Meta-Analysis Comparing Transcatheter Aortic Valve Implantation to Surgical Aortic Valve Replacement in Low Surgical Risk Patients

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Transcatheter aortic valve implantation (TAVI) is recommended for inoperable and high risk surgical patients with severe aortic stenosis. It is noninferior to surgical aortic valve replacement (SAVR) in intermediate risk candidates. TAVI is currently being assessed for low surgical risk individuals. We performed a meta-analysis of randomized controlled trials (RCTs) and matched observational studies between TAVI and SAVR in low surgical risk patients. The primary outcomes were short-term and mid-term mortality and neurologic events. Secondary outcomes were other periprocedure complications. A total of 8 studies (3 RCTs and 5 matched observational studies) totaling 6,686 patients were included. No difference was seen in short-term mortality and neurologic events (risk ratio [RR] 0.68, 95% confidence interval [CI] 0.45 to 1.03, p 0.07 and RR 0.76, 95% CI 0.52 to 1.13, p 0.18) as well as mid-term mortality and neurologic events (RR 0.89, 95% CI 0.54 to 1.47, p 0.65 and RR 1.04, 95% CI 0.55 to 1.97, p 0.9) between the 2 groups. Reduced risk of new onset atrial fibrillation (RR 0.14, 95% CI 0.08 to 0.25, p <0.00001), acute kidney injury (RR 0.43, 95 CI 0.23 to 0.82, p 0.01), and bleeding (RR 0.43, 95% CI 0.27 to 0.69, p 0.0005) whereas increased risk of ≥ moderate aortic regurgitation (RR 6.53, 95% CI 3.48 to 12.24, p <0.00001), pacemaker or defibrillator implantation (RR 3.11, 95% CI 1.96 to 4.94, p <0.00001) and vascular complications (RR 5.29, 95% CI 1.58 to 17.70, p 0.007) was noted in TAVI arm. In conclusion, TAVI is comparable to SAVR in terms of short-term and mid-term mortality and neurologic events in low surgical risk patients. The risk of periprocedure events is variable. **(Am J Cardiol 2019;124:1257−1264)**

Surgical aortic valve replacement (SAVR) has been the mainstay of treatment for severe aortic stenosis for decades. In recent years, transcatheter aortic valve implantation (TAVI) has shown superiority over SAVR or medical treatment in extreme or high surgical risk patients and comparability to SAVR in intermediate surgical risk patients.[1−7] Several societies now recommend TAVI as an alternative to SAVR in such patients.[8,9] As less invasive option, there has been a growing interest in extending TAVI to low surgical risk patients.[10,11] There have been 4 randomized controlled trials (RCTs) on TAVI in these patients, 2 were published in 2019 (PARTNER 3 Trial, Evolut Low Risk Trial), 1 in 2015 (NOTION 1 Trial) whereas 1 was prematurely terminated due to safety issues (STACCATO Trial, 2012).[10,12−14] A few observational studies also exist but meta-analyses are extremely limited with most done on intermediate surgical risk patients which had also included low-risk patients.[15,16] There are only 2 meta-analyses exclusively on low surgical risk patients in which 1 only looked at 30-day outcomes and included 4 studies out of which 2 were from the same registry (Fraccaro et al, Rosato et al) and thus a possible potential for overlap of population existed.[17−19] The other meta-analysis had 6 studies but included the STACCATO trial which was prematurely terminated due to safety issues.[20] We have conducted an updated meta-analysis to compare TAVI and SAVR exclusively in low surgical risk patients.

Methods

We searched PubMed, Cochrane Library, and Google Scholar databases using the search term: (transcatheter OR trans-catheter OR TAVR OR TAVI) AND (low-risk OR low risk) AND stenosis. Articles published through April, 2019 with data on outcomes of interest were included. Inclusion criteria were (1) Studies comparing TAVI and SAVR in low surgical risk patients determined by either a mean Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score <4% and/or a mean Logistic EuroSCORE 1 (LES 1) <10% (or Logistic EuroSCORE 2 [LES 2] <5% if LES 1 was not reported) for both the TAVI and SAVR arms. STS-PROM score took precedence over LES in case of discordance between the 2. (2) RCTs or observational studies with matched TAVI and SAVR arms. Duplicate studies and incomplete or prematurely terminated studies were excluded. The Newcastle-Ottawa scale was used to assess the quality of the included observational studies.[21] Validation of study eligibility and extraction of data were independently performed by 2 reviewers (SS and

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See page 1263 for disclosure information.

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SY). The primary outcomes were short-term mortality (in-hospital or 30 day), short-term stroke and/ or transient ischemic attack (TIA) (in-hospital or 30 day), mid-term mortality (1 to 3 years, whichever was the longest reported follow-up) and mid-term stroke and/ or TIA (1 to 3 year, whichever was the longest reported follow-up). The secondary outcomes were other in-hospital or 30-day periprocedure events; these included new-onset atrial fibrillation, ≥ moderate (Grade ≥2) aortic regurgitation, the need for permanent pacemaker (PM) or defibrillator implantation, myocardial infarction (MI), acute kidney injury (AKI), bleeding, and vascular complications which we have explained in regards to each individual study in the supplementary material.

Statistical analysis was performed using RevMan5.3 software. Events and total sample size for TAVI and SAVR arms were entered as a dichotomous data set into the software. Heterogeneity in studies was assessed using the chi-squared test for heterogeneity and the I^2 statistics. If heterogeneity was significant (I^2 statistic >50%), the random effect model was chosen otherwise, fixed effect model was used. A Mantel-Haenszel statistical method was used to calculate a weighted risk ratio (RR) with 95% confidence interval (CI) for each outcome. A p value of <0.05 was assigned as clinically significant. Funnel plots were used to look for publication bias.

