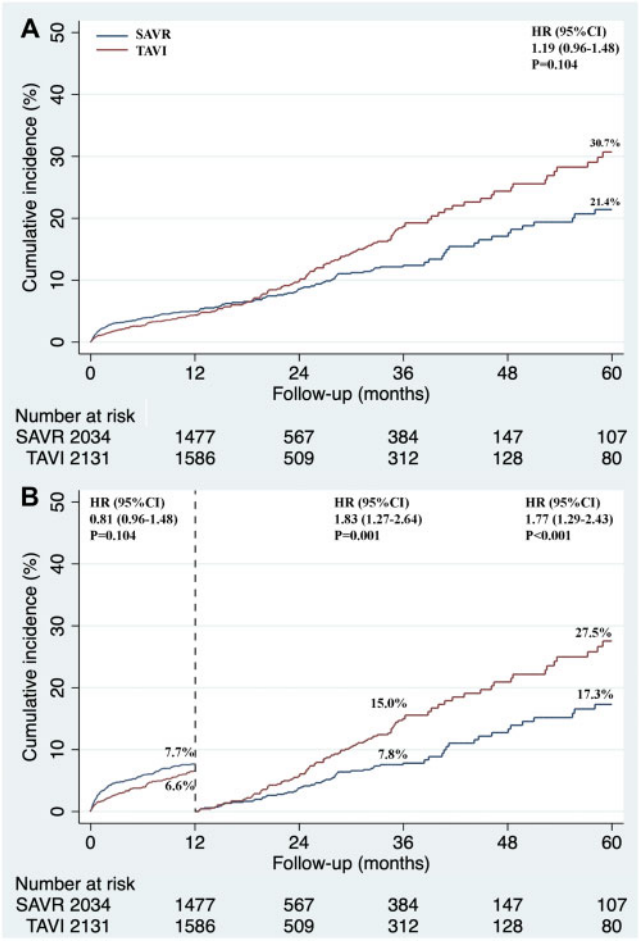

Figure 2: Reconstructed pooled individual patient cumulative incidence of all-cause mortality in patients with low-surgical risk undergoing either TAVI or SAVR. (**A**) The overall curve; HR given for 5 years. (**B**) A landmark analysis; HRs are given for 1, 3 and 5 years with the 3-year mark designating the 10% of patients still at risk for an event. CI: confidence interval; HR: hazard ratio; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

Future outlook

Given the data from recently published RCTs, the surgical risk is no longer the single determinant for the eligibility of patients. Other important variables, including anatomy and comorbidities, should lead to patient allocation. Multidisciplinary heart team decision-making is becoming more important for the treatment of aortic valve disease because of the increasing overlap of indications for SAVR and TAVI. Formal heart team meetings are recommended to assess and allocate patients accordingly. Nevertheless, we need to be cautious and await long-term data from RCTs before changing the current standards of care.

Limitations

It is important to emphasize that this study has several limitations. First, this meta-analysis includes both RCTs and PSM cohort studies. Whereas both types of studies account for baseline characteristics, a difference in magnitude of effect size can be noted [37]. However, differences in effect estimates are not significantly different, and consistency is evident [37, 38]. Second, we were very strict in our definition of surgical risk: We adopted only the STS surgical risk score. The STS score accurately predicts SAVR outcomes [39, 40] yet overestimates 30-day mortality in patients having TAVI. The lack of TAVI risk scores is an issue that needs to be considered in future studies. [41]. Third, it was impossible to perform a network meta-analysis to indirectly compare the transfemoral and transapical approaches because of the low number of studies comparing the SAVR to the transapical TAVI procedure, which will become the procedure of choice only for highly selected patients. Finally, the most important limitation of the present study is the limited follow-up period of the 2 largest RCTs.

