Cardiovascular Revascularization Medicine 20 (2019) 838–842

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Clinical

Transcatheter versus surgical aortic valve replacement in low-risk surgical patients: A meta-analysis of randomized clinical trials

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ARTICLE INFO

Article history:
Received 23 October 2018
Received in revised form 9 December 2018
Accepted 27 December 2018

Keywords:
Aortic stenosis
TAVR
SAVR
Low risk

ABSTRACT

Background: Transcatheter aortic valve replacement (TAVR) is a valid option for patients with high or intermediate surgical risk. However, clinical outcomes of TAVR in low-risk patients are lacking. Our aim was to evaluate the efficacy and safety of TAVR versus surgical aortic valve replacement (SAVR) in low-surgical-risk patients.
Methods: Electronic database review was conducted for all randomized clinical trials (RCTs) that compared TAVR versus SAVR in low-risk patients. We calculated risk ratios (RRs) and 95% confidence intervals (CIs) using a random-effects model.
Results: We included 3 RCTs totaling 604 patients (310 TAVR and 294 SAVR). Our results showed no significant difference in mortality between TAVR compared with SAVR (RR = 0.71; 95% CI = 0.22–2.30; $P = 0.56$), however, there was a significantly increased risk of pacemaker implantation (RR = 7.28; 95% CI = 3.94–13.42; $P < 0.01$) and moderate/severe paravalvular leakage (PVL) (RR = 6.74; 95% CI = 1.31–34.65; $P = 0.02$) with TAVR. Nevertheless, TAVR demonstrated a significantly reduced risk of post-procedural bleeding (RR = 0.40; 95% CI = 0.30–0.54; $P < 0.01$) and new-onset atrial fibrillation (RR = 0.36; 95% CI = 0.27–0.47; $P < 0.01$). Other clinical outcomes were not significantly different between the groups and included cardiovascular mortality, stroke, transient ischemic attack, and myocardial infarction.
Conclusions: Among low-risk patients, TAVR offered comparable efficacy outcomes and fewer bleeding events compared with SAVR. There were increased risks of pacemaker implantation and PVL associated with TAVR, though lower atrial fibrillation risks.

1. Introduction

When approaching patients with symptomatic severe aortic stenosis, transcatheter aortic valve replacement (TAVR) is typically preferable over surgical aortic valve replacement (SAVR) in inoperable and high-risk-surgical patients who often have multiple risk factors such as frailty [1,2]. Regarding intermediate-surgical-risk patients, TAVR is considered a valid option as well [3]. However, in low-risk patients, SAVR continues to be the standard of care (Ib recommendation) [4]. Nevertheless, the desire for expansion of TAVR for low-surgical risk patients has grown largely due to a combination of successful results in intermediate- and high-surgical risk patients, technical advancements, TAVR device improvements, and increased operator experience [5]. Registry data show mixed results with regard to low-risk patients undergoing TAVR [5–8], thus, we conducted our study to evaluate the efficacy and safety of TAVR in low-surgical-risk patients when compared with SAVR.

2. Materials and methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) Statement 2015 was followed [9]. HA and AS independently performed a comprehensive search of electronic databases from establishment to July 2018 using the following terms: "transcatheter aortic valve replacement", "TAVR", "surgical aortic valve replacement", "SAVR", "TAVI", "SAVI", AND "low risk." Our inclusion criteria were: (1) the study must be a RCT, (2) patients have low surgical risk (defined as a mean STS score < 4% and/or EuroSCORE <10%).

Risk ratios (RRs), 95% confidence intervals (CIs), and heterogeneity (I^2) were calculated using the Mantel-Haenszel random effects method.

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https://doi.org/10.1016/j.carrev.2018.12.023
1553-8389/

We performed a sensitivity analysis by excluding each trial sequentially. Subgroup analysis comparing self- vs balloon-expandable bioprosthesis was performed for the primary outcome. Analyses were performed with the aid of RevMan v5.3.

