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ORIGINAL STUDIES

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Comparison of single versus dual antiplatelet therapy after TAVR: A systematic review and meta-analysis

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Abstract

Objective: We aim to evaluate the efficacy of dual versus single anti-platelet therapy (SAPT) after TAVR through a systematic review and meta-analysis of published research.

Background: Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel is a commonly practiced strategy after transcatheter aortic valve replacement (TAVR). However, there is lack of sufficient evidence supporting this approach.

Method: We searched PubMed, EMBASE, the Cochrane Central Register of Controlled trials, and the clinical trial registry maintained at clinicaltrials.gov for randomized control trials (RCT) and observational studies comparing DAPT with SAPT post TAVR. Event rates were compared using a forest plot of relative risk with 95% confidence intervals using a random-effects model assuming inter-study heterogeneity.

Results: A total of six studies (3 RCTs and 3 observational studies, $n = 840$) were included in the final analysis. Compared to SAPT, DAPT was associated with increased risk of significant bleeding (life threatening and major) [RR = 2.52 (95% CI 1.62–3.92, $P < 0.0001$)] with the number needed to harm for major or life-threatening bleeding calculated to be 10.4. There was no significant difference in the incidence of stroke [RR = 1.06 (95% CI, 0.43–2.60, $P = 0.90$)], spontaneous myocardial infarction [RR = 2.08 (95% CI, 0.56–7.70, $P = 0.27$)] and all-cause mortality [RR = 1.18 (95% CI, 0.68–2.05, $P = 0.56$] in the DAPT and SAPT groups.

Conclusion: In this small meta-analysis of DAPT versus SAPT after TAVR, DAPT did not prevent stroke, myocardial infarction or death while the risk of bleeding was higher. Results from ongoing trials are awaited to determine the best anti-thrombotic approach after TAVR.

KEYWORDS

anthithrombotic, antiplatelet, aspirin, P2Y receptor antagonist, TAVI, TAVR, transcatheter aortic valve implantation, transcatheter aortic valve replacement

1 | INTRODUCTION

TAVI has now become a viable therapy for patients with severe aortic stenosis who are at increased surgical risk, and has also shown encouraging initial results even among low-risk patients [1–3]. TAVR is associated with several intraprocedural and postprocedural complications [4]. Efforts have been mainly focused to reduce the risks of thromboembolic events and paravalvular leak. Incidence of stroke is still in the 4–10% range for all strokes, and 2–3% for major strokes [5]. However, leaflet thrombosis with its potential complications like stroke and decreased valve durability is the focus of recent investigations [6].

Early antithrombotic regimens in TAVR were based on experience from implantation of coronary stents. Grube et al. in a 2006 study, first reported using aspirin 100 mg day^{-1} and clopidogrel 75 mg day^{-1}

indefinitely in all TAVI patients and a 300 mg clopidogrel loading dose in most of the patients (21 out of 25) before undergoing TAVI [7]. Current guidelines recommend dual anti-platelet therapy (DAPT) with aspirin (ASA) and clopidogrel for first 3–6 months after TAVR in individuals without an indication for oral anticoagulation (OAC) [1,2]. These recommendations are based on expert consensus derived from limited observational data. Randomized trials like the PARTNER trial used DAPT for 6 months and the CoreValve trial used DAPT for 3 months followed by aspirin or clopidogrel monotherapy indefinitely [8,9]. Recently, few dedicated RCTs have attempted to compare DAPT with single antiplatelet therapy (SAPT), however were underpowered to assess for differences in individual end-points [10,11]. Further, previous meta-analyses either included limited RCT data or had patients on oral anticoagulation leading to potential for bias [12,13]. Therefore, optimal antithrombotic strategy after TAVR remains an important knowledge gap that has resulted in a large variability, ranging from triple therapy (DAPT + OAC) to either DAPT or OAC alone. Accordingly, we conducted an updated systematic review and meta-analyses of the published literature to assess outcomes with DAPT versus SAPT in patients after TAVR.

2 | METHODS

2.1 | Study design

This meta-analysis was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-analysis of Observational studies in Epidemiology) guidelines [14,15].

