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Comparative Efficacy of Local and General Anesthesia for Transcatheter Aortic Valve Implantation: A Meta-Analysis and Systematic Review

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ABSTRACT

Background: This meta-analysis aimed to compare the potential effects of local anesthesia (LA) and general anesthesia (GA) for transcatheter aortic valve implantation (TAVI).

Measurements: All relevant studies were searched from Pubmed, EMbase, Web of Science, and the Cochrane Library (January 1, 2016, to June 1, 2021). The main outcomes of this literature meta-analysis were 30-day mortality, procedural time, new pacemaker implantation, total stay in the hospital, use of the vasoactive drug, and intra-and postoperative complications and emergencies, including conversion to open, myocardial infarction, pulmonary complication, vascular complication, renal injury/failure, stroke, transesophageal echocardiography, life-threatening/major bleeding, cardiac tamponade, and emergency PCI. Pooled risk ratio (RR) and mean difference (MD) together with a 95% confidence interval (CI) were calculated.

Results: A total of 17 studies, including 20938 patients, in the final analysis, fulfilled the inclusion criteria. Intra-and postoperative complications (myocardial infarction, vascular complication, renal injury/failure, stroke, and cardiac tamponade) undergoing TAVI in severe AS patients under GA do not offer a significant difference compared with LA. No differences were observed between LA and GA for new pacemaker implantation, total stay in the hospital, transesophageal echocardiography, and emergency PCI. LA has lower mortality compared with GA (RR 0.69, $P = 0.600$), pulmonary complications (RR 0.54, $P = 0.278$), life-threatening/major bleeding (RR 0.85, $P = 0.855$), and lower times of conversion to open (RR 0.22, $P = 0.746$). LA has many advantages, including a shorter procedure duration (MD=-0.38, $P = 0.000$) and reduction of the use of the vasoactive drug (RR 0.57, $P = 0.000$).

Conclusions: For TAVI, both LA with or without sedation and GA are feasible and safe. LA appears a feasible alternative to GA for AS patients undergoing TAVI.

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INTRODUCTION

Aortic stenosis (AS) is the most common valvular disease in patients and a major cause of mortality and morbidity. Aortic valve replacement through surgery of AS is the class-I therapy advocated by the American College of Cardiology Foundation, American Heart Association, and European Society of Cardiology guideline [Bonow 2008; Joint Task Force on the Management of Valvular Heart Disease of the European Society of C 2012]. Over the last few years, transcatheter aortic valve implantation (TAVI) has become an effective therapy for increased aged patients with symptomatic severe AS and left ventricular dysfunction or coexisting comorbidities or not suitable for surgical correction with lower long-term mortality compared with patients undergoing surgical valve replacement [Nishimura 2014].

Severe cardiac conditions, old age, and coexisting medical problems of AS patients usually increase the risk of anesthesia for TAVI. Many aspects of the TAVI procedure demand the surveillance of anesthesiologists during the operation period, such as hemodynamic manipulation and respiratory tract management. With the original experience, a number of centers preferred to perform TAVI under general anesthesia (GA) [Durand 2012]. So far, the anesthetic strategy of TAVI has adopted both GA and local anesthesia with or without sedation (LA). This further development of anesthetic strategy leads to increasing concern and discussion about performing TAVI under GA or LA. GA with the tracheal intubation and consequent surveillance of the patients normally performed well; however, it may also result in an increase of risks, such as hemodynamic instability and pulmonary morbidity [Greif 2014].

To reveal the optimal anesthesia strategy for undergoing TAVI, we performed a meta-analysis and literature review to evaluate the differences in procedural complication rates due to the use of LA compared with GA.

METHODS

To perform this systematic literature review, we adopted the principles proposed by the Cochrane Handbook [Frohlich 2014] and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [Moher 2010]. Registration number: CRD420212582569 (PROSPERO).

Search strategy: Two authors independently searched the Pubmed, EMbase, Web of Science, and The Cochrane Library databases for relevant articles written in English and published from January 1, 2016, to July 1, 2021. We used the following contextual query language: "Aortic valve" AND ("TAVI" OR "TAVR" OR "Transcatheter Aortic Valve Implantation" OR "Transcatheter Aortic Valve Replacement") AND "General Anaesthesia" AND ("Local Anaesthesia" OR "Sedation"). The syntax for the other databases was similar. The titles and abstracts of the potentially relevant articles were scanned by the same two authors. The reference lists of all identified studies were manually checked, and relevant review articles were used to select potentially eligible articles. We planned to include only randomized controlled trials; however, due to the few of these articles, we modified the originally composed protocol to include both randomized controlled trials (RCTs) and retrospective studies.

Study selection: The study's inclusion and exclusion criteria were determined before the systematic search. Inclusion criteria are as follows: 1) the target population is subjects who underwent TAVI surgery; 2) the study included comparisons between TAVI under LA or sedation and under GA; 3) publication date after 1 January 2016. Exclusion criteria are as follows: 1) studies that only compared regional anesthesia techniques or varying dose regimens of local anesthetics during the same perioperative period; 2) studies focused on the effect of timing; 3) letter, review, meta-analysis, and case report. Duplicates and irrelevant articles were excluded by assessing titles, abstracts, and full texts, and then the finally relevant studies were selected by two authors. The discriminations were resolved through discussion. Agreement between reviewers regarding trial inclusion was assessed using the Cohen K statistics [Liberati 2009].