3. Results

Among 142 studies, we included 3 RCTs totaling 604 patients (310 TAVR and 294 SAVR) [6,10,11]. The median follow-up period was 12 months. The mean age was 79.5 ± 4.7 with an average aortic valve area of 0.7 cm^2 and a gradient of 59 mmHg. The average STS and EuroScore were 2.8% and 8.8%, respectively. Two trials used a self-expandable bioprosthesis (SURTAVI and NOTION), and one trial utilized a balloon-expandable one (STACCATO). The majority of TAVR procedures were performed via transfemoral access (85.2%). All included trials were multicenter, and one trial was prematurely terminated due to safety concerns (STACCATO). The baseline characteristics of the included patients are summarized in Table 1.

With regard to all-cause mortality (primary outcome), there was no significant difference in TAVR compared with SAVR (3.9% vs 5.6%; RR = 0.71; 95% CI = 0.22–2.30; $P = 0.56$; $I^2 = 39\%$) (Fig. 1). Examination of the funnel plot did not suggest any publication bias. Furthermore, subgroup analysis based on the type of TAVR bioprosthesis (self- vs balloon-expandable) showed no significant interaction ($P = 0.16$).

Concerning secondary outcomes, there were no significant differences between both groups regarding cardiovascular mortality (RR = 0.71; 95% CI = 0.34–1.46; $P = 0.35$), stroke (RR = 0.63; 95% CI = 0.30–1.31; $P = 0.21$), transient ischemic attack (RR = 1.81; 95% CI = 0.65–5.04; $P = 0.26$), or myocardial infarction (RR = 1.08; 95% CI = 0.31–3.77; $P = 0.90$). Notably, there was a significantly increased risk of pacemaker implantation (RR = 7.28; 95% CI = 3.94–13.42; $P < 0.01$) and moderate/severe paravalvular leakage (PVL) (RR = 6.74; 95% CI = 1.31–34.65; $P = 0.02$) in patients who underwent TAVR compared with SAVR. In contrast, TAVR was associated with significantly reduced risk of post-procedural bleeding (RR = 0.40; 95% CI = 0.30–0.54; $P < 0.01$) and atrial fibrillation (AF) (RR = 0.36; 95% CI = 0.27–0.47; $P < 0.01$) (Fig. 1).

4. Discussion

Our meta-analysis revealed that TAVR was associated with similar efficacy, lower bleeding, and higher risks of pacemaker implantation and PVL compared with SAVR, however, the risk of AF was increased with SAVR.

In addition to surgical risk assessment, the mode of intervention should be carefully determined based on the patients' individual risk factors, characteristics, anatomical aspects, and operator experience in a heart team [10,12]. Current guidelines recommend surgical intervention for those deemed low-surgical-risk [4].

In our study, we found a numerically lower all-cause mortality with TAVR compared with SAVR at a median of 1-year in low-risk surgical patients (3.9% vs 5.6%; $P = 0.56$). In a recent study of low surgical risk patients, the short-term (30-day) mortality was found to be numerically lower in the TAVR group compared with the SAVR group (0% vs 1.7%; $P = 0.08$) [5]. These results indicate an inaccurate prediction of short- and long-term mortality with the contemporary surgical risk scores—a finding that encourages the need for TAVR-specific risk models for better stratification [13].

It is worth noting that the STACCATO trial was prematurely terminated due to the overall high rate of adverse events in the TAVR group [11]. Nevertheless, the trial used trans-apical access for TAVR placement – an approach that is rarely used nowadays.

In our study we found an increased risk of clinically relevant PVL and pacemaker implantation in the TAVR group. Although the valve-annulus interface may allow for positive remodeling and possible improvement of associated PVL over time [10], further data on the long-term durability of TAVR valves are needed. Nevertheless, advances in newer TAVR devices, along with precise CT-guided valve sizing and high implantation strategies, may further reduce the associated pacemaker implantations and PVL risks. In a recent contemporary practice of TAVR among lower-risk surgical patients, Waksman et al. reported promising lower rates of 30-day moderate-to-severe PVL (0.5%) and new pacemaker implantation (6.5%), which represent the lowest rates of all previous major TAVR studies [5]. Moreover, a tradeoff with the significantly higher incidence of new-onset AF and post-procedural bleeding among SAVR groups should be also weighed in such low-surgical risk patients.