We carried out a literature search using MEDLINE, EMBASE, EBSCO, CINAHL, Web of Science and Cochrane databases, of all studies published between January 1, 2000, and July 31, 2017, reporting on comparison between DAPT and SAPT for patients who underwent TAVR. No language restrictions were applied. We used the following MeSH search headings: "transcatheter aortic valve implantation," "transcatheter aortic valve replacement," "TAVI," "TAVR." "antiplatelet," "anthithrombotic," "aspirin," and "P2Y receptor antagonist."

The following criteria were applied for study inclusion: (1) RCTs and observational studies, preferably with propensity matched samples, comparing DAPT and SAPT after TAVR; (2) published in peer reviewed journals; (3) mean follow-up of at least 1 month; (4) reporting at least one clinical end-point based on antiplatelet approach. Exclusion criteria were: (1) studies reporting use of oral anticoagulation (OAC) either alone or combined with APT; (2) abstract presentations or non-published studies.

2.2 | Data collection

Two reviewers (HR and AG) independently screened study reports for eligibility, assessed risk of bias, and collected data from each eligible study using pre-determined forms. Any disparities between the two investigators were discussed with a third investigator (SG) until consensus was reached.

We collected information on study characteristics (study design, year of publication, inclusion and exclusion criteria, sample size, antiplatelet regimen and dose, length of follow-up, funding source, and primary and secondary end-point definitions), baseline patient characteristics, transcatheter valve systems (balloon expandable or self expandable), and event-rate of primary and secondary outcomes from the studies that met inclusion criteria. Included studies were also assessed for quality using the Cochrane guidelines for risk of bias assessment [16]. We compared the two groups for the following outcomes: all-cause mortality, stroke, myocardial infarction (MI), and major and life threatening bleeding at the longest available follow-up.

2.3 | Statistical analysis

We conducted this meta-analysis according to recommendations from the Cochrane Collaboration using Review Manager, version 5.3 [17]. We undertook independent pooling of data from RCTs and observational studies to minimize the risk of bias. For each clinical end-point, pooled risk ratio (RR) and 95% confidence interval (CI) were calculated using the random-effects model with the Mantel-Haenszel method. A P value of <0.05 was assigned as the measure of statistical significance. Heterogeneity between studies was calculated using the I^2 statistic. Heterogeneity was considered significant if the $I^2 > 50\%$. Further, forest plots were generated to show the relative effect size of DAPT versus SAPT for each clinical outcome.

3 | RESULTS

3.1 | Study characteristics

As reported in Figure 1, the initial search identified 191 publications that were screened at abstract level. Fourteen reports were eligible for full-text review after exclusion of duplicate and irrelevant studies. After full-text review, six studies (three RCTs and three observational studies) were included in the final analysis [10,11,18–21]. Out of three observational studies, two studies reported propensity-matched patient and outcomes data [19,20]. Together, these studies included a total of 840 patients (using propensity matched); 404 treated with DAPT and 436 treated with SAPT. The mean duration of follow up was 4.8 months (range: 1–12 months).

Characteristics of individual studies, including definitions of primary and secondary end-points are described in Table 1. All included studies were low to intermediate-bias risk studies as assessed by the Cochrane metrics for quality assessment risk (Supporting Information table) [11]. Overall, patients in the two arms were well matched for baseline characteristics (Table 2). The mean age of patients was 81.6 years, and 59% were males. Among SAPT group, five studies exclusively utilized aspirin [10,11,18,20,21]; clopidogrel was utilized in case of prior aspirin use in one study [19]. Similarly, clopidogrel was used exclusively in the DAPT group in four studies [10,18,19,21], whereas two studies used either clopidogrel or ticlopidine [11,20]. Four studies