The study selection process is depicted in Figure 1. The STACCATO trial was the only study excluded on grounds of premature termination.[14] Previous meta-analyses on low-to-intermediate surgical risk patients have been criticized for including STACCATO trial.[22] The STACCATO trial protocol was not consistent with current clinical practice and was restricted only to the far less commonly performed transapical route for TAVI resulting in unusually high rate of adverse events.[14] We have also excluded the study by Fraccaro et al as a duplicate publication of the study by Rosato et al as both were from the same registry with the former only restricted to population older than 80 years of age.[17,18]

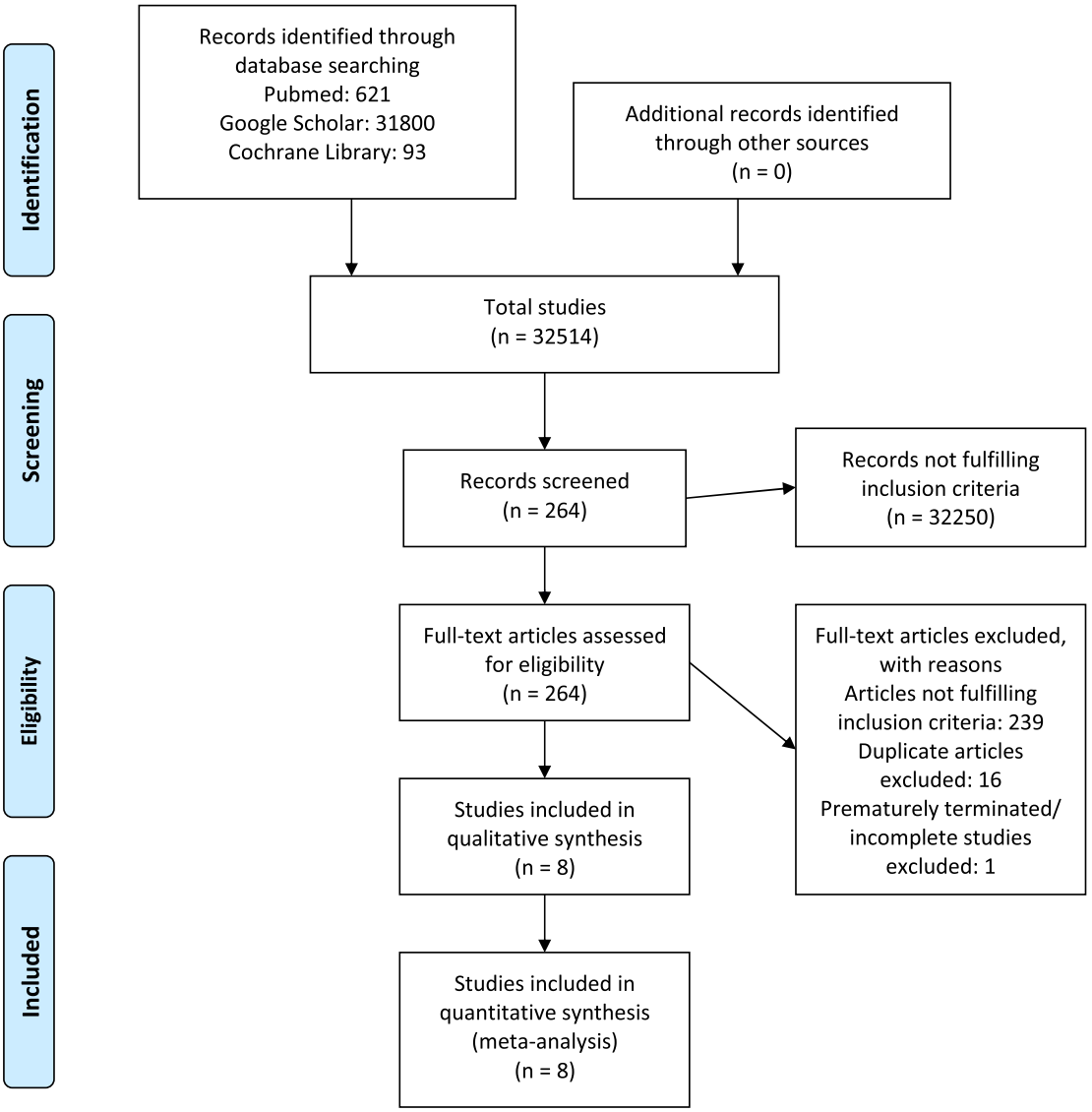


Figure 1. Study selection process.