Quality assessment: The quality of cohort and case-control studies was assessed independently by two authors using the methods recommended by the Newcastle–Ottawa Quality Assessment Scale (NOS) [Landis 1977]. Those who scored over 7 were regarded as high-quality studies. The quality of the randomization-controlled trial was assessed by the Cochrane Collaboration Assessment Scale. If there was any disagreement, a third author would reevaluate the original study.

Data extraction: With standard data extraction forms, two authors independently performed all interrelated data extraction: publication information (name of the first author, year, and name of journal), characteristics of participants (sample size, age, gender, type of surgery, and registration of clinical trial) and outcome information: 30-day mortality, procedural time, new pacemaker implantation, total stay in the hospital, use of the vasoactive drug, intra-and postoperative complications and emergencies, including conversion to open, myocardial infarction, pulmonary complication, vascular complication, renal injury/failure, stroke, transesophageal echocardiography, life-threatening/major bleeding, cardiac tamponade, and emergency PCI. Any discrepancies were resolved by discussion and consensus with the corresponding author.

Statistical analysis: We conducted this meta-analysis using Stata 12.0 software (Stata Corporation, College Station, TX, USA). Dichotomous data of the studies were combined to calculate pooled risk ratio (RR) and 95% confidence intervals (CIs) of LA versus GA. If the 95% CI included a value of 1, we considered the difference not statistically significant. We calculated the standard mean difference (SMD) for continuous data, also reported with 95% CI. We used the Chi-squared test and the I-squared test for heterogeneity. A level of 10% significance ($P \leq 0.1$) for the Chi-squared statistic or I^2 greater than 50% was considered to indicate considerable heterogeneity. The Mantel-Haenszel random-effect model was used for these studies. The Mantel-Haenszel fixed model was used for studies that did not demonstrate significant heterogeneity [Hozo 2005].

RESULTS

Study identification and selection: We searched a total of 281 records, of which five were excluded after correcting for duplicates. Based on irrelevant titles and abstracts, 255 studies were excluded. The remaining 21 full-text studies were reviewed for a more detailed assessment, of which four studies were excluded for the reasons of not reporting both LA and GA. (Figure 1) At last, 17 articles were included [Thiele 2020; Martins 2019; Stragier 2019; He 2017; Husser 2018; Kesimci 2016; Jabbar 2016; Cuadrado 2016; Palermo 2016; D'Errigo 2016; Debry 2016; Mayr 2016; Brecker 2016; Miles 2016; Kiramijyan 2016; Hyman 2017; Pani 2017].

Study characteristics and quality: The main characteristics of the 17 articles included in this meta-analysis are shown in Table 1. (Table 1) These articles were published between 2016 and 2021. Almost all these studies were non-randomized with respect to the anesthetic type and either a prospective or retrospective study, except for two controlled parallel-group trials with balanced randomization [Thiele 2020; Mayr 2016]. LA and GA groups were compared based on age, sex, logistic Euro Score, Society of Thoracic Surgeons (STS), NYHA III-IV, prior transient ischemic attack (TIA) or cerebrovascular accident (CVA), diabetes mellitus, hypertension, aortic valve area, value types and surgical approaches. The logistic Euro Score was significantly higher for the GA group in two studies [Mayr 2016; Pani 2017], and the hypertension was significantly higher in four studies [Martins 2019; Stragier 2019; Miles 2016; Hyman 2017]. Other significant differences in main characteristics are marked in Table 1. Rating of the quality of studies based on the NOS and the Cochrane Collaboration score is presented in Table 2 and Table 3. (Table 2) (Table 3) Quality scores ranged from 6 to 9. Three trials were determined as moderate quality [Brecker 2016; Hyman 2017; Pani 2017]; the others were considered as high (≧7).

Outcomes – Overall mortality: Fourteen studies including 19070 participants compared mortality at 30 days between the LA and GA groups [Thiele 2020; Martins 2019; Stragier 2019; He 2017; Husser 2018; Kesimci 2016; Jabbar 2016; Cuadrado 2016; Palermo 2016; D'Errigo 2016; Debry 2016; Miles 2016; Kiramijyan 2016; Hyman 2017]. The average 30-day mortality rate, which was 189 of 5921 patients in the LA group and 564 of 13149 patients in the GA group, demonstrated statistically significant differences between the

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Table 1. Main characteristics of studies included in the analysis between LA and GA