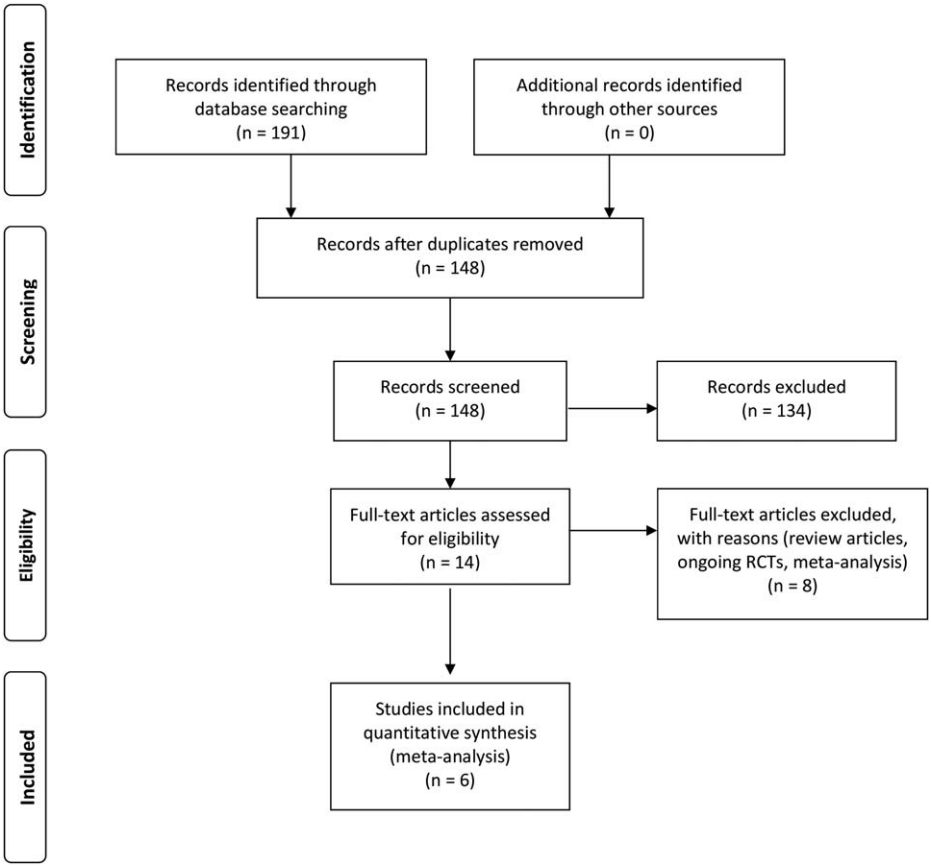

FIGURE 1 Flowchart describing systematic literature search and study selection process

reported administration of loading clopidogrel dose of 300 mg as their protocol [10,18,19,21]. Finally, duration of DAPT varied across studies; 1–6 months [19], 3 months [10,18] and 6 months [11,20,21].

3.2 | Outcomes

All-cause mortality occurred in 48 patients (6.4%) among 752 patients included in 5 studies (Figure 2) at the end of longest reported follow-up, with no significant differences in DAPT compared with SAPT [RR 1.18; 95% CI 0.68–2.05]. Similar findings were noted in the analyses of RCTs and observational studies when pooled separately [RR 1.07; 0.48–2.41, RR 1.34; 0.51–3.48, respectively].

In 5 studies involving 752 patients, stroke or TIA occurred in 20 patients (2.6%) at the longest reported follow up (Figure 3) with similar risks between DAPT and SAPT [RR 1.06; 95% CI 0.43–2.60] in the pooled analysis. No significant differences in stroke or TIA were observed with RCTs [0.93; 0.28–3.06] as well as observational studies [1.25; 0.32–4.92].

Incidence of MI was low (1.3%) among 752 patients included in 5 studies. Risk of MI was not significantly different in DAPT versus SAPT [RR 2.08; 95% CI 0.56–7.70] (Figure 4). The results were consistent between RCTs [3.62; 0.60–21.76] and observational studies [1.18; 0.14–9.98].

Major and life-threatening bleeding was reported in 92 (10.9%) patients among 6 studies involving 840 patients at the longest reported follow up. Overall, risk of bleeding was significantly higher in DAPT arm compared to SAPT arm [RR 2.52; 95% CI 1.62–3.92, $P < 0.0001$] (Figure 5). Pooled estimates of observational studies showed a consistent risk [3.24; 1.82–5.75]; however, a nonsignificant trend was noted for RCTs [1.75; 0.88–3.50]. Number needed to harm was calculated as 10.4.

Finally, there was no significant heterogeneity observed between studies for each end-point.