Results

Our meta-analysis included a total of 8 studies which enrolled a total of 6,686 patients. Of these studies, 3 were RCTs and 5 were matched observational studies (4 studies used propensity score matching whereas 1 study used inverse probability weighting to balance potential confounders between the TAVI and SAVR arms).[10,12,13,18,23–26] We only included patients with STS-PROM <4% from the study by Piazza et al as it also included intermediate risk patients. All observational studies were ranked good quality on Newcastle-Ottawa scale assessment. The study details and baseline demographics are shown in Table 1. The major baseline co-morbidities and clinical characteristics of population in each study are summarized in Table 2 (See supplementary material for description of co-morbidities from each study). A trend toward decreased short-term mortality was noted in TAVI arm, however, it was not statistically significant (7 studies, RR 0.68, 95% CI 0.45 to 1.03, p 0.07, I^2 0%). In terms of short-term stroke/TIA, no difference was seen (6 studies, RR 0.76, 95% CI 0.52 to 1.13, p 0.18, I^2 22%). There was no difference between TAVI and SAVR in terms of mid-term mortality (5 studies, RR 0.89, 95% CI 0.54 to 1.47, p 0.65, I^2 67%) and mid-term stroke/TIA (4 studies, RR 1.04, 95% CI 0.55 to 1.97, p 0.9, I^2 74%). Forest plots for these findings are shown in Figures 2 and 3. Funnel plots in regards to primary outcomes overall do not indicate publication bias and are available in supplementary material. Furthermore, no difference in 1-year mortality and 1-year stroke/TIA was also noted (See supplementary material). Analysis of periprocedure events showed significantly reduced risk of new onset atrial fibrillation, AKI, and bleeding whereas an increased risk of device (PM or ICD) implantation, ≥ moderate aortic regurgitation regurgitation and vascular complications in TAVI group. No difference in MI

Table 1
Study details and baseline demographics

Study (Year)	Design	Sample Size (N)	TAVI (N)	SAVR (N)	Age TAVI (Years)	Age SAVR (Years)	Male TAVI	Male SAVR	STS TAVI	STS SAVR	LES-1 TAVI	LES-1 SAVR	Femoral access	Follow-up (Years)
Mack (2019)[13]	RCT	950	496	454	73.3 ± 5.8	73.6 ± 6.1	67.5%	71.1%	1.9 ± 0.7	1.9 ± 0.6	1.5 ± 1.2[†]	1.5 ± 0.9[†]	100%	1
Popma (2019)[12]	RCT	1403	725	678	74.1 ± 5.8	73.6 ± 5.9	64%	66.2%	1.9 ± 0.7	1.9 ± 0.7	NA	NA	99%	2
Thyregod (2015)[10]	RCT	280	145	135	79.2 ± 4.9	79± 4.7	53.8%	52.6%	2.9 ± 1.6	3.1± 1.7	8.4 ± 4	8.9 ± 5.5	96.5%	1
Frerker (2017)[23]	PSM	1610	805	805	77.5 ± 4.4	77.5 ± 4.4	39.6%	39.6%	NA	NA	6.8 ± 1.7	4.2 ± 1.4	100%	Inhospital
Rosato (2016)[18]	PSM	710	355	355	80.1 ± 6.4	80 ± 5.1	58%	58.9%	NA	NA	6.3 ± 2.7	6.3 ± 3	NA	3
Schymik (2015)[25]	PSM	432	216	216	78.3± 5.2	78.2± 4.6	46.3%	51.4%	NA	NA	8.7 ± 2.7	8.8± 2.8	NA	3
Piazza* (2013)[24]	PSM	382	191	191	NA	NA	NA	NA	STS<4	STS<4	NA	NA	NA	1
Waksman (2018)[26]	IPW	919	200	719	71.7 ± 14.9	70.9 ± 9.2	59.4%	61%	1.7 ± 1	1.7 ± 0.7	NA	NA	100%	1 m

IPW = inverse probability weighting; LES 1 = Logisitic EuroSCORE 1; m = months; N = number of patients; NA = not available; PSM = propensity score matching; RCT = Randomized controlled trial; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; TAVI: transcatheter aortic valve implantation.

* A subgroup analysis from a larger study.

† Logistic Euroscore II was calculated in the Mack et al.

Table 2
Baseline comorbidities and clinical characteristics of study population

Study		CKD or Cr>2 mg/dl	CVA or Neurologic disease	DM	NYHA III-IV	COPD	PVD
Mack[13]	TAVI	0.2%	3.4%	31.2%	31.2%	5.1%	6.9%
	SAVR	0.2%	5.1%	30.2%	23.8%	6.2%	7.3%
Popma[12]	TAVI	0.4%	10.2%	31.4%	25.1%	15%	7.5%
	SAVR	0.1%	11.8%	30.5%	28.4%	18%	8.3%
Thyregod[10]	TAVI	1.4%	16.6%	17.9%	48.6%	11.7%	4.1%
	SAVR	0.7%	16.3%	20.7%	45.5%	11.9%	6.7%
Frerker[23]	TAVI	10.6%	4.1%	23.6%	76.4%	1.7%	0.6%
	SAVR	10.6%	4.1%	23.6%	76.4%	1.7%	0.6%
Rosato[18]	TAVI	NA	4.2%	14.9%	50.7%	NA	8.7%
	SAVR	NA	4.2%	6.1%	51.3%	NA	10.1%
Schymik[25]	TAVI	NA	2.8%	NA	NA	NA	5.1%
	SAVR	NA	3.7%	NA	NA	NA	6.9%
Piazza*,[24]	TAVI	NA	NA	NA	NA	NA	NA
	SAVR	NA	NA	NA	NA	NA	NA
Waksman[26]	TAVI	4.3%	5%	24%	26%	12.4%	16.6%
	SAVR	7.7%	7.9%	26.1%	20.6%	15.4%	5.5%

COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; Cr = creatinine; CVA = cerebrovascular accident; DM = diabetes mellitus; NA = not available; NYHA = New York Heart Association; PVD = peripheral vascular disease; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve implantation.

* A subgroup analysis from a larger study.