Source	*N*		Age (years)	Female (%)	Logistic EuroS-core	STS score	NYHA III-IV	Prior TIA or CVA	DM (%)	HTN (%)	AVA (cm^2)	Valve	Access site
Thiele 2020	LA	218	81.8	50.9	13.8	4.5	69	NA	32.1	91.3	0.7	EV MCV	TF
	GA	220	81.4	51.4	15.6	5.1	62.9	NA	35.2	90.0	0.8	EV MCV	TF
Martins 2019	LA	47	82	51.1	NA	NA	72.3	10.6	29.8	91.5*	0.63	NA	TF TSC
	GA	102	81	59.8	NA	NA	60.8	15.7	28.4	76.5*	0.61	NA	TF TSC
Stragier 2019	LA	93	86.3	46.2	9.6	NA	68.8	16.1	22.6	94.7*	NA	EV	TF
	GA	85	81.7	51.8	10.1	NA	81.2	11.8	24.7	82.4*	NA	EV	TF
He 2017	LA	77	74.09	31.17	NA	NA	70.13	NA	16.9	54.6	NA	MCV	TF
	GA	36	75.94	41.67	NA	NA	83.33	NA	19.4	47.2	NA	MCV	TF
Husser 2018	LA	2624	81	58.6	15	4.6	84.1	NA	11.6	90.6	NA	EV MCV DFM etc	TF
	GA	2624	81	58.2	15	4.5	84.8	NA	12.1	90.5	NA	EV MCV DFM etc	TF
Kesimci 2016	LA	72	77.4	44.4*	NA	NA	NA	13.9*	8.3*	NA	NA	EV MCV	TF TA
	GA	79	76.3	68.4*	NA	NA	NA	3.8*	27.8*	NA	NA	EV MCV	TF TA
Jabbar 2016	LA	71	80.2	NA	18.8	NA	14.1	NA	15.5	NA	0.67	EV DFM	TF
	GA	145	80.9	NA	18.5	NA	13.1	NA	18.6	NA	0.66	EV DFM	TF
Cuadrado 2016	LA	65	82.37	69	NA	NA	NA	NA	34	83	0.62	EV MCV	TF
	GA	35	83.65	66	NA	NA	NA	NA	40	85	0.56	EV MCV	TF
Palermo 2016	LA	44	85.4*	31.8	13.5	6.9	NA	11.4	29.5	77.3	0.64	MCV	TF
	GA	21	79.6*	23.8	13.1	6.2	NA	19	42.9	81	0.74	MCV	TF
D'Errigo 2016	LA	310	82.7	35.5	13.3	NA	69.4	NA	29.4	NA	0.6	EV	TF
	GA	310	82.0	38.1	13.4	NA	67.1	NA	29	NA	0.6	EV	TF
Debry 2016	LA	52	81	19.2	20.9	8.7	80.7	11.5	23	NA	0.42	EV MCV etc	TC
	GA	122	80.3	34.7	19.5	7.3	85.2	14.7	35.2	NA	0.43	EV MCV etc	TC
Mayr 2016	LA	31	84	42	11.66*	5.0	71	NA	NA	NA	0.63	MCV	TF
	GA	31	80	58	9.72*	4.3	77	NA	NA	NA	0.70	MCV	TF
Brecker 2016	LA	245	81.3	51.4	16.1	5.3	79.2	12.7	24.5	NA	0.7	MCV	TF, TSC
	GA	245	81.6	53.1	16.3	5.2	78.8	11.8	24.1	NA	0.7	MCV	TF, TSC
Miles 2016	LA	44	81.5*	34	NA	NS	86	18	27	73*	NA	EV	TF
	GA	44	77.8*	25	NA	NA	82	18	46	48*	NA	EV	TF
Kiramijyan 2016	LA	467	82.9	49.4	NA	8.5*	87	12.2	33.8	93.8	0.67	EV MCV	TF
	GA	66	81.3	50	NA	9.8*	93.5	13.1	35.5	88.7	0.69	EV MCV	TF
Hyman 2017	LA	1737	82.4*	45.8	NA	NA	79.2*	12.1	38.2	91.1*	0.7	EV MCV	TF
	GA	9260	81.8*	46.4	NA	NA	81.6*	11.9	37.7	89.3*	0.7	EV MCV	TF
Pani 2017	LA	961	81.8	53.3	19*	NA	73.5	9.2	28.5	NA	0.4	MCV	TF TC TSC
	GA	355	81.2	53.0	21*	NA	69.6	9.6	30.8	NA	0.4	MCV	TF TC TSC

STS, Society of Thoracic Surgeons; NYHA, New York Heart Association; EV, Edward Value (Edward Sapien; Sapien XT; Cribier Edwards; Edwards Life science); MCV, Medtronic Core Valve; MC, MitraClip®; TIA, transient ischemic attack; CVA, cerebrovascular accident; DM, diabetes mellitus; HTN, hypertension; AVA, aortic valve area; TF, transfemoral; TA, transaxillary; TSC, transsubclavian; TA, transaortic. *significant difference

Table 2. Newcastle-Ottawa Assessment Scale for cohort studies and case-control studies