Our study has limitations, largely attributable to the small number of RCTs included, limited sample size, and few events. Additionally, our patient cohort is older and, therefore, has limited generalizability to younger populations. Moreover, as we lacked patient-level data, we could not assess the effect of transfemoral vs transthoracic access on the clinical outcomes of TAVR. Furthermore, there was substantial heterogeneity in all-cause mortality and moderate-severe PVL (>20%). Due to the limited number of RCTs included, we were unable to perform a meta-regression analysis. However, subgroup analysis based on the type of TAVR bioprosthesis (self- vs balloon-expandable) showed no significant interaction. Finally, we lacked long-term data necessary for assessing valve durability. There are currently ongoing trials in low-risk patients that may shed further light on this rapidly evolving area (NCT02825134, NCT02675114, and NCT02701283).

Table 1
The baseline demographics.

Variable	SURTAVI		NOTION		STACCATO	
	TAVR = 131	SAVR = 123	TAVR = 145	SAVR = 135	TAVR = 34	SAVR = 36
Age	75.1 ± 6.5	75.4 ± 5.5	79.2 ± 4.9	79.0 ± 4.7	80 ± 3.6	82 ± 4.4
Male	89 (67.9)	84 (68.3)	78 (53.8)	71 (52.6)	9 (26.5)	12 (33.3)
STS score	2.3	2.3	2.9	3.1	3.1	3.4
Diabetes mellitus	30 (22.9)	21 (17.1)	26 (17.9)	28 (20.7)	1 (2.9)	3 (8.3)
Hypertension	–	–	103 (71.0)	103 (76.3)	–	–
Creatinine > 2 mg/dl	0	1 (0.8)	2 (1.4)	1 (0.7)	1 (2.9)	0
Prior stroke	6 (4.6)	9 (7.3)	24 (16.6)	22 (16.3)	1 (2.9)	1 (2.8)
Peripheral vascular disease	25 (19.1)	18 (14.6)	6 (4.1)	9 (6.7)	2 (5.9)	3 (8.3)
Prior coronary artery bypass graft	10 (7.6)	9 (7.3)	–	–	–	–
Prior percutaneous coronary intervention	28 (21.4)	18 (14.6)	11 (7.6)	12 (8.9)	–	–
Prior myocardial infarction	14 (10.7)	10 (8.1)	8 (5.5)	6 (4.4)	–	–
Prior atrial fibrillation/flutter	33 (25.2)	28 (22.8)	40 (27.8)	34 (25.6)	–	–

All values in mean ± SD or number (%).
Abbreviations: SAVR: surgical aortic valve replacement; SURTAVI: Surgical Replacement and Transcatheter Aortic Valve Implantation; STACCATO: A Prospective, Randomized Trial of Transapical Transcatheter Aortic Valve Implantation vs. Surgical Aortic Valve Replacement in Operable Elderly Patients with Aortic Stenosis; STS: Society of Thoracic Surgeons; NOTION: The Nordic Aortic Valve Intervention; TAVR: transcatheter aortic valve replacement.

5. Conclusions

In low-risk-surgical patients undergoing aortic valve replacement, TAVR is associated with comparable efficacy compared with SAVR. TAVR does, however, have an increased risk of pacemaker implantation and PVL. In contrast, SAVR is associated with a higher risk of AF and post-procedural bleeding.

Acknowledgments

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

Dr. Deepak L. Bhatt discloses the following relationships - Advisory Board: Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: American

