DOI: 10.1111/joic.12141

STRUCTURAL

Impact of Access on TAVI Procedural and Midterm Follow-Up: A Meta-Analysis of 13 Studies and 10,468 Patients

FEDERICO CONROTTO, M.D.,[1] FABRIZIO D'ASCENZO, M.D.,[1] GIORDANA FRANCESCA, M.D.,[1] CHIARA COLACI, M.D.,[1] PAOLO SACCIATELLA, M.D.,[1] GIUSEPPE BIONDI-ZOCCAI, M.D.,[2] CLAUDIO MORETTI, M.D.,[1] MAURIZIO D'AMICO, M.D.,[1] FIORENZO GAITA, M.D.,[1] and SEBASTIANO MARRA, M.D.[1]

From the [1]Division of Cardiology, Città della Salute e della Scienza Hospital, Turin, Italy; and [2]Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

***Introduction**: Transcatheter aortic valve implantation (TAVI) may be performed using the transfemoral (TF) or transapical (TA) approach in most patients with aortic stenosis. The impact of access choice on peri-procedural and midterm results remains to be defined.*
***Methods**: Medline and Cochrane Library were searched for articles describing differences in baseline, peri-procedural, and midterm outcomes among patients undergoing TF or TA TAVI. The primary end-point was all-cause mortality after at least 1-year follow-up, while secondary end-points were 30 days mortality and in-hospital complications (bleeding and cerebrovascular events). The independent impact of access choice was evaluated with pooled analysis using a random-effect model.*
***Results**: Thirteen studies with 10,468 patients were included. TF was the most exploited strategy (69.5% vs. 30.5%). After adjusting for confounding variables, 30-day and midterm follow-up mortality (median 365 days, range 222–400) were lower in TF patients with a pooled adjusted odds ratio of 0.81 (0.68–0.97 I^2 99%) and 0.85 (0.80–0.90 I^2 96%), respectively. Regarding periprocedural outcomes, TF reduced risk of bleedings and strokes (OR of 0.74 [0.66–0.82 I^2 95%] and 0.91 [0.83–0.99] I^2 86%, respectively).*
***Conclusions**: The TF approach reduces mortality in TAVI patients, due to lower rates of periprocedural bleedings and strokes.* (J Interven Cardiol 2014;27:500–508)

Introduction

High-risk patients with severe aortic stenosis may be treated with transcatheter aortic valve implantation (TAVI) as an alternative to cardiac surgery.[1,2] Recently, the European Society of Cardiology has included TAVI in the valvular heart disease management guidelines, with a Class I/B recommendation for inoperable patients and a Class IIa/B recommendation for high-risk surgical patients.[3]

Two main access sites have been largely exploited: transfemoral (TF) and transapical (TA). Transfemoral aortic valve implantation (TF-AVI) has the advantage of being a completely percutaneous procedure while transapical aortic valve implantation (TA-AVI) represents a more invasive procedure, needing direct puncture of the left ventricle. In clinical practice, TF-AVI is preferred over TA-AVI whenever a good vascular access is present. The TA route is usually limited to patients with small or unapproachable femoral vessels, although some experiences have been reported with TA-AVI as a first-line option for all patients,[4,5] and dedicated devices have been recently proposed.[6] There is a lack of randomized studies investigating the different TAVI approaches, and a comparison between the effects of TF and TA strategies on TAVI clinical outcome remains challenging. Some

Disclosure statement: The authors report no financial relationships or conflicts of interest regarding the content herein.
Address for reprints: Federico Conrotto, M.D., Department of Cardiology, Città della Salute e della Scienza Hospital, Turin, Italy. Fax: +390116335565; e-mail: federico.conrotto@gmail.com

registry data suggested that the TA access could be associated with a worse prognosis[7,8] though the bias of a higher baseline risk may have influenced these results. Thus, to clarify the impact of TF versus TA approach on short- and midterm TAVI outcome, we performed a meta-analysis including the observational studies reporting the independent impact of access choice on TAVI outcome.