Source cohort studies	Selection			Comparability			Outcome			Total
	Representativeness	Selection of controls	Ascertainment of exposure	Outcome not present at start	On age	On other risk factors	Assessment of outcome	Long enough follow-up	Adequacy of follow-up	
Martins 2019	1	1	1	1	1	0	1	1	1	8
Stragier 2019	1	1	1	1	1	0	1	1	1	8
He 2017	1	1	1	1	1	1	1	1	1	9
Husser 2018	1	1	1	1	1	1	1	1	1	9
Kesimci 2016	1	1	1	1	1	0	1	1	1	8
Jabbar 2016	1	1	1	1	1	1	1	1	0	8
Cuadrado 2016	1	1	1	1	1	1	1	1	1	9
D'Errigo 2016	1	1	1	1	1	1	1	1	1	9
Debry 2016	1	1	1	1	1	1	1	1	1	9
Brecker 2016	1	1	1	1	1	0	1	0	0	6
Miles 2016	1	1	1	1	1	0	1	1	0	7
Kiramijyan 2016	1	1	1	1	1	0	1	1	1	8
Hyman 2017	1	1	1	1	0	0	1	1	0	6
Pani 2017	1	1	1	1	1	0	1	0	0	6
Palermo 2016	1	1	1	1	1	0	1	1	1	8

Table 3. Cochrane Collaboration Assessment Scale for randomized controlled trials

Source	Random sequence generation	Allocation concealment	Blinding – Participants	Blinding-Outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Thiele 2020	Low risk	Low risk	High risk	Unclear	Low risk	Low risk	Low risk
Mayr 2016	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Low risk

two groups. The mortality of the LA group was lower than the GA group. The overall pooled RR of mortality at 30 days was 0.69 [95%CI 0.57 to 0.82; I^2=0%]. (Figure 2)

Procedural time: Five studies compared procedural time between the LA and GA groups [Kesimci 2016; Jabbar 2016; Palermo 2016; Miles 2016; Hyman 2017]. The LA group experienced a statistically significant short procedural time when compared with the GA group. The overall difference in means was -0.38 [95%CI -0.74 to -0.01; I^2=88.7%]. (Figure 3)

New pacemaker implantation: Data for the need of definitive new pacemaker implantation postoperatively between the LA and GA groups were extracted from 12 trials [Martins 2019; Stragier 2019; He 2017; Husser 2018; Kesimci 2016; Jabbar 2016; D'Errigo 2016; Debry 2016; Miles 2016; Kiramijyan 2016; Hyman 2017; Pani 2017]. As Figure 4 shows, the LA group yielded a statistical significance in the need of pacemaker implantation when compared with GA (RR 1.08; [95%CI 1.00 to 1.16; I^2=25.5%). (Figure 4)

Total stay in hospital: Five studies including 11437 patients compared the total stay in hospital between the two groups [He 2017; Palermo 2016; Debry 2016; Miles 2016; Hyman 2017]. In LA for TAVI, there was no significantly longer hospital stay when compared with GA (SMD -0.28; [95%CI -0.58 to 0.02; I^2=79.4%]). (Figure 5)

The use of the vasoactive drug: The use of the vasoactive drug was reported in five studies [Martins 2019; Stragier 2019; He 2017; Miles 2016; Hyman 2017]. LA was associated with significantly higher use of the vasoactive drug (RR 0.57; [95%CI 0.42 to 0.78; I^2=89.4%]. (Figure 6)

Intra-and postoperative complications and emergencies: A comprehensive analysis of these complications, such as myocardial infarction, pulmonary complication, vascular complication, renal injury/failure, stroke, life-threatening/major bleeding, and cardiac tamponade, was suggested. Both groups did not statistically differ in the incidence of myocardial infarction, vascular complication, renal injury/failure, stroke, cardiac tamponade, except pulmonary complication and life-threatening/major bleeding. As Figure 7 shows, for the incidence of pulmonary complication [Thiele 2020; Martins 2019; He 2017; Husser 2018; Cuadrado 2016], the RR was 0.54 [95%CI 0.41 to 0.72;

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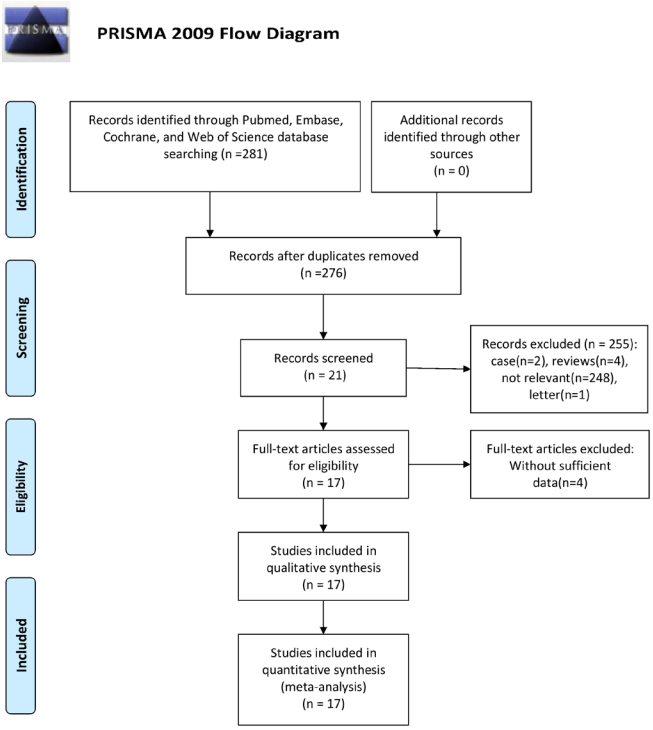