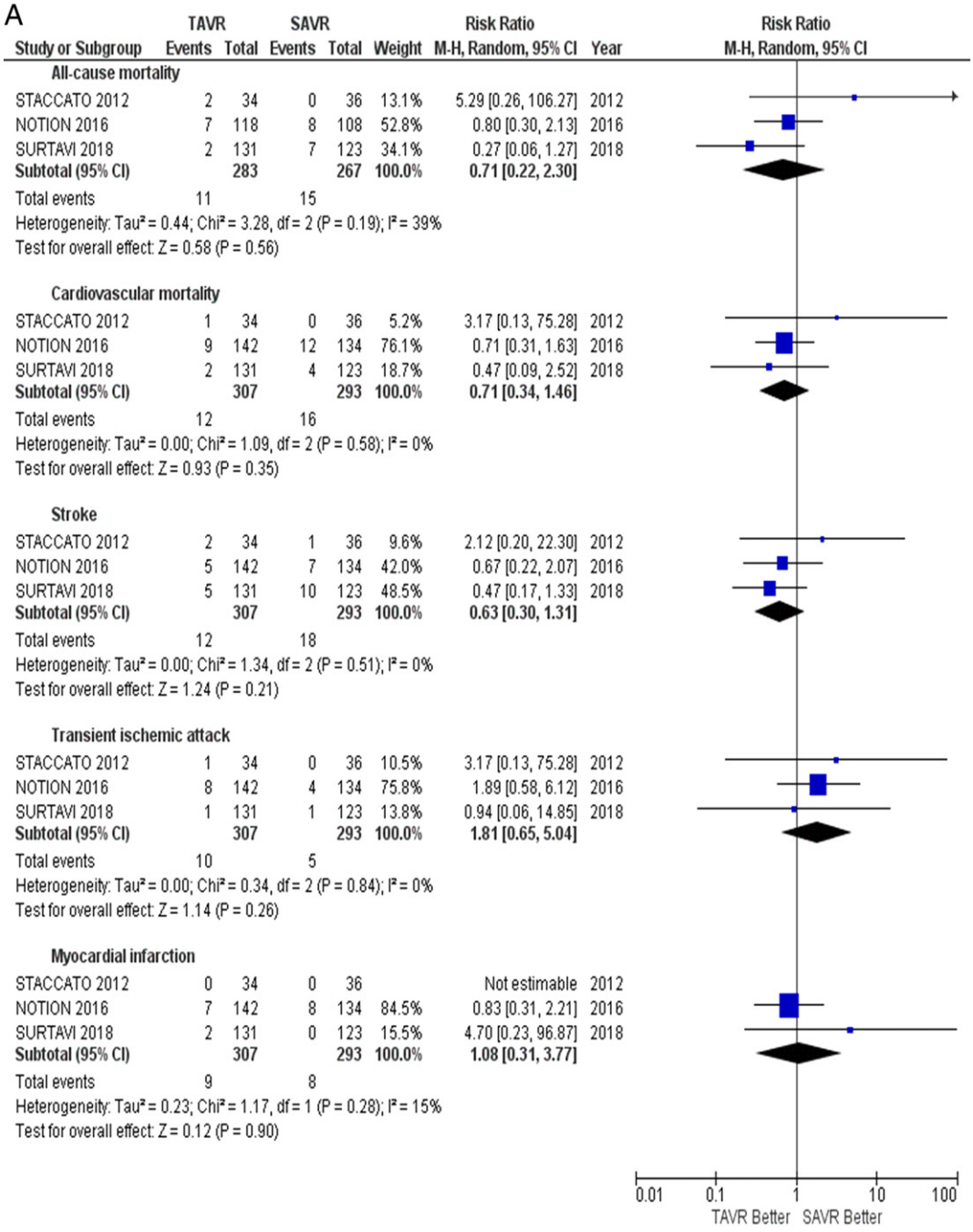

Fig. 1. Forest plot of the clinical outcomes in patients who presented with ischemic stroke and transient ischemic attack. Abbreviations: SAVR: surgical aortic valve replacement; SURTAVI: Surgical Replacement and Transcatheter Aortic Valve Implantation; STACCATO: A Prospective, Randomized Trial of Transapical Transcatheter Aortic Valve Implantation vs. Surgical Aortic Valve Replacement in Operable Elderly Patients with Aortic Stenosis; NOTION: The Nordic Aortic Valve Intervention; TAVR: transcatheter aortic valve replacement.