Methods

The present research was conducted following current guidelines, including the recent Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) amendment to the Quality of Reporting of Meta-analyses (QUOROM) statement, and recommendations from The Cochrane Collaboration and Meta-analysis of Observational Studies in Epidemiology (MOOSE).[9–11]

Search Strategy and Study Selection

Search strategy. Possible articles for inclusion were found using established search methods[12] looking for the terms "TAVI" or "trans catheter aortic valve replacement" or "percutaneous aortic valve replacement" and "transfemoral" or "transapical" or "access." Moreover abstract presentations at congresses were reviewed to identify other studies. Two independent reviewers (FC, FDA) initially screened the title and/or abstract of all possible articles for inclusion, with disagreement resolved by consensus. If potentially eligible, the complete article was then reviewed according to the following strict selection criteria. Inclusion/exclusion criteria. Inclusion criteria were studies (i) investigating patients undergoing TAVI, (ii) reporting independent predictive value of the access choice, and (iii) with at least 6 months follow-up. Exclusion criteria were any of: (i) nonhuman study and (ii) duplicate reporting (in which case the manuscript reporting the largest sample of patients was selected).

Data selection. Baseline features of patients included in each study (age, gender, cardiovascular risk factors, previous myocardial infarction and coronary revascularization, previous cerebrovascular accident, renal, and pulmonary function) as of procedural data (kind of valve and of access) were abstracted.

End-points. The primary end-point was all cause mortality after at least 1-year follow-up, while in-hospital complications (major bleedings, cerebrovascular events) and 30-day all-cause mortality were the secondary ones. All clinical variables and end-points were adjudicated according to VARC criteria.[13]

Internal validity and quality appraisal. Two unblinded independent reviewers (FC, FDA) evaluated the quality of the selected studies on pre-specified data collection forms using modified MOOSE criteria to take into account the specific features of included studies.[11] The independent reviewers separately appraised study design, setting, data source, and statistical methods for multivariable analysis, as well as risk of analytical, selection, adjudication, detection, and attrition bias (expressed as low, moderate, or high risk of bias).

Data analysis. Statistical pooling was performed according to a random-effect model with generic inverse-variance weighting, computing risk estimates with 95% confidence intervals, using RevMan 5.2 (The Cochrane Collaboration, The Nordic Cochrane Centre, and Copenhagen, Denmark). Graphical inspection of funnel plots was used to assess for study bias. Sensitivity analysis was performed for the primary end-point according to study design. Using rates of event as dependent variable, a meta-regression was performed to test whether an interaction between baseline clinical features (age, gender, diabetes mellitus, coronary artery disease, PAD, logistic EuroSCORE, STS score, self-expandable, and balloon expandable valves) and access choice was present for the primary end-point.

Standard hypothesis testing was set at the 2-tailed 0.05 level.

Results

Four hundred sixty eight citations were first screened at abstract level and 29 were analyzed. Among them, 16 were excluded because not reporting multivariable adjustment. Finally, 13 studies were included,[14–26] 12 deriving from published articles and 1 from congress' abstract (Fig. 1). Ten thousand four hundred sixty-eight patients with symptomatic severe aortic stenosis were included and their main characteristics are reported in Table 1. Median age was 82 years (80.5–83.6) and half of the patients were male (50%: 37.3–57.8). Twenty-six percent (22.8–35.4) of the patients were diabetic, 17.8% (6.7–71) had renal dysfunction, 61% (45.4–74.9) had a known CAD, and median ejection fraction was 52.4% (51–55.6). Mean Logistic EuroSCORE was more than 20% in all the studies, except for one (18.5%), and was higher in TA patients if compared to TF patients in the 4 studies that reported it. Mean STS score was greater than 5% in all papers that reported it. Table 2 summarizes the procedural features of the included studies. The TF-approach was the preferred

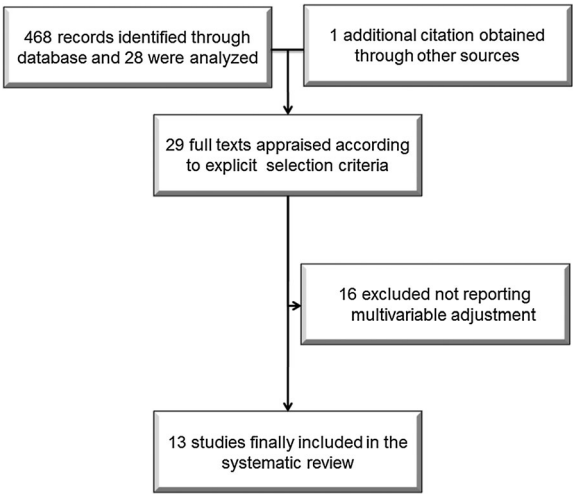

Figure 1. Study flow-chart.