Figure 1. Flow chart for selection of studies for inclusion in this meta-analysis

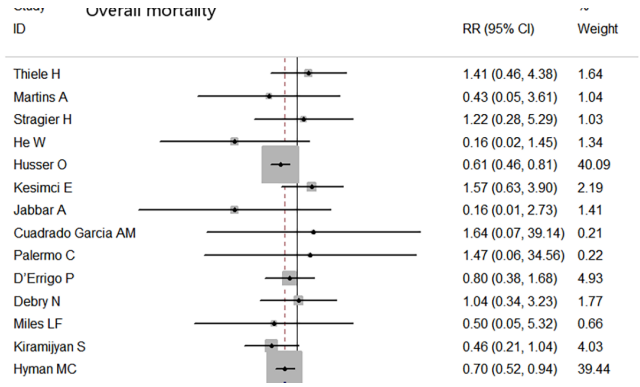

Figure 2. Forest plot of risk ratios for 30-day mortality. 95% CI, 95% confidence interval; RR, risk ratio

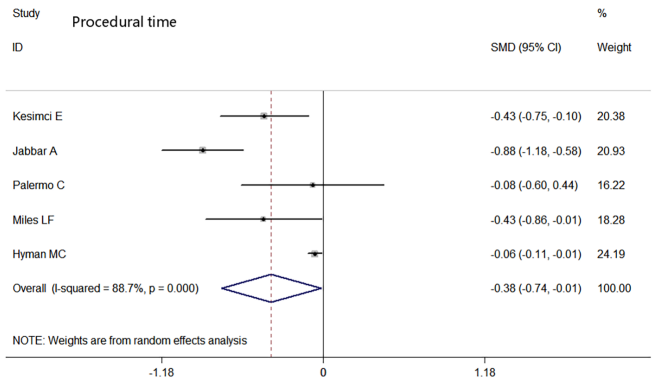

Figure 3. Forest plot for procedure time (minutes). 95% CI, 95% confidence interval; SMD, standard mean difference

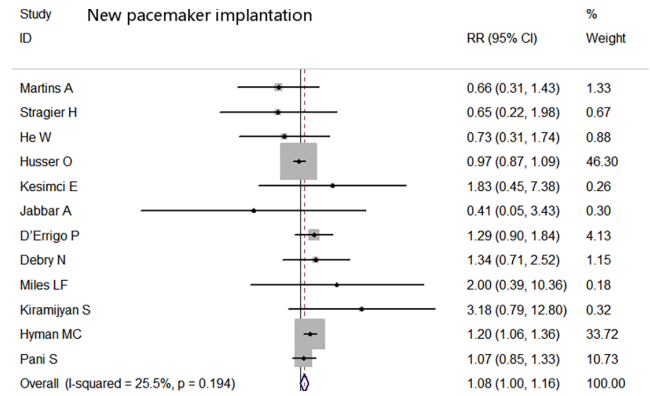

Figure 4. Forest plot of risk ratios for new pacemaker implantation. 95% CI, 95% confidence interval; RR, risk ratio

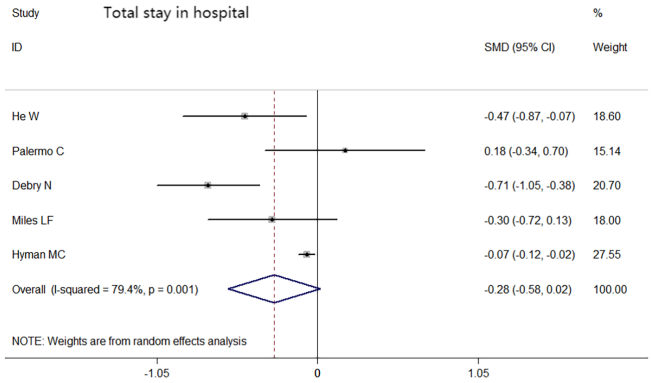

Figure 5. Forest plot of total stay in hospital (days). 95% CI, 95% confidence interval; SMD, standard mean difference

I^2=21.4%], the RR of life-threatening/major bleeding was 0.85 [95%CI 0.77 to 0.94; I^2=0%] in eight studies [Thiele 2020; Martins 2019; Stragier 2019; Husser 2018; Jabbar 2016; D'Errigo 2016; Debry 2016; Miles 2016; Kiramijyan 2016]. (Figure 7)

The incidence of emergency PCI in four studies [Jabbar 2016; Cuadrado 2016; D'Errigo 2016; Miles 2016] that included 1024 participants during intra-and post operation yielded statistically significance between the two groups (RR 1.31; [95%CI 0.25 to 6.88; I^2=11.6%]). The incidence of transesophageal echocardiography was reported in three studies [Thiele 2020; Jabbar 2016; Kiramijyan 2016] that