3.3 | 30-day analysis

A smaller 30-day analysis was also performed including five out of six studies [10,11,18,19,21] which reported outcomes at 30-day follow up period. All-cause mortality occurred in 42 among 752 patients with no significant difference between DAPT and SAPT group [RR 1.17; 95% CI 0.64–2.12] (Supporting Information Figure 1). Myocardial Infarction occurred in 9 out of 752 patients with no significant difference in DAPT compared with SAPT [RR 1.94; 95% CI 0.46–8.16] (Supporting Information Figure 2). Major and life-threatening bleed was reported in 82 among 752 (10.9%) patients. The risk was significantly higher in DAPT group compared to SAPT group [RR 2.38; 95% CI 1.44–3.93, $P = 0.0007$] (Supporting Information Figure 3). Stroke/TIA outcomes were identical to that of the longest follow up period analysis (Supporting Information Figure 4).

TABLE 1 Study characteristics

Study	STABILE 2014	DURAND 2014	POLIACIKOVA 2013	USSIA 2011	ARTE 2017	ICHIBORI 2017
Design	Randomized	Prospective	Prospective	Randomized	Randomized	Retrospective
Multi-center/ Single-center	Single-center	Multicenter	Single-center	Single-center	Multicenter	Single-center
Combined/composite endpoint/primary endpoint	30-day mortality	Combination of mortality, major stroke, LTB, MI, and major vascular complications	MACE (all-cause mortality, ACE or stroke) and NACE (combined endpoint of all-cause mortality, ACE, stroke or major bleeding)	MACCE: Composite of death from any cause, MI, major stroke, urgent or emergency conversion to surgery, and LTB	Death, MI, stroke or TIA, or major or LTB at 3 months.	Composite end point: all-cause death, nonfatal MI, nonfatal stroke, and major or LTB.
Secondary endpoint	30-day bleedings and MACCE. 6-month valve failures and neurologic events	30-day transfusion, vascular complication, any stroke, any bleeding, acute kidney injury and success rate.	NA	NA	Incidence of MI, ischemic stroke, major or LTB, and death at 3 months.	NA
Inclusion criteria	1.Severe AS: AVA < 0.8 cm^2 (or AVA index <0.5 cm^2 m^{-2}) and mean AVG > 40 mm Hg or peak jet velocity > 4.0 m $s^{-1;}$ 2. Cardiac symptoms: NYHA functional class II, syncope; 3. High surgical risk.	1. Patients with symptomatic severe AS who were not candidates for surgical AV replacement; 2. AVA < 0.8 cm^2, mean aortic gradient 40 mm Hg or a peak aortic jet velocity 4.0 m s^{-1}; 3. NYHA functional class II/III/IV	All patients who underwent TAVI	1. Severe symptomatic AS with AVA < 1 cm^2; 2. Not candidates for standard AV replacement.	Patients with clinical indications for TAVR with a balloon-expandable valve.	Patients who underwent TAVI with balloon expandable valve.
Exclusion criteria	1. Aortic annular diameter < 18 mm or > 25 mm; 2. Aortic dissection, or iliac-femoral dimensions or disease precluding safe sheath insertion. 3. Untreated CAD requiring revascularization. 4. Severe AR or MR, or prosthetic valve. 5. Acute MI within 1 month. 6. UGI bleed within 3 months. 7. CVA or TIA within 6 months. 8. Any cardiac procedure, other than balloon aortic valvuloplasty, within 1 month or within 6 months of DES placement. 9. Indication for OAC. 10.Aspirin or thienopyridine intolerance/allergy.	No particular exclusion criteria.	None	1. Vascular disease that precluded access. 2. Severe deformation of the chest. 3. Intracardiac thrombus; 4. Unprotected stenosis of the left main coronary artery not amenable to PCI; 5. MI within 7 days; 6. Prosthetic heart valve 7. Active infection; 8. Blood dyscrasias or active bleeding or anemia. 9. Nondilatable aorta with a 23-mm aortic valvuloplasty balloon; 10. Aortic annulus size <19 mm or >24 mm; 11. Liver cirrhosis; 12. Recurrent PE; 13. Porcelain aorta; 14. Respiratory failure; 15. History of radiotherapy to mediastinum; 16. Severe connective tissue disease; 17. Previous PCI or MI requiring DAPT; 18. Need for OAC; 19. Allergy or intolerance to study drugs	Need for chronic anticoagulation treatment, major bleeding within the 3 months before the TAVR procedure, prior intracranial bleeding, DES implantation within the year before the TAVR procedure, and allergy to clopidogrel and/or aspirin.	Indication for OAC.