one (69.5%) while most of the patients received an Edwards-Sapien valve (72%, 35–100). Thirty-day and midterm events are reported in Table 3. Thirty days mortality was 7.5% (3.4-11-3), while follow-up mortality was 19.5% (13–25.5). Regarding the primary end-point, a better midterm survival for TF patients was shown, with a pooled adjusted odds ratio 0.85 (0.80–0.90 I^2 96%) (Fig. 2). Significance did not change after excluding the only retrospective study (0.84 [0.77, 0.93] I^2 0), the only randomized controlled trial (0.85 [0.77, 0.93], I^2 95%), or when including only multicenter study (0.85 [0.77, 0.93], I^2 95%, all CI 95%). At meta-regression analysis, baseline and procedural characteristics did not influence these results (Tables 4 and 5).

After adjusting for confounding variables, 30-day mortality was lower in TF patients compared to TA patients, with a pooled adjusted odds ratio of 0.81 (0.68–0.97 I^2 99%) (Fig. 3). Regarding periprocedural outcomes, TF reduced risk of bleedings and strokes (OR respectively of 0.74 [0.66–0.82 I^2 95] and 0.91 [0.83–0.99 I^2 86%]), respectively (Figs. 4 and 5).

Discussion

This systematic review of contemporary literature, including more than ten thousand patients treated for symptomatic severe AS between 2005 and 2012, represents a wide range of TAVI experience. It aims to identify the impact of TF versus TA approach on TAVI outcomes. Mayor findings of our meta-analysis are: (i) 30-day survival is higher in TF group than in TA patients; (ii) the rate of periprocedural bleedings and strokes is significantly lower in TF-TAVI; (iii) short-term advantage of TF approach remains statistically significant at midterm follow-up.

A comparison between short and midterm results of TF-AVI and TA-AVI remains difficult, as in TAVI patients, in the absence of anatomical contraindications, TF approach has traditionally represented the default access. The TA approach instead is limited by the invasiveness of the surgical thoracotomy, albeit short delivery distance makes an accurate valve positioning easier. Consequently in most studies the access choice is based on baseline clinical characteristics of the population, and a bias favoring TF-AVI in less sick patients is usually present. To date direct randomized comparisons are not yet available. Recently a meta-analysis on this topic reported a better short-term survival for TF patients.[27] However, as the included studies were not adjusted for confounding variables, it still remains unclear if differences in outcomes among TF-AVI and TA-AVI may be attributable to the different clinical presentations or to an independent prognostic role of the chosen approach**.** Moreover more accurate data on midterm follow-up are still lacking.

Also in the present review, EuroSCORE was higher in TA-AVI patients, although we appraised the impact of different accesses independently from clinical features. Moreover at metaregression analysis, no clinical or procedural features influenced the outcomes, in particular for patients with peripheral artery disease or according to balloon expandable or self-expandable valves.

The higher mortality in TA-AVI patients at 30 days directly translated into a higher mortality at a median follow-up of 1 year. These results may be influenced by the significantly higher incidence of bleeding and strokes. These two complications severely worsen outcome in TAVI patients, as it has been highlighted by various studies[28–35] while are still not accurately predicted by dedicated score.[32]

In a multicenter work by our group, bleedings increased in-hospital mortality and, in a recent report by Borz et al., bleedings were independent predictors of midterm mortality.[30,33] Moreover bleedings represent a common pathway for other significant complications after TAVI, such as vascular injuries and acute renal failure, thus worsening patients' a prognosis, especially when blood transfusion is necessary.[36,37]