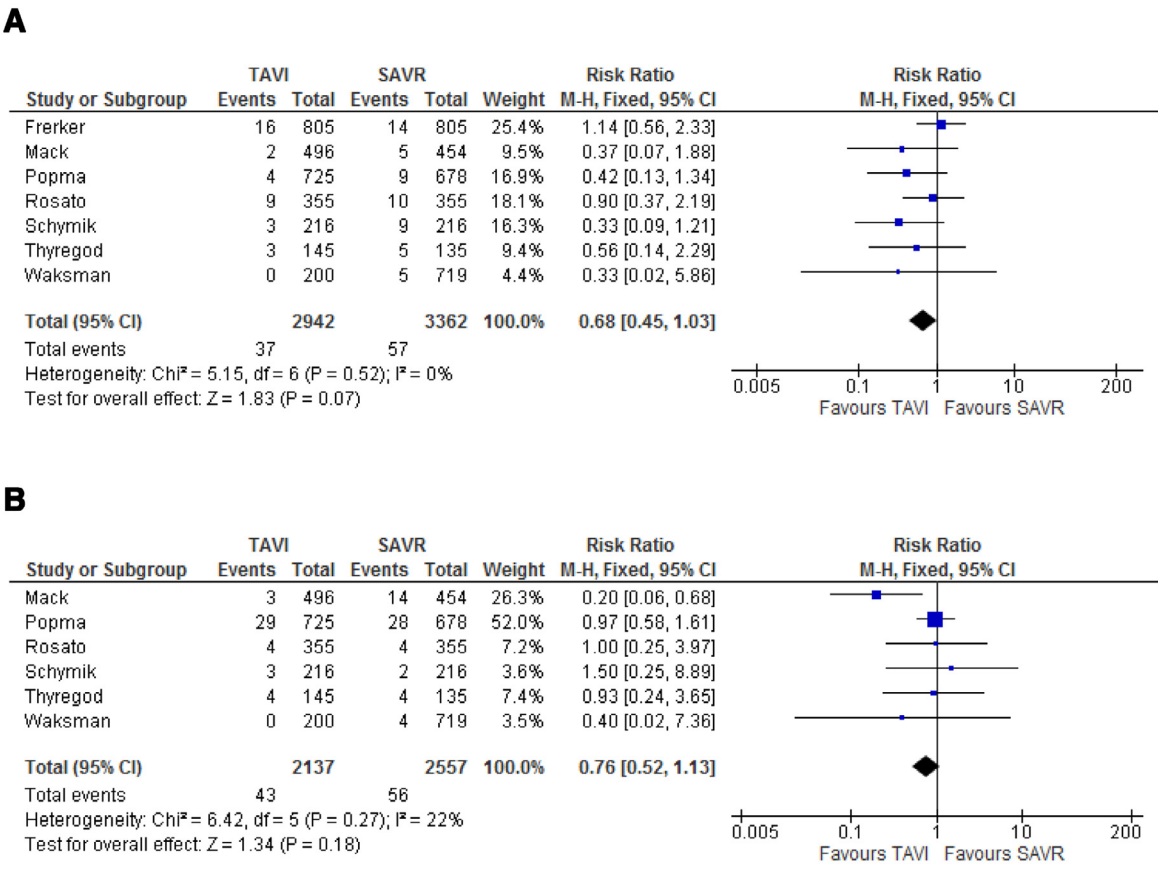


Figure 2. Forest plots of risk ratio for short-term outcomes between TAVI and SAVR; (*A*) showing in-hospital or 30 day mortality, (*B*) showing in-hospital or 30 day stroke and/or transient ischemic attack (TIA).

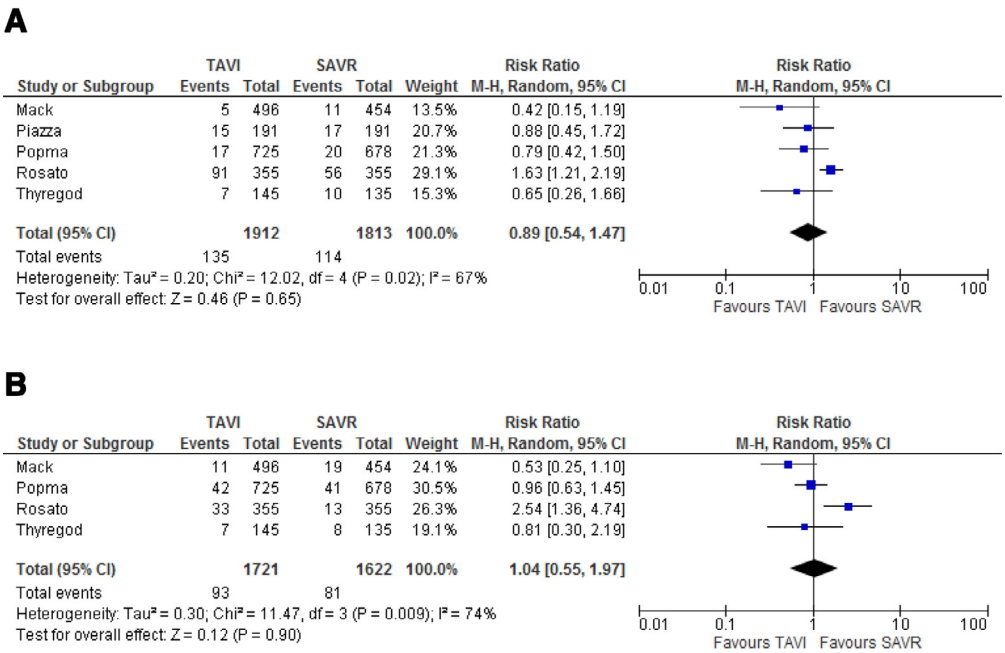


Figure 3. Forest plots of risk ratio for midterm outcomes between TAVI and SAVR; (*A*) showing 1 to 3 year mortality, (*B*) showing 1 to 3 year stroke and/or transient ischemic attack (TIA).