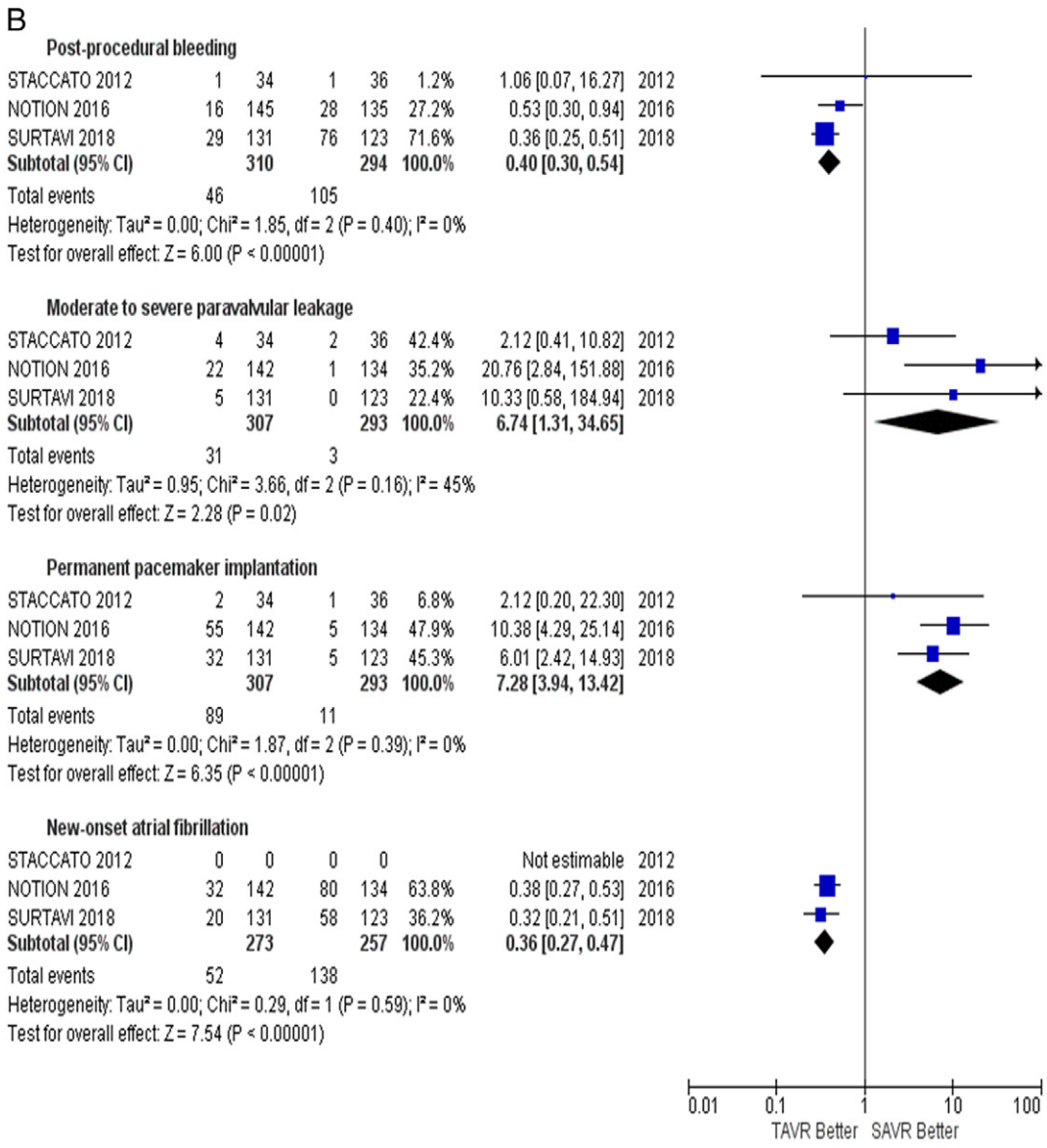

Fig. 1 (*continued*).

Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo), Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); Research Funding: Abbott, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Eisai, Ethicon, Forest Laboratories, Idorsia, Ironwood, Ischemix, Lilly, Medtronic, PhaseBio, Pfizer, Regeneron, Roche, Sanofi Aventis, Synaptic, The Medicines Company; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Biotronik, Boston Scientific, St. Jude Medical (now Abbott), Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Merck, Novo Nordisk, PLx Pharma, Takeda.

The remaining authors report no relationships that could be construed as a conflict of interest.

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