Table 1. Baseline Characteristics

Article	Number of Patients	Male n (%)	Age	CAD n (%)	Renal Insufficiency	Diabetes n (%)	COPD n (%)	PAD n (%)	FE (%)	Logistic Euro SCORE (%)	STS Score	AVA cm^2	Mean Transvalvular Gradient (mmHg)
Amabile	171	80 (47)	83.5 ± 6.2	107 (63)	121 (71)	43 (25)	46 (27)	52 (31)	54.7 ± 14.9	22.1 ± 12.3			49.4 ± 17.5
Gilard	3,195	1,630 (51)	82.7 ± 7.2	1,483 (47.9)			790 (25.5)	643 (20.8)	53.2 ± 14.1	21.9 ± 14.3	14.4 ± 11.9	0.7 ± 0.2	48.1 ± 16.5
Hemman	426	131 (48) TF	80 ± 8 TF	151 (55) TF	19 (7) TF	90 (33) TF				19.5 ± 14.2 TF	7.4 ± 6.2 TF		51.2 ± 17.1 TF
		143 (52) TA	81 ± 7 TA	93 (61) TA	14 (9) TA	61 (40) TA				24.21 ± 14.9 TA	7.9 ± 5.9 TA		51.6 ± 17.6 TA
Himbert	75	41 (55)	82 ± 8	45 (61)	28 (38)		20 (27)	11 (15)	51 ± 15	26 ± 13	16 ± 7	0.64 ± 16	52 ± 15
Moat	870	456 (52.4)	81.9 ± 7.1	394 (47.6)	55 (6.7)	196 (22.8)	239 (28.7)	241 (29)		18.5			
PARTNER	348	201 (57.8)	83.6 ± 6.8	260 (74.9)	38 (11.1)		151 (43.4)	148 (43)	52.5 ± 13.5	29.3 ± 16.5	11.8 ± 3.3	0.7 ± 0.2	42.7 ± 14.6
Pilgrim	389	165 (42)	82,4	238 (61)	268 (69)	105 (27)	72 (19)	87 (22)	52 ± 15	24 ± 14	6.8 ± 5.3		44 ± 17
Schymik	300	112 (37.3)	81 ± 5	181 (60.3)	21 (7)		41 (13.7)	58 (19.3)	55.6 ± 14.7	24 ± 16.9			
SOURCE	2,344	975 (41.6)	81.1	TA 56.1 TF 47.8	TA 31.2 TF 24.8					28.1 TA 21.5 TF			
Turin	1,100	489 (44.5)	81.5 ± 6.6		196 (17.8)	341 (31)	332 (30.2)	374 (34)	52.2 ± 12.7	17.2 ± 9.4 TF 23.1 ± 14 TA	9.7 ± 7.4	0.73 ± 0.2	51.1 ± 18
Van der boon	882	470 (53.3)	81.2 ± 7.0	400 (45.4)	553 (63.0)	250 (28.3)	290 (32.9)	200 (22.8)	152 (17.2)	20.8 (13.0–28.5)	7.0 (3.8–10.2)	0.70 ± 0.20	
Webb	168	87 (51.8)	84	114 (67.9)	20 (11.9)	39 (23.2)	35 (20.8)	60 (35.7)		28.6	9.1	0.6	46
Wenaweser	200	85 (42.5)	82 ± 6.5	125 (62.5)		50 (25)		47 (23.5)	51 ± 14	24.6 ± 15.3	6.4 ± 4.9	0.7 ± 0.2	43 ± 15

Table 2. Procedural Characteristics

Article	TF n° (%)	TA n°(%)	TS n°(%)	Edwards Sapien n°(%)	Core Valve Sapien	Mean Valve Diameter (mm)
Amabile	139 (81)	32 (19)	0	132 (77)	39 (23)	
Gilard	2,383 (74.6)	569 (17.8)	185 (5.8)	2,137 (66.9)	1,058 (33.1)	
Hemman	274 (64.3)	152 (35.7)	0	240 (56.3)	186 (43.7)	51.2 ± 17.1 (TF) 51.6 ± 17.6 (TA)
Himbert	51 (68)	24 (32)	0	75 (100%)	0	
Moat	599 (68.9)	271 (31.1)		410 (47.1)	452 (51.9)	
Pilgrim	308 (79)	76 (19)	5 (2)	164 (42)	225 (58)	
Schymik	174 (58)	126 (42)	0	257 (85.6)	43 (14.4)	
PARTNER	244 (70)	104 (30)	0	699 (100)	0	
Turin	634 (75.8)	335 (30.5)	131 (11.9)	548 (49,8)	552 (50,2)	
SOURCE	946 (39.9)	1,398 (60.1)	0	2,344 (100)	0	
Van der Boon	793 (89.9)	89 (10.1)		429 (48.7)	453 (51.3)	
Webb	113 (67)	55 (33)	0	168 (100)	0	22.74 + 2.01 (annulus)
Wenaweser	154 (77)	43 (21.5)	3 (1.5)	70 (35)	130 (65)	21.8 ± 1.9