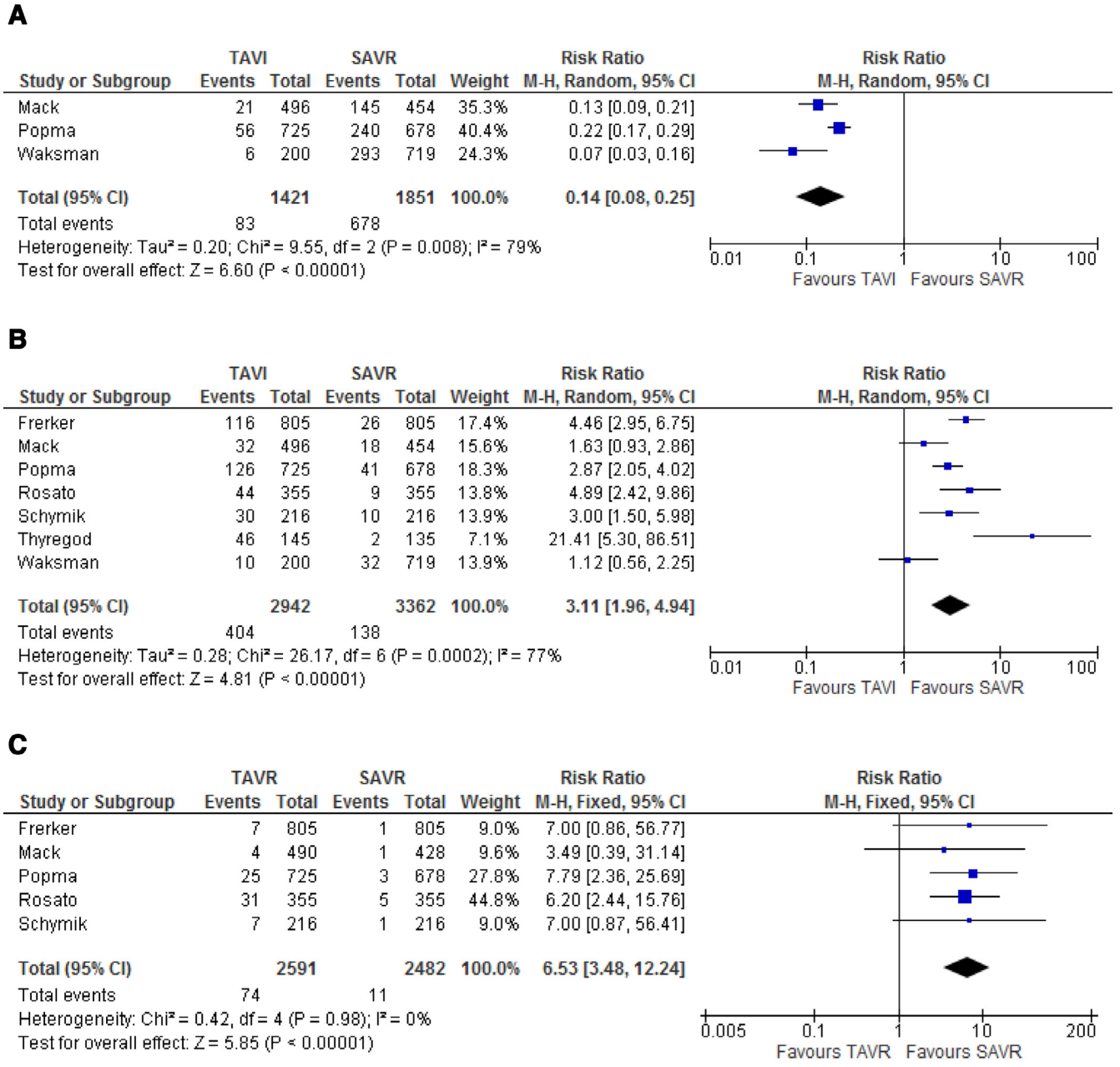


Figure 4. Forest plots of risk ratio for atrial fibrillation (*A*), pacemaker or defibrillator implantation (*B*) and ≥ moderate aortic regurgitation (*C*) between TAVI and SAVR.

risk was seen between the 2 groups. Forest plots for these findings are shown in Figures 4–6.

Discussion

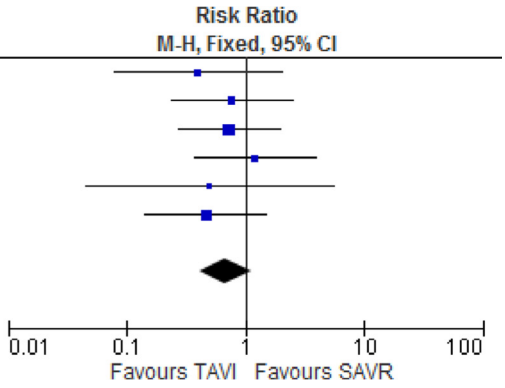
Our meta-analysis is the most updated and the first to include data from the recently published PARTNER-3 Trial and Evolut Low Risk Trial. We found no statistically significant difference between TAVI and SAVR in mortality and stroke/ TIA whether short-term or mid-term.