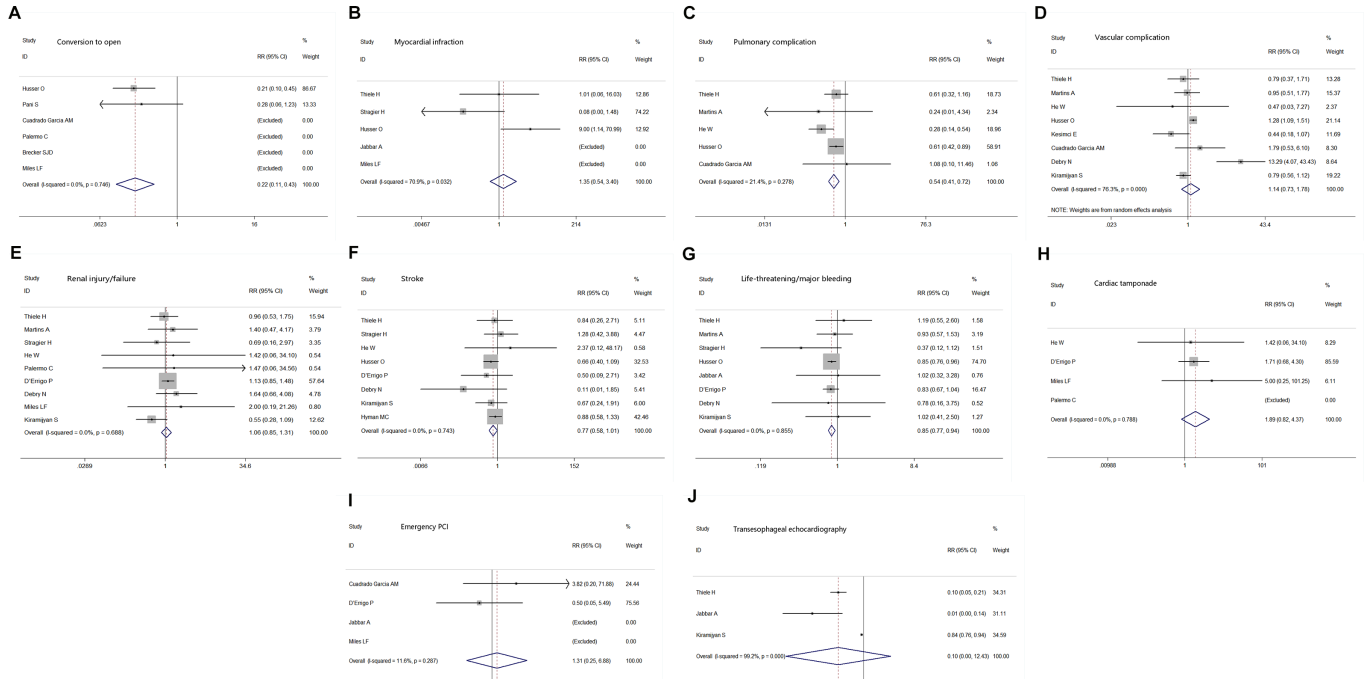

Figure 6. Forest plot of the use of vasoactive drug. 95% CI, 95% confidence interval; RR, risk ratio

included 1187 participants (RR 0.10; [95%CI 0.00 to 12.43; I^2=99.2%]). The difference in the incidence of conversion to open between the two groups (RR 0.22; [95%CI 0.11 to 0.43; I^2=0.0%]) was statistically significant. However, there was no statistical significance for other common complications, such as myocardial infarction (RR 1.35; [95%CI 0.54 to 3.40; I^2=70.9%]), vascular complication (RR 1.14; [95%CI 0.73 to 1.78; I^2=76.3%]), renal injury/failure (RR 1.06; [95%CI 0.85 to 1.31; I^2=0.0%]), stoke (RR 0.77; [95%CI 0.58 to 1.01; I^2=0.0%]), and cardiac tamponade (RR 1.89; [95%CI 0.82 to 4.37; I^2=0.0%]) between the two groups. All results comparing each analyzed data point between LA and GA are presented in Table 4. (Table 4)

Subgroup analysis of overall mortality based on STS score: Five studies listed patients' STS scores between the LA and GA groups [Thiele 2020; Husser 2018; Palermo 2016; Debry 2016; Kiramijyan 2016]. STS scores that ranged from 4 to 6 and were considered low-risk groups [Thiele 2020; Husser 2018]. The STS score range from 7 to 9 was considered a high-risk group [Palermo 2016; Debry 2016; Kiramijyan 2016]. In the low-risk group, LA experienced statistical significance over mortality when compared with GA. The overall pooled RR of mortality was 0.64 [95%CI 0.49 to 0.84; I^2=50.4%]. The LA group yielded a statistical significance of mortality when compared with GA in the high-risk group (RR 0.67; [95%CI 0.36 to 1.27; I^2=0.0%). (Figure 8)

DISCUSSION

Up until now, TAVI has become a less invasive percutaneous procedure as an alternative management option for serious AS patients, accompanying with the forthcoming of percutaneous suture devices. The selection between GA and LA with or without sedation is a point of dispute. Generally, there is no consensus regarding which methods should be preferred and reached. The difference in safety and efficacy of GA and LA has been studied in the present meta-analysis. Outcomes of the analysis of 15 case-control studies and two cohort studies provisionally suggest that LA is not statistically significant and independently associated with GA of new pacemaker implantation, total stay in the hospital, emergency PCI and some certain intra and post-procedural endpoints, such as myocardial infarction, vascular complication, renal injury/failure, stroke, and cardiac tamponade. Compared with the LA group, patients who had TAVI performed under GA experienced a significantly increased procedure time, mortality in hospital, use of the vasoactive drug, the time's conversion to open, pulmonary complications, life-threatening/major bleeding.