Eggebrecht et al.[38] demonstrated a 3.5-fold higher 30-day mortality in patients with postprocedural stroke. Open heart surgery represents well-known risk factors for this complication, which is related to acute mortality and increased morbidity, physical disability and resources use.[14,39–41] A less invasive procedure may reduce the stroke risk. For example, a conventional sternotomy increases the risk of stroke when compared to less invasive approaches in patients undergoing mitral valve replacement,[42] and percutaneous coronary interventions reduce ischemic cerebral events when compared to coronary artery bypass grafting.[43,44] Further explanations for the worse TA-AVI outcome may be attempted. A longer hospitalization among patients undergoing TA-AVI compared with patients undergoing TF-AVI was reported in previous studies.[14,16,24] Longer hospital stay not only may lead to increased costs but also may be associated with an increased risk of hospital-acquired infections and consequently may have negative implications on patients' prognosis. Moreover, recent large multicenter registries reported an enhanced risk of renal injury in TA patients.[36,45]

Table 3. 30-Day and Midterm Outcome

Article	Periprocedural Strokes n (%)	Periprocedural Major or Life Threatening Bleedings n (%)	30-Day Mortality n (%)	Follow-Up Length (Days)	Follow-Up Mortality n (%)
Amabile		23 (34.5)		265	30 (17.5)
Webb	7 (4.2)	19 (11.5)	19 (11.3)	222	
Gilard	131 (4.1)	183 (5.7)	293 (9.7)	365	528 (24)
Hemman			32 (7.5)	365	70 (16.5)
Himbert	3 (4)		8 (10)	365	17 (22)
Moat	35 (4.1)		62 (7.1)	365	186 (21.4)
Pilgrim				400	
Schymik	8 (2.7)	47 (19)	18 (6)	365	(17.3)
PARTNER	19 (5.5)	32 (9.3)	12 (3.4)	365	84 (24.2
Turin	16 (3.8%)	205 (21)	53 (9)	365	144 (17)
SOURCE			221 (9.4)	365	597 (25.5)
Van der Boon	25 (2.8)	302 (34.2)	65 (7.4)	365	
Wenaweser	9 (4.5)	88 (44)	15 (7.5)	180	26 (13.0)

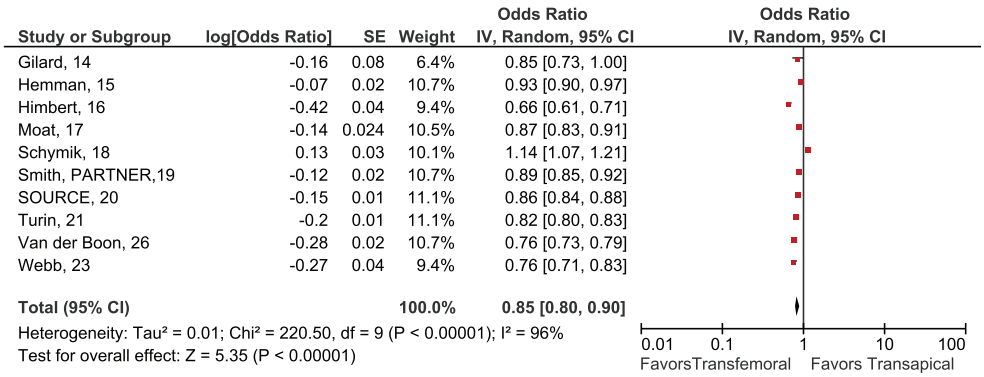

Figure 2. Pooled adjusted OR for midterm mortality.

Table 4. Main Features of Included Study

Article	Number of Patients	Number of Center	Study Design	Adjudication Bias	Attrition Bias	Kind of Multivariate Analysis
Amabile	171	Single	Prospective, observational	Unclear	Unclear	Cox multivariate model
Gilard	3,195	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model with stepwise regression
Hemman	426	Multicenter	Retrospective, observational	Medium risk	Medium risk	Cox multivariate model
Himbert	75	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model
Moat	870	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model
PARTNER	348	Multicenter	Prospective, randomized	Low risk	Low risk	Generalized linear model
Pilgrim	389	Single	Prospective, observational	Low risk	Low risk	Cox multivariate model
Schymik	300	Single	Prospective, observational	Unclear risk	Low risk	Multivariate logistic regression analysis
SOURCE	2344	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model
Turin	1,100	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model
Van der boon	882	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model
Webb	168	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model
Wenaweser	200	Multicenter	Prospective, observational	Low risk	Low risk	Cox multivariate model

Table 5. Meta Regression Analysis for the Primary End Point

	Beta	LCI	UCI	P-Value
Male gender	0.003	−0.001	0.009	0.12
Age	0.011	−0.06	0.02	0.77
Previous CAD	0.002	−0.004	0.003	0.57
PAD	0.002	−0.001	0.004	0.91
Logistic euroscore	0.001	−0.003	0.002	0.81
STS score	−0.003	−0.007	0.002	0.35
Balloon expandable	−0.007	−0.009	0.12	0.56
Self expandable	0.01	−0.001	0.03	0.74

CAD, coronary artery disease; PAD, peripheral artery disease.