Abbreviations- MI: Myocardial Infarction; TIA: Transient Ischemic Attack; LTB: Life threatening bleed; TAVI: Trans-catheter Aortic Valve Implantation; TAVR: Trans-catheter Aortic Valve Replacement; OAC: Oral Anti-Coagulation; DES: Drug Eluting Stent; PCI: Percutaneous Coronary Intervention; UGI- Upper Gastrointestinal; DAPT: Dual Anti-platelet therapy; AS: Aortic Stenosis; AVA: Aortic Valve Area; AVG: Aortic Valve Gradient; CAD: Coronary artery disease, AR: Aortic Regurgitation, MR: Mitral Regurgitation.

TABLE 2 Baseline characteristics of patients included in the studies

Study	Stabile 2014		Durand 2014		Poliacikova 2013		Ussia 2011		ARTE 2017		Ichibori 2017	
	SAPT	DAPT	SAPT	DAPT	SAPT	DAPT	SAPT	DAPT	SAPT	DAPT	SAPT	DAPT
No. of patients	60	60	164	128	91	58	39	40	111	111	78	66
Age (y)	81.1 ± 4.8	80.2 ± 5.7	82.7 ± 6.3	84.6 ± 5.8	82 ± 6.9	81 ± 4	81 ± 4	80 ± 6	79 ± 9	79 ± 9	83 ± 6	84 ± 6
Female (%)	36 (60)	44 (66.7)	74 (45.1)	78 (60.9)	42 (46.2)	36 (44.8)	23 (59)	20 (50)	52 (46.8)	41 (36.9)	50 (64.1)	42 (63.6)
Euro Score (%)	25.1 ± 12	23.34 ± 8.15	20.0 ± 12.4	20.2 ± 11.6	–	–	21 ± 16	23 ± 15			24.2 ± 15.6	25.5 ± 18.5
STS score (%)	10.4 ± 6.8	9.7 ± 5.1	7.4 ± 6.1	6.9 ± 4.0	–	–	7 ± 3	8 ± 5	6.4 ± 4.6	6.2 ± 4.4	10.7 ± 7.4	12.2 ± 12.7
Diabetes (%)	17 (28.3)	15 (25)	40 (24.4)	30 (23.4)	16 (17.6)	16 (27.6)	8(21)	13(33)	36(32.7)	41 (36.9)	24 (30.8)	22 (33.3)
Dyslipidemia (%)	–	–	97 (59.1)	55 (43)	–	–	–	–			59 (75.6)	47 (71.2)
Hypertension (%)	57 (95)		116 (70.7)	90 (70.3)	–	–	31 (80)	35 (88)	87 (79.8)	86 (77.5)		
Previous CAD (%)	–	57 (95)	82 (50)	39 (30.5)	50 (54.9)	37 (63.8)	–	–			29 (37.2)	35 (53.0)
Previous MI (%)	–	–	22 (13.4)	14 (10.9)	–		4 (10)	7 (18)	20 (18.4)	26 (23.4)		
Previous CABG (%)	–	–	30 (18.3)	10 (7.8)	19 (20.9)	17 (29.3)	4 (10)	2 (5)	42 (38.5)	39 (35.1)	10 (12.8)	10 (15.2)
Previous stroke (%)	–	–	13 (7.9)	12 (9.4)	–	–	4 (10)	2 (5)			22 (28.2)	13 (19.7)
Peripheral artery disease (%)	–	–	28 (17.1)	10 (7.8)	–	–	4 (10)	3 (8)	22 (20.0)	28 (25.2)	–	–
Atrial fibrillation	–	–	37 (23)	45 (35.2)	10(11)	16 (27.6)	6 (15)	4 (10)			–	–
Chronic kidney disease (%)	–	–	12 (7.3)	11 (8.6)	5 (5.5)	3 (5.2)	5 (13)	6 (15)	70 (63.1)	70 (63.1)	–	–
EF (mean ± SD)	51.5 ± 11.0	52.4± 14.4	54.4 ± 13.6	60.5 ± 14.0	–	–	54 ± 8	51 ± 12	54 ± 13	55 ± 12	–	–
Aortic valve area (cm2)	–	–	0.61 ± 0.16	0.63 ± 0.14	0.71 ± 0.22	0.67± 0.17	0.6 ± 0.3	0.6 ± 0.2	0.40 ± 0.11	0.42 ± 0.13	0.70 ± 0.19	0.62 ± 0.17
PCI before index procedure (%)	14 (23.3)	13 (21.3)	–	–	20 (22)	16 (27.6)	9 (23)	12 (30)	–	–	11 (14.1)	25 (37.9)
Procedural access												
Trans-femoral	–	–	138 (84.1)	98 (76.6)	–	–	39 (100)	38 (95)	73 (65.8)	80 (72.1)	–	–
Trans-apical	–	–	24 (14.6)	30 (23.4)	–	–			20 (18.0)	18 (16.2)	42 (53.9)	29 (43.9)
Subclavian	–	–	2 (0.7)	2 (1.2)	–	–	0	2(5%)	–	–	–	–
Surgical cut-down	–	–	64 (45.7)	3 (3.1)	–	–			–	–	–	–