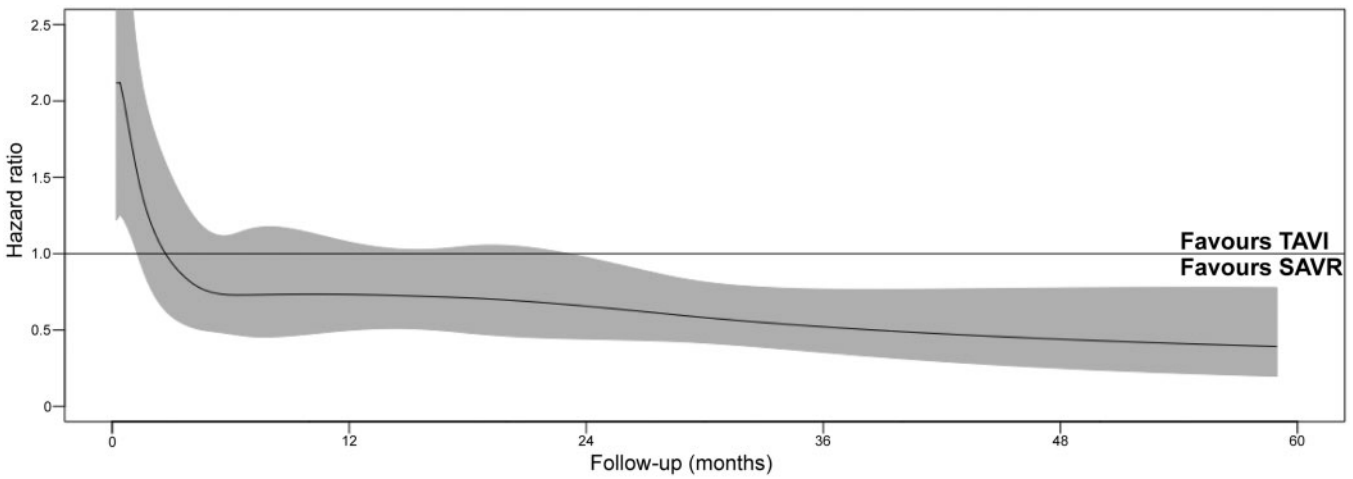

Figure 3: Transcatheter aortic valve implantation. The hazard ratio is given as all-cause mortality after the index procedure. A hazard ratio <1.0 favours surgical aortic valve replacement, whereas a hazard ratio >1.0 favours a transaortic valve implant. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

CONCLUSIONS

In this reconstructed individual patient data analysis of studies comparing low-surgical risk patients with AS who had either a surgical or an interventional procedure, the data showed that the 5-year mortality did not significantly differ in patients receiving either TAVI or SAVR. In particular, the benefit of SAVR over TAVI was shown in patients surviving up to 1 year after the index procedure. Longer follow-up from well-conducted RCTs and large national registries are warranted to better define mortality differences between these 2 complementary procedures.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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Conflict of interest: none declared.

Author contributions

Mevlüt Çelik: Conceptualization; Data curation; Formal analysis; Methodology; Validation; Visualization; Writing—original draft; Writing—review & editing. **Milan M. Milojevic:** (Conceptualization; Formal analysis; Methodology; Validation; Writing—original draft; Writing—review & editing. **Andras P. Durko:** Conceptualization; Data curation; Formal analysis; Writing—review & editing. **Frans B.S. Oei:** Conceptualization; Supervision; Writing—original draft; Writing—review & editing. **Ad J.J.C. Bogers:** Conceptualization; Supervision; Validation; Writing—original draft; Writing—review & editing. **Edris A.F. Mahtab:** Conceptualization; Methodology; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing.

Reviewer information

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REFERENCES

[1] Brennan JM, Edwards FH, Zhao Y, O'Brien SM, Douglas PS, Peterson ED. Long-term survival after aortic valve replacement among high-risk elderly patients in the United States: insights from the Society of Thoracic Surgeons Adult Cardiac Surgery Database, 1991 to 2007. Circulation 2012;126:1621–9.

[2] Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F *et al.* Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002; 106:3006–8.

[3] Kapadia SR, Tuzcu EM, Makkar RR, Svensson LG, Agarwal S, Kodali S *et al.* Long-term outcomes of inoperable patients with aortic stenosis randomly assigned to transcatheter aortic valve replacement or standard therapy. Circulation 2014;130:1483–92.

[4] Gleason TG, Reardon MJ, Popma JJ, Deeb GM, Yakubov SJ, Lee JS *et al.* 5-year outcomes of self-expanding transcatheter versus surgical aortic valve replacement in high-risk patients. J Am Coll Cardiol 2018;72: 2687–96.

[5] Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM *et al.* 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. Lancet 2015;385:2477–84.

[6] Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK *et al.* Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016;374:1609–20.

[7] Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M *et al.* Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med 2017;376:1321–31.

[8] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd. Fleisher LA *et al.* 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;70:252–89.

[9] Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ *et al.* 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739–91.

[10] Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M *et al.* Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695–705.

[11] Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D *et al.* Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med 2019;380:1706–15.

[12] Thourani VH, Suri RM, Gunter RL, Sheng S, O'Brien SM, Ailawadi G *et al.* Contemporary real-world outcomes of surgical aortic valve replacement in 141,905 low-risk, intermediate-risk, and high-risk patients. Ann Thorac Surg 2015;99:55–61.

[13] Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;349: g7647.

[14] Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of observational studies in epidemiology (MOOSE) group. JAMA 2000;283:2008–12.

[15] Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.

[16] Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M *et al.* ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.

[17] Guyot P, Ades AE, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. BMC Med Res Methodol 2012;12:9.

[18] Wei Y, Royston P. Reconstructing time-to-event data from published Kaplan-Meier curves. Stata J 2017;17:786–802.

[19] Rosato S, Santini F, Barbanti M, Biancari F, D'Errigo P, Onorati F *et al.* Transcatheter aortic valve implantation compared with surgical aortic valve replacement in low-risk patients. Circ Cardiovasc Interv 2016;9: e003326.

[20] Schaefer A, Schofer N, Goßling A, Seiffert M, Schirmer J, Deuschl F *et al.* Transcatheter aortic valve implantation versus surgical aortic valve replacement in low-risk patients: a propensity score-matched analysis. Eur J Cardiothorac Surg 2019;56:1131–9.