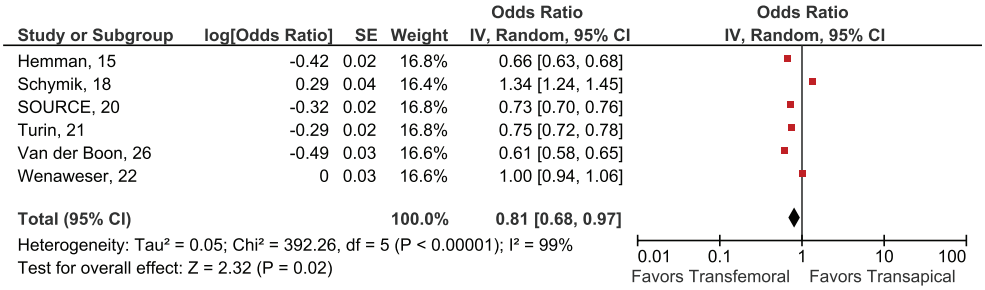

Figure 3. Pooled adjusted OR for 30-day mortality.

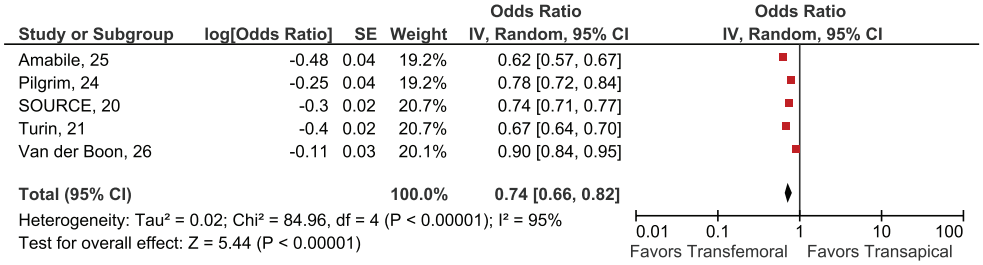

Figure 4. Pooled adjusted OR for periprocedural bleeding.

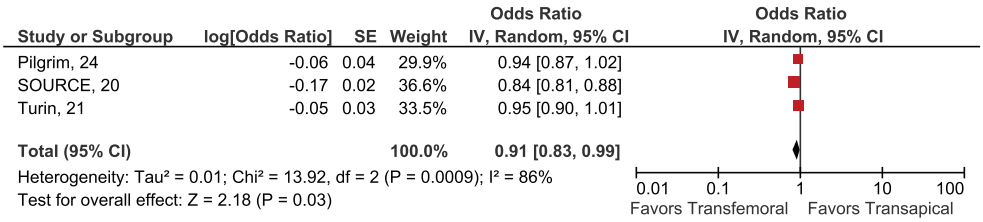

Figure 5. Pooled adjusted OR for periprocedural stroke.

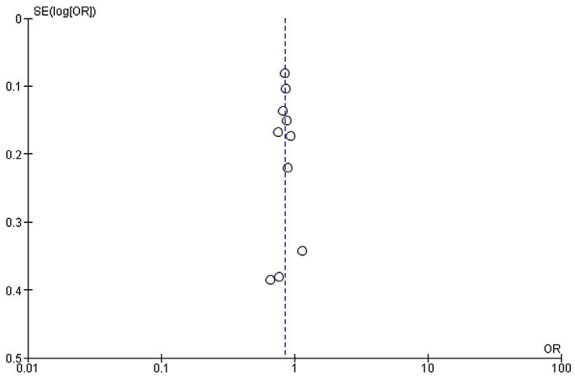

Figure 6. Funnel plot of included studies.

Limitations

All of the data were drawn from either observational studies or unbalanced subgroups of a randomized trial; none were direct comparisons from randomized trials. To minimize the selection bias of patients undergoing TAVI via different access routes we included in our meta-analysis only studies adjusted for the baseline differences. Yet, residual confounding factors may still be present and the higher baseline risk profile of TA-TAVI patients, could exceed the multivariate adjustments. Although the present meta-analysis was based only on published studies publication bias still remains a problem, while small study bias was unapparent at funnel plot inspection (Fig. 6). Meta-analysis which is

not patient level may represent another weakness. A comparison of impact of different approach on midterm cardiac mortality could be more appropriate but adjusted cardiac midterm mortality data were not available.