The meta-analysis by Witberg et al enrolled 3,484 patients and included patients from STACCATO trial, which however were excluded in the sensitivity analysis.[20] Findings of short-term mortality, cerebrovascular accident, MI, major bleeding, AKI, PM implantation and vascular complications agreed with our findings however, increased mid-term mortality in TAVI arm (RR 1.45, 95% CI 1.11 to 1.89, p 0.006) was seen as opposed to no difference (RR 0.89, 95% CI 0.54 to 1.47, p 0.65) in our study. Our study contained more RCTs (3 as opposed to only 1) and had bigger sample size (3,725 as opposed to 1,804 patients) for evaluation of mid-term mortality. Our results show a higher ≥ moderate aortic regurgitation and a lower new onset atrial fibrillation risk with TAVI, 2 outcomes that Witberg et al did not analyze. The inverse probability weighting study of 919 patients by Waksman et al found no difference between short-term mortality and stroke between TAVI and SAVR.[26] The Partner 3 Trial comparing transfemoral,

A

Study or Subgroup	TAVI Events	TAVI Total	SAVR Events	SAVR Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Frerker	2	805	5	805	13.9%	0.40 [0.08, 2.06]
Mack	5	496	6	454	17.5%	0.76 [0.23, 2.48]
Popma	7	725	9	678	25.9%	0.73 [0.27, 1.94]
Rosato	6	355	5	355	13.9%	1.20 [0.37, 3.90]
Schymik	1	216	2	216	5.6%	0.50 [0.05, 5.47]
Thyregod	4	145	8	135	23.1%	0.47 [0.14, 1.51]
Total (95% CI)		**2742**		**2643**	**100.0%**	**0.68 [0.41, 1.13]**
Total events	25		35			

Heterogeneity: Chi² = 1.81, df = 5 (P = 0.87); I² = 0%
Test for overall effect: Z = 1.48 (P = 0.14)



B

Study or Subgroup	TAVI Events	TAVI Total	SAVR Events	SAVR Total	Weight	Risk Ratio M-H, Random, 95% CI
Mack	7	496	39	454	20.0%	0.16 [0.07, 0.36]
Popma	7	725	19	678	19.0%	0.34 [0.15, 0.81]
Rosato	87	355	146	355	27.8%	0.60 [0.48, 0.74]
Schymik	44	216	39	216	26.0%	1.13 [0.77, 1.66]
Thyregod	1	145	9	135	7.3%	0.10 [0.01, 0.81]
Total (95% CI)		**1937**		**1838**	**100.0%**	**0.43 [0.23, 0.82]**
Total events	146		252			

Heterogeneity: Tau² = 0.38; Chi² = 25.43, df = 4 (P < 0.0001); I² = 84%
Test for overall effect: Z = 2.56 (P = 0.01)

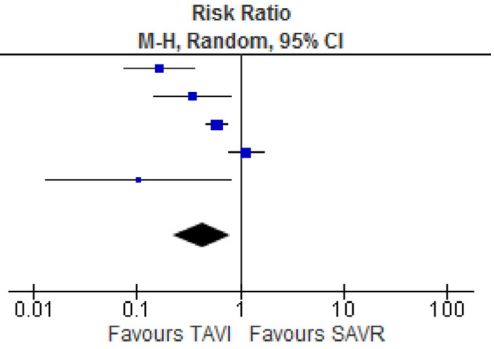
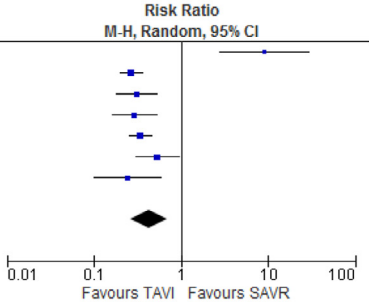


Figure 5. Forest plots of risk ratio for myocardial infarction (*A*) and acute kidney injury (*B*) between TAVI and SAVR.

A

Study or Subgroup	TAVI Events	TAVI Total	SAVR Events	SAVR Total	Weight	Risk Ratio M-H, Random, 95% CI
Frerker	27	805	3	805	8.7%	9.00 [2.74, 29.55]
Mack	45	496	153	454	17.5%	0.27 [0.20, 0.37]
Popma	17	725	51	678	15.2%	0.31 [0.18, 0.53]
Rosato	14	355	48	355	14.8%	0.29 [0.16, 0.52]
Schymik	39	216	114	216	17.5%	0.34 [0.25, 0.47]
Thyregod	16	145	28	135	14.9%	0.53 [0.30, 0.94]
Waksman	5	200	74	719	11.4%	0.24 [0.10, 0.59]
Total (95% CI)		**2942**		**3362**	**100.0%**	**0.43 [0.27, 0.69]**
Total events	163		471			

Heterogeneity: Tau² = 0.31; Chi² = 35.57, df = 6 (P < 0.00001); I² = 83%
Test for overall effect: Z = 3.47 (P = 0.0005)



B

Study or Subgroup	TAVI Events	TAVI Total	SAVR Events	SAVR Total	Weight	Risk Ratio M-H, Random, 95% CI
Frerker	28	805	0	805	10.9%	57.00 [3.49, 932.03]
Mack	34	496	22	454	24.6%	1.41 [0.84, 2.38]
Popma	28	725	22	678	24.5%	1.19 [0.69, 2.06]
Rosato	25	355	0	355	10.8%	51.00 [3.12, 834.49]
Schymik	26	216	0	216	10.9%	53.00 [3.25, 864.19]
Thyregod	8	145	2	135	18.3%	3.72 [0.81, 17.23]
Total (95% CI)		**2742**		**2643**	**100.0%**	**5.29 [1.58, 17.70]**
Total events	149		46			

Heterogeneity: Tau² = 1.47; Chi² = 31.25, df = 5 (P < 0.00001); I² = 84%
Test for overall effect: Z = 2.70 (P = 0.007)