[21] Thyregod HGH, Ihlemann N, Jorgensen TH, Nissen H, Kjeldsen BJ, Petursson P *et al.* Five-year clinical and echocardiographic outcomes from the Nordic Aortic Valve Intervention (NOTION) randomized clinical trial in lower surgical risk patients. Circulation 2019; 139:2714–23.

[22] Virtanen MPO, Eskola M, Jalava MP, Husso A, Laakso T, Niemela M *et al.* Comparison of outcomes after transcatheter aortic valve replacement vs surgical aortic valve replacement among patients with aortic stenosis at low operative risk. JAMA Netw Open 2019;2:e195742.

[23] Petronio AS, Capranzano P, Barbato E, Piazza N, Baumbach A, Haude M *et al.* Current status of transcatheter valve therapy in Europe: results from an EAPCI survey. EuroIntervention 2016;12:890–5.

[24] Cockburn J, Dooley M, de Belder A, Trivedi U, Hildick-Smith D. A comparison between surgical risk scores for predicting outcome in patients undergoing transcatheter aortic valve implantation. J Cardiovasc Surg (Torino) 2017;58:467–72.

[25] Butchart EG, Gohlke-Barwolf C, Antunes MJ, Tornos P, De Caterina R, Cormier B *et al.* Recommendations for the management of patients after heart valve surgery. Eur Heart J 2005;26:2463–71.

[26] Hyman MC, Vemulapalli S, Szeto WY, Stebbins A, Patel PA, Matsouaka RA *et al.* Conscious sedation versus general anesthesia for transcatheter aortic valve replacement: insights from the National Cardiovascular Data Registry Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. Circulation 2017;136: 2132–40.
[27] Vemulapalli S, Carroll JD, Mack MJ, Li Z, Dai D, Kosinski AS *et al.* Procedural volume and outcomes for transcatheter aortic-valve replacement. N Engl J Med 2019;380:2541–50.
[28] Carroll JD, Vemulapalli S, Dai D, Matsouaka R, Blackstone E, Edwards F *et al.* Procedural experience for transcatheter aortic valve replacement and relation to outcomes: the STS/ACC TVT registry. J Am Coll Cardiol 2017;70:29–41.
[29] Auffret V, Lefevre T, Van Belle E, Eltchaninoff H, Iung B, Koning R *et al.* Temporal trends in transcatheter aortic valve replacement in France: FRANCE 2 to FRANCE TAVI. J Am Coll Cardiol 2017;70:42–55.
[30] Gaede L, Blumenstein J, Kim WK, Liebetrau C, Dorr O, Nef H *et al.* Trends in aortic valve replacement in Germany in 2015: transcatheter versus isolated surgical aortic valve repair. Clin Res Cardiol 2017;106: 411–19.
[31] Waksman R, Rogers T, Torguson R, Gordon P, Ehsan A, Wilson SR *et al.* Transcatheter aortic valve replacement in low-risk patients with symptomatic severe aortic stenosis. J Am Coll Cardiol 2018;72:2095–105.
[32] Ando T, Takagi H, Telila T, Afonso L. Comparison of outcomes in new-generation versus early-generation heart valve in transcatheter aortic valve implantation: a systematic review and meta-analysis. Cardiovasc Revasc Med 2018;19:186–91.
[33] Dafni U. Landmark analysis at the 25-year landmark point. Circ Cardiovasc Qual Outcomes 2011;4:363–71.
[34] Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F *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.
[35] Kapadia SR, Leon MB, Makkar RR, Tuzcu EM, Svensson LG, Kodali S *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. Lancet 2015;385:2485–91.
[36] Navarese EP, Andreotti F, Kołodziejczak M, Wanha W, Lauten A, Veulemans V *et al.* Age-related 2-year mortality after transcatheter aortic valve replacement: the YOUNG TAVR Registry. Mayo Clin Proc 2019;94: 1457–66.
[37] Dahabreh IJ, Sheldrick RC, Paulus JK, Chung M, Varvarigou V, Jafri H *et al.* Do observational studies using propensity score methods agree with randomized trials? A systematic comparison of studies on acute coronary syndromes. Eur Heart J 2012;33:1893–901.
[38] Anglemyer A, Horvath HT, Bero L. Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials. Cochrane Database Syst Rev 2014;MR000034.
[39] Ferguson TB Jr, Dziuban SW Jr, Edwards FH, Eiken MC, Shroyer AL, Pairolero PC *et al.* The STS National Database: current changes and challenges for the new millennium. Committee to Establish a National Database in Cardiothoracic Surgery, The Society of Thoracic Surgeons. Ann Thorac Surg 2000;69:680–91.
[40] Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9–13.
[41] Debonnaire P, Fusini L, Wolterbeek R, Kamperidis V, van Rosendael P, van der Kley F *et al.* Value of the "TAVI2-SCORe" versus surgical risk scores for prediction of one year mortality in 511 patients who underwent transcatheter aortic valve implantation. Am J Cardiol 2015;115: 234–42.