Due to these limitations, the results of the present meta-analysis should be viewed as hypothesis generating only; however, they suggest that TA access should be reserved as a last option in TAVI patients. More studies are needed to validate new delivery systems with smaller diameters and emerging access routes as the transaortic one.

References

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–1607.
2. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012;366:1686–1695.
3. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC), European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2012;33:2451–2596.
4. Higgins J, Ye J, Toggweiler S, et al. Transapical aortic valve implantation: The Vancouver experience. Ann Cardiothorac Surg 2012;1(2):138–144.
5. Holzhey DM, Hänsig M, Walther T, et al. Transapical aortic valve implantation: The Leipzig experience. Ann Cardiothorac Surg 2012;1:129–137.
6. Holzhey D, Linke A, Treede H, et al. Intermediate follow-up results from the multicenter engager European pivotal trial. Ann Thorac Surg 2013;96:2095–2100.
7. Thomas M, Schymik G, Walther T, et al. Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis in patients at very high or prohibitive surgical risk. J Am Coll Cardiol 2010;55:1080–1090.
8. Eltchaninoff H, Prat A, Gilard M, et al. Transcatheter aortic valve implantation: Early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. Eur Heart J 2011;32:191–197.
9. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ 2009;339:b2535.
10. Moher D, Cook DJ, Eastwood S, et al. Improving the quality of reports of meta-analyses of randomised controlled trials: The QUOROM statement. Quality of Reporting of Meta-analyses. Lancet 1999;354:1896–1900.
11. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008–2012.
12. McManus RJ, Wilson S, Delaney BC, et al. Review of the usefulness of contacting other experts when conducting a literature search for systematic reviews. BMJ 1998;317:1562–1563.
13. Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for Transcatheter Aortic Valve Implantation clinical trials: A consensus report from the Valve Academic Research Consortium. J Am Coll Cardiol 2011;57:253–269.
14. Gilard M, Eltchaninoff H, Iung B, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. N Engl J Med 2012;366:1705–1715.
15. Hemmann K, Sirotina M, De Rosa S, et al. The STS score is the strongest predictor of long-term survival following transcatheter aortic valve implantation, whereas access route (transapical versus transfemoral) has no predictive value beyond the periprocedural phase. Interact Cardiovasc Thorac Surg 2013;17:359–364.
16. Himbert D, Descoutures F, Al-Attar N, et al. Results of transfemoral or transapical aortic valve implantation following a uniform assessment in high-risk patients with aortic stenosis. J Am Coll Cardiol 2009;54:303–311.
17. Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. J Am Coll Cardiol 2011;58:2130–2138.
18. Schymik G, Schröfel H, Schymik JS, et al. Acute and late outcomes of Transcatheter Aortic Valve Implantation (TAVI) for the treatment of severe symptomatic aortic stenosis in patients at high- and low-surgical risk. J Interv Cardiol 2012;25:364–374.
19. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–2198.
20. Thomas M, Schymik G, Mohr F, et al. Final one-year outcomes of >2,300 patients in the source of registry, using the Edwards Sapien bioprostesis for TAVI in Europe. Abstract, presented at PCR 2011.
21. Conrotto F, D'Ascenzo F, Giordana F, et al. Impact of diabetes mellitus on early and midterm outcomes after transcatheter aortic valve implantation (from a multicenter registry). Am J Cardiol 2014;113:529–534.
22. Wenaweser P, Pilgrim T, Roth N, et al. Clinical outcome, predictors for adverse events after transcatheter aortic valve implantation with the use of different devices, access routes. Am Heart J 2011;161:1114–1124.
23. Webb JG, Altwegg L, Boone RH, et al. Transcatheter aortic valve implantation: Impact on clinical and valve-related outcomes. Circulation 2009;119:3009–3016.
24. Pilgrim T, Kalesan B, Wenaweser P, et al. Predictors of clinical outcomes in patients with severe aortic stenosis undergoing TAVI: A multistate analysis. Circ Cardiovasc Interv 2012;5:856–861.
25. Amabile N, Azmoun A, Ghostine S, et al. Incidence, predictors and prognostic value of serious hemorrhagic complications following transcatheter aortic valve implantation. Int J Cardiol 2013;168:151–156.
26. van der Boon RM, Marcheix B, Tchetche D, et al. Transapical versus transfemoral aortic valve implantation: A multicenter collaborative study. Ann Thorac Surg 2014;97:22–28.
27. Li X, Kong M, Jiang D, et al. Comparison 30-day clinical complications between transfemoral versus transapical aortic valve replacement for aortic stenosis: A meta-analysis review. Cardiothorac Surg 2013;8:168.
28. Tamburino C, Capodanno D, Ramondo A, et al. Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. Circulation 2011;123:299–308.
29. Rodés-Cabau J, Webb JG, Cheung A, et al. Long-term outcomes after transcatheter aortic valve implantation. J Am Coll Cardiol 2012;60:1864–1875.
30. Borz B, Durand E, Godin M, et al. Incidence, predictors and impact of bleeding after transcatheter aortic valve implantation