Our results were conducted mostly in accordance with the finding by Pedro A. Villablanca published in 2017, which included 10572 patients from 26 individual studies in a systematic review [Villablanca 2018]. The incidence of 30-day mortality, stroke, myocardial infarction, renal injury, and vascular complication was similar between the two meta-analyses. Otherwise, Villablanca reported the length of hospital stay was significantly shorter in the LA group among patients undergoing TAVI. In our analyses, there was no significantly longer hospital stay in LA for TAVI when compared with GA. The result was unsimilar from ours because we excluded the articles when the study offered

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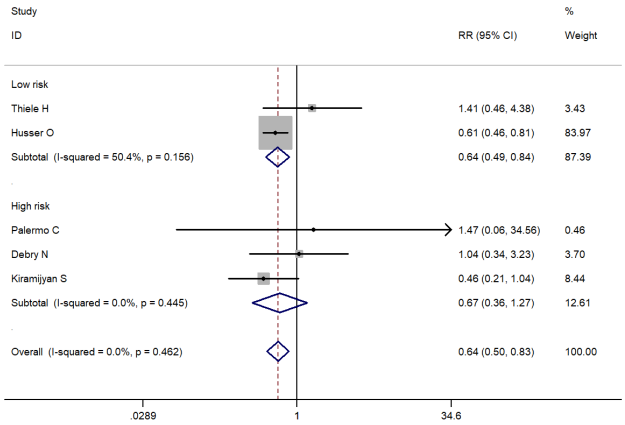

Figure 7. Forest plot of risk ratios for intra-and postoperative complication. A) conversion to open; B) myocardial infarction; C) pulmonary complication; D) vascular complication; E) renal injury/failure; F) stroke; G) life-threatening/major bleeding; H) cardiac tamponade; I) emergency PCI; J) transesophageal echocardiography. 95% CI, 95% confidence interval; RR, risk ratio

medians and included means and SDs; we did not calculate medians into the means and SDs, considering the accuracy of the data. Although the number of included articles was smaller, it increased the stability of the results after sensitivity analysis, supported the validity of the results, and proved the rationality of the conclusion. We double the number of selected articles compared with Villablanca's study, with a total of 17 articles enrolled and based on accepted guidelines with 20938 patients and conducted a newest search from January 1, 2016 to July 1, 2021. Ehret et al.'s meta-analysis, which totally collected one RCT and 19 observational studies from 1 January 2006 to 26 June 2016 that compare LA to GA in an adult study population, also was published in 2017 [Ehret 2017]. Ehret et al. concluded there was no significant difference in 30-day mortality between the LA and GA groups. However, the confidence interval was large, and when we increased the sample size, the difference was very significant. This result is consistent with that of Villablanca. In our analysis, there were significant differences between the LA and GA groups, in terms of life-threatening/major bleeding, pulmonary complication, and the usage of vascular activators. This also is one of the reasons for the difference in 30-day mortality. In the GA group, the increased mortality was attributable to the use of endotracheal intubation, mechanical ventilation, and hemodynamic instability. Besides, Fröhlich's quantitative synthesis included 1,542 patients from seven non-randomized studies and was short of prospective observation [Holmes 2012]. Also, we provide more primary safety endpoints with the closest contact comparison between LA and GA. In addition, we added two single centers, controlled parallel-group trials with a balanced randomization study, and include not only perspective but also retrospective ones.

GA can alleviate pain while maintaining immobility of the body and guarantee airway safety, by placing the patient in a state of "unconsciousness" through a variable intermixture of an intravenous agent, muscle relaxants, and endotracheal intubation. In particular, the complete immobilization of patients is influential when the prosthesis valve deploys in the correct position. Using the different sizes of the sheath through the femoral or subclavian artery can be poorly tolerated or awakened in conscious sedated patients. As we all know, patients under conscious sedation can significantly increase the risk of respiratory depression, especially the octogenarians and fragile patients. It will be difficult to balance the proper conscious sedation and maintain airway patency. Under GA, the airway can be protected by endotracheal intubation and endotracheal intubation. GA also can facilitate the utilization of transesophageal echocardiography (TEE) by cardiologists. TEE usually is required in the initial training period if the transthoracic echocardiographic (TTE) images are of poor quality to portray the aortic valve or root anatomy. TEE, providing real-time three-dimensional geometry, has proven to be a standard method in monitoring the valve size decision, left ventricular outflow tract during interoperation of TAVI [Guarracino 2016]. TEE almost always necessitates GA and endotracheal intubation, because of the intolerance of an awake patient. GA is indicated for patients who suffer from Parkinson's, dyspnea, orthopnea, or neurological alterations and can provide a comfortable scenario without pain during TAVI [Ben-Dor 2012; Babaliaros 2014]. GA also is strongly performed by less experienced cardiologists when the TAVI team's competence is limited. Besides, advanced cardiac life support, mechanical circulatory support, and cardiopulmonary bypass can be instituted by the cardiovascular anesthesiologist as quickly as possible if necessary. If life-threatening complications (aortic annular rupture, aortic perforation, pericardial tamponade, massive hemorrhage, and acute aortic dissection, etc.) occur, GA is more quickly and easily able to resuscitate and stabilize the patient.