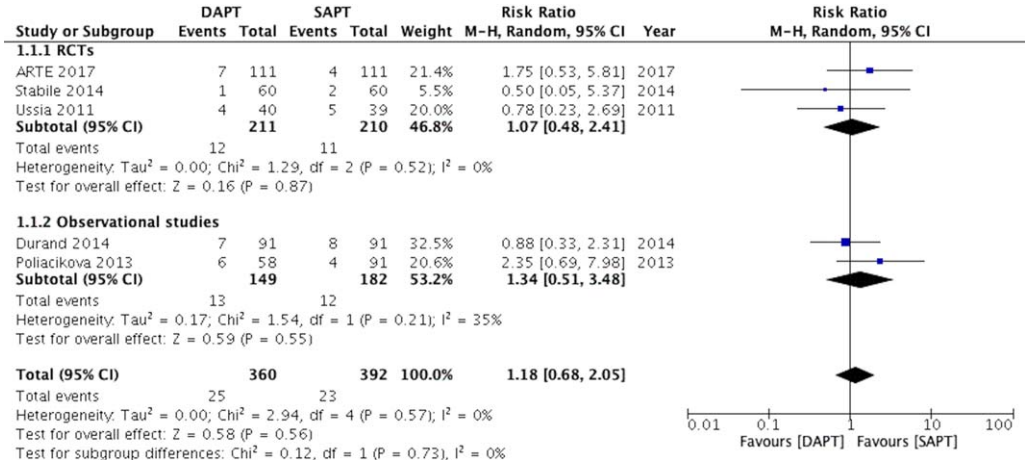

FIGURE 2 Forrest plot showing meta-analysis of all-cause mortality comparing dual versus single antiplatelet therapy [Color figure can be viewed at wileyonlinelibrary.com]

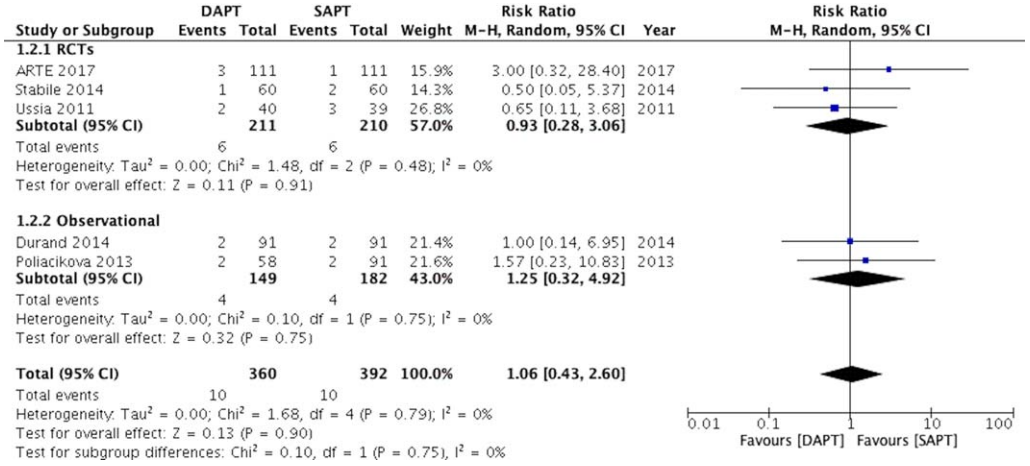

FIGURE 3 Forrest plot showing meta-analysis of stroke or TIA comparing dual versus single antiplatelet therapy. TIA: Transient ischemic attack [Color figure can be viewed at wileyonlinelibrary.com]