using the balloon-expandable Edwards prosthesis. Heart 2013;99:860–865.
31. Pilgrim T, Stortecky S, Luterbacher F, et al. Transcatheter aortic valve implantation and bleeding: Incidence, predictors and prognosis. J Thromb Thrombolysis 2013;35:456–462.
32. D'Ascenzo F, Ballocca F, Moretti C, et al. Inaccuracy of available surgical risk scores to predict outcomes after transcatheter aortic valve replacement. J Cardiovasc Med (Hagerstown) 2013;14:894–898.
33. Moretti C, D'Amico M, D'Ascenzo F, et al. Impact on prognosis of periprocedural bleeding after TAVI: Midterm Follow-Up of a Multicenter Prospective Study. J Interv Cardiol 2014;27(3): 293–299
34. D'Ascenzo F1, Gonella A, Moretti C, et al. Gender differences in patients undergoing TAVI: A multicentre study. EuroIntervention 2013;9:367–372.
35. D'Ascenzo F, Moretti C, Salizzoni S, et al. 30 days and midterm outcomes of patients undergoing percutaneous replacement of aortic valve according to their renal function: A multicenter study. Int J Cardiol 2013;167:1514–1518.
36. Nuis RJ, Rodés-Cabau J, Sinning JM, et al. Blood transfusion and the risk of acute kidney injury after transcatheter aortic valve implantation. Circ Cardiovasc Interv 2012;5:680–688.
37. Tchetche D, Van der Boon RM, Dumonteil N, et al. Adverse impact of bleeding and transfusion on the outcome post-transcatheter aortic valve implantation: Insights from the Pooled-RotterdAm-Milano-Toulouse In Collaboration Plus (PRAGMATIC Plus) initiative. Am Heart J 2012;164:402–409.
38. Eggebrecht H, Schmermund A, Voigtländer T, et al. Risk of stroke after transcatheter aortic valve implantation (TAVI): A meta-analysis of 10,037 published patients. EuroIntervention 2012;8:129–138.
39. Fairbairn TA, Mather AN, Bijsterveld P, et al. Diffusion-weighted MRI determined cerebral embolic infarction following transcatheter aortic valve implantation: Assessment of predictive risk factors and the relationship to subsequent health status. Heart 2012;98:18–23.
40. Chevreul K, Brunn M, Cadier B, et al. Cost of transcatheter aortic valve implantation and factors associated with higher hospital stay cost in patients of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. Arch Cardiovasc Dis 2013;106:209–219.
41. O'Brien SM, Shahian DM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: Part 2-isolated valve surgery. Ann Thorac Surg 2009;88(Suppl 1):S23–S42.
42. Cao C, Gupta S, Chandrakumar D, et al. A meta-analysis of minimally invasive versus conventional mitral valve repair for patients with degenerative mitral disease. Ann Cardiothorac Surg 2013;2:693–703.
43. D'Ascenzo F, Barbero U, Moretti C, et al. Percutaneous coronary intervention versus coronary artery bypass graft for stable angina: Meta-regression of randomized trials. Contemp Clin Trials 2014;38(1):51–58.
44. Palmerini T, Biondi-Zoccai G, Reggiani LB, et al. Risk of stroke with coronary artery bypass graft surgery compared with percutaneous coronary intervention. J Am Coll Cardiol 2012;60:798–805.
45. Saia F, Ciuca C, Taglieri N, et al. Acute kidney injury following transcatheter aortic valve implantation: Incidence, predictors and clinical outcome. Int J Cardiol 2013;168(2):1034–1040.