Avoiding GA, LA also presents several other advantages, such as lower mortality in hospital, lower risk of life-threatening/major bleeding, lower risk of intraoperative conversion to thoracotomy, lower the incidence of pneumonia, lower the duration of intraoperative operation, and fewer vasoactive drugs. In the low-risk group (STS score:4-6), LA experienced statistically significant mortality when compared with GA. In our study, the mean operative procedural time for LA was 128.74 minutes, while the mean operative procedural time for GA was 144.46 minutes. The additional requirements of anesthesia induction and recovery may be the main reason for prolonged operation time. Patients who underwent GA were more likely to require vasoactive drug treatment. With the cardiac depressant effect of the intravenous agent under GA, it may trigger cardiovascular instability and collapse, because of the patient's elder and fragile physical condition. Hypotension and bradycardia are especially common during anesthesia induction, so the need for vasopressor medication will certainly increase during the procedure. LA instead requires a reduced need for vasopressor medication, due to its stable hemodynamics. As is known, uncontrolled hemodynamic alterations induced by anesthesia induction can significantly increase the perioperative danger

Table 4. The results comparing each analyzed data point between LA and GA

Outcomes	No. of studies	Test of association			Test of heterogeneity	
		RR (SMD)	95%CI	Weight (%)	I^2 (%)	*P*
Overall mortality	14	0.69	0.57 to 0.82	100	0	0.600
Procedural time	5	-0.38	-0.74 to -0.01	100	88.7	0.000
New pacemaker implantation	12	1.08	1.00 to 1.16	100	25.5	0.194
Total stay in hospital	5	-0.28	-0.58 to 0.02	100	79.4	0.001
The use of vasoactive drug	5	0.57	0.42 to 0.78	100	89.4	0.000
Myocardial infarction	5	1.35	0.54 to 3.40	100	70.9	0.032
Pulmonary complication	5	0.54	0.42 to 0.72	100	21.4	0.278
Vascular complication	8	1.14	0.73 to 1.78	100	76.3	0.000
Renal injury/failure	9	1.06	0.85 to 1.31	100	0.0	0.688
Stroke	8	0.77	0.58 to 1.01	100	0.0	0.743
Life-threatening/major bleeding	8	0.85	0.77 to 0.94	100	0.0	0.855
Cardiac tamponade	4	1.89	0.82 to 4.37	100	0.0	0.788
Emergency PCI	4	1.31	0.25 to 6.88	100	11.6	0.287
Transesophageal echocardiography	3	0.10	0.00 to 12.43	100	99.2	0.000

in patients affected by severe AS. LA also presents a lower risk of patients with pulmonary complications, such as pulmonary edema, pneumonia, respiratory depression, and refractory bronchospasm in comparison with GA controlled by mechanical ventilation. Whatever anesthetic drug or mechanical ventilation, once patients are associated with depressed ventilation or hypercapnia, the pulmonary complication can probably turn worse. Nevertheless, LA limits the use of TEE for procedural guidance. Real-time TEE monitoring during TAVI is commonly performed under GA and requires endotracheal intubation because of the toleration of awake patients. However, Guarracino once selected awake patients under profound sedation to perform intraoperative TEE via noninvasive ventilation (NIV) face mask [Thiele 2020]. Combined with the modified facial mask, patients under deep sedation can tolerate the discomfort induced by the TEE probe, and adequate ventilation also can be maintained throughout the procedure. Bartel et al. provided a potential replacement for TEE in the intracardiac echocardiography (ICE) [Bartel 2016]. ICE guidance has been demonstrated to be effective and safe for solving the common dilemma that TAVI almost always necessitates GA and endotracheal intubation combined with TEE.

LIMITATIONS

The present meta-analysis was based on 15 non-randomized studies, with respect to the anesthetic type and either prospective or retrospective studies and only two controlled parallel-group trials with balanced randomization. The following limitations should be considered when interpreting these results. First, the nonuniform definitions of some endpoints might result in the emergence of heterogeneity among the different studies. Second, patients were not randomized with regard to the standardized anesthesia techniques, both LA and GA. Moreover, the outcome of LA-only performance of might be different from that of the LA-plus sedation performance. Besides, a further identifier for the selection of severe LA patients might cause a selection bias, which could be hardly discriminated in the present meta-analysis.

CONCLUSIONS

To conclude, we believe that both anesthetic regimens are suitable for TAVI and suggest a more careful preoperative evaluation to determine the best strategy for each patient. Of course, more prospective, large-scale, and randomized controlled trials should be warranted to confirm any firm conclusions. In general, LA with or without sedation may be an optimal alternative to GA in TAVI in appropriate patients. LA appears a feasible alternative to GA for AS patients undergoing TAVI.

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