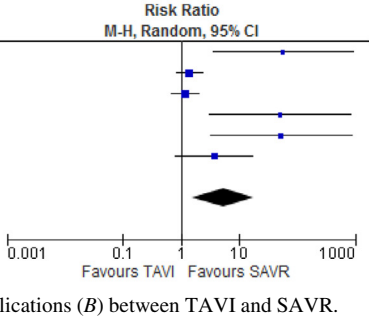


Figure 6. Forest plots of risk ratio for bleeding (*A*) and vascular complications (*B*) between TAVI and SAVR.

balloon expandable TAVI and SAVR in low risk patients showed significantly lower composite of death, stroke, and rehospitalization at 1 year in TAVI, however analyzed separately, there was no statistically significant difference at 1 year in the death or stroke between TAVI and SAVR.[13] This could possibly mean that the difference seen in the composite data was mostly driven by the reduced rehospitalization rate in TAVI arm, an outcome that we did not assess in our analysis. As opposed to our findings, no difference was seen in periprocedure vascular complications, (≥ moderate) aortic regurgitation and PM implantation which other than restriction to transfemoral route and exclusion of patients with left ventricular outflow tract calcium, adverse aortic root and poor transfemoral access can also be explained by the evolution of TAVI technique and improved valve design over the years.[13] New onset atrial fibrillation and bleeding were lower in TAVI arm similar to our analysis.[13] The Evolut Low Risk Trial, a randomized noninferiority trial comparing self-expanding TAVI with SAVR in low risk patients showed noninferiority between TAVI and SAVR in terms of composite end point of death and disabling stroke at 24 months.[12] There was no difference between short-term and mid-term mortality or stroke between the 2 groups. The risk of new onset atrial fibrillation, device implantation, aortic regurgitation, MI, and bleeding were consistent with our analysis, however, the risk of vascular complications was not different between TAVI and SAVR in the Evolut Low Risk Trial.[12] The positive results of TAVI in studies on low surgical risk patients have led to the comparability of TAVI to SAVR in severe aortic stenosis across the whole spectrum of surgical risk, indicating that the choice between TAVI and SAVR should be dictated by life expectancy and valve durability rather than surgical risk.[27]

Our study has several limitations. We do not have complete data on the type of valve used and the access pursued for TAVI for every study as the rate of complications may differ depending on the type of valve and the access chosen. Although, the observational studies included in our meta-analysis are matched and thus have a lower risk of bias, they cannot be considered equivalent to RCTs leaving a room for confounders to affect outcomes. Moreover, although we have excluded STACCATO trial, some of the data taken may have still been from studies performed at the time when TAVI was in its early stages of evolution. With more experience and better delivery techniques, we believe that some of the complications from TAVI can be reduced. Lastly, TAVI in low surgical risk population has been gaining consideration recently and we do not have data on long-term outcomes of TAVI in this group of patients.

In conclusion, TAVI is comparable to SAVR in regards to short-term and mid-term mortality and neurologic events. The risk of new onset atrial fibrillation, AKI, and bleeding complications is lower whereas the risk of device implantation, ≥ moderate aortic regurgitation and vascular complications is higher in TAVI than SAVR.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.07.029.

1. Makkar RR, Fontana GP, Jilaihawi H, Kapadia S, Pichard AD, Douglas PS, Thourani VH, Babaliaros VC, Webb JG, Herrmann HC, Bavaria JE, Kodali S, Brown DL, Bowers B, Dewey TM, Svensson LG, Tuzcu M, Moses JW, Williams MR, Siegel RJ, Akin JJ, Anderson WN, Pocock S, Smith CR, Leon MB. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. *N Engl J Med* 2012;366:1696–1704.
2. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–1607.
3. Kapadia SR, Leon MB, Makkar RR, Tuzcu EM, Svensson LG, Kodali S, Webb JG, Mack MJ, Douglas PS, Thourani VH, Babaliaros VC, Herrmann HC, Szeto WY, Pichard AD, Williams MR, Fontana GP, Miller DC, Anderson WN, Akin JJ, Davidson MJ, Smith CR. 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 (London, England)* 2015;385:2485–2491.
4. Siontis GC, Praz F, Pilgrim T, Mavridis D, Verma S, Salanti G, Sondergaard L, Juni P, Windecker S. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials. *Eur Heart J* 2016;37:3503–3512.
5. Deeb GM, Reardon MJ, Chetcuti S, Patel HJ, Grossman PM, Yakubov SJ, Kleiman NS, Coselli JS, Gleason TG, Lee JS, Hermiller JB Jr., Heiser J, Merhi W, Zorn GL 3rd, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Maini B, Mumtaz M, Conte J, Resar J, Aharonian V, Pfeffer T, Oh JK, Qiao H, Adams DH, Popma JJ. 3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol* 2016;67:2565–2574.
6. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609–1620.
7. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med* 2017;376:1321–1331.
8. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 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. *Circulation* 2017;135:e1159–e1195.
9. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Munoz D, Rosenhek R, Sjogren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739–2791.
10. Thyregod HG, Steinbruchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, Chang Y, Franzen OW, Engstrom T, Clemmensen P, Hansen PB, Andersen LW, Olsen PS, Sondergaard L. Transcatheter Versus surgical aortic valve replacement in patients with severe aortic

valve stenosis: 1-year results from the all-comers NOTION randomized clinical trial. *J Am Coll Cardiol* 2015;65:2184–2194.
11. Huynh K. TAVR versus surgery in low-risk patients. *Nat Rev Cardiol* 2019;16:319.
12. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, Askew J, Sorajja P, Rovin J, Chetcuti SJ, Adams DH, Teirstein PS, Zorn GL 3rd, Forrest JK, Tchetche D, Resar J, Walton A, Piazza N, Ramlawi B, Robinson N, Petrossian G, Gleason TG, Oh JK, Boulware MJ, Qiao H, Mugglin AS, Reardon MJ. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. *N Engl J Med* 2019;380:1706–1715.
13. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Genereux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;380:1695–1705.
14. Nielsen HH, Klaaborg KE, Nissen H, Terp K, Mortensen PE, Kjeldsen BJ, Jakobsen CJ, Andersen HR, Egeblad H, Krusell LR, Thuesen L, Hjortdal VE. A prospective, randomised trial of transapical transcatheter aortic valve implantation vs. surgical aortic valve replacement in operable elderly patients with aortic stenosis: the STACCATO trial. *EuroIntervent* 2012;8:383–389.
15. Khan SU, Lone AN, Saleem MA, Kaluski E. Transcatheter vs surgical aortic-valve replacement in low- to intermediate-surgical-risk candidates: a meta-analysis and systematic review. *Clin Cardiol* 2017;40:974–981.
16. Tam DY, Vo TX, Wijeysundera HC, Ko DT, Rocha RV, Friedrich J, Fremes SE. Transcatheter vs surgical aortic valve replacement for aortic stenosis in low-intermediate risk patients: a meta-analysis. *Can J Cardiol* 2017;33:1171–1179.
17. Fraccaro C, Tarantini G, Rosato S, Tellaroli P, D'Errigo P, Tamburino C, Onorati F, Ranucci M, Barbanti M, Grossi C, Santoro G, Santini F, Covello RD, Fusco D, Seccareccia F. Early and midterm outcome of propensity-matched intermediate-risk patients aged >/=80 years with aortic stenosis undergoing surgical or transcatheter aortic valve replacement (from the Italian Multicenter OBSERVANT Study). *Am J Cardiol* 2016;117:1494–1501.
18. Rosato S, Santini F, Barbanti M, Biancari F, D'Errigo P, Onorati F, Tamburino C, Ranucci M, Covello RD, Santoro G, Grossi C, Ventura M, Fusco D, Seccareccia F. Transcatheter aortic valve implantation compared with surgical aortic valve replacement in low-risk patients. *Circ Cardiovasc Interv* 2016;9:e003326.
19. Arora S, Strassle PD, Ramm CJ, Rhodes JA, Vaidya SR, Caranasos TG, Vavalle JP. Transcatheter versus surgical aortic valve replacement in patients with lower surgical risk scores: a systematic review and meta-analysis of early outcomes. *Heart Lung Circ* 2017;26:840–845.
20. Witberg G, Lador A, Yahav D, Kornowski R. Transcatheter versus surgical aortic valve replacement in patients at low surgical risk: a meta-analysis of randomized trials and propensity score matched observational studies. *Catheter Cardiovasc Intervs* 2018;92:408–416.
21. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, Petticrew M, Altman DG. Evaluating non-randomised intervention studies. *Health Technol Assess* 2003;7:iii–iix. 1-173.
22. Siemieniuk RA, Agoritsas T, Manja V, Devji T, Chang Y, Bala MM, Thabane L, Guyatt GH. Transcatheter versus surgical aortic valve replacement in patients with severe aortic stenosis at low and intermediate risk: systematic review and meta-analysis. *BMJ* 2016;354:i5130.
23. Frerker C, Bestehorn K, Schluter M, Bestehorn M, Hamm CW, Mollmann H, Katus HA, Kuck KH. In-hospital mortality in propensity-score matched low-risk patients undergoing routine isolated surgical or transfemoral transcatheter aortic valve replacement in 2014 in Germany. *Clin Res Cardiol* 2017;106:610–617.
24. Piazza N, Kalesan B, van Mieghem N, Head S, Wenaweser P, Carrel TP, Bleiziffer S, de Jaegere PP, Gahl B, Anderson RH, Kappetein AP, Lange R, Serruys PW, Windecker S, Juni P. A 3-center comparison of 1-year mortality outcomes between transcatheter aortic valve implantation and surgical aortic valve replacement on the basis of propensity score matching among intermediate-risk surgical patients. *JACC Cardiovasc Interv* 2013;6:443–451.
25. Schymik G, Heimeshoff M, Bramlage P, Herbinger T, Wurth A, Pilz L, Schymik JS, Wondraschek R, Suselbeck T, Gerhardus J, Luik A, Gonska BD, Tzamalis P, Posival H, Schmitt C, Schrofel H. A comparison of transcatheter aortic valve implantation and surgical aortic valve replacement in 1,141 patients with severe symptomatic aortic stenosis and less than high risk. *Catheter Cardiovasc Interv* 2015;86:738–744.
26. Waksman R, Rogers T, Torguson R, Gordon P, Ehsan A, Wilson SR, Goncalves J, Levitt R, Hahn C, Parikh P, Bilfinger T, Butzel D, Buchanan S, Hanna N, Garrett R, Asch F, Weissman G, Ben-Dor I, Shults C, Bastian R, Craig PE, Garcia-Garcia HM, Kolm P, Zou Q, Satler LF, Corso PJ. Transcatheter aortic valve replacement in low-risk patients with symptomatic severe aortic stenosis. *J Am Coll Cardiol* 2018;72:2095–2105.
27. Otto CM. Informed shared decisions for patients with aortic stenosis. *N Engl J Med* 2019;380:1769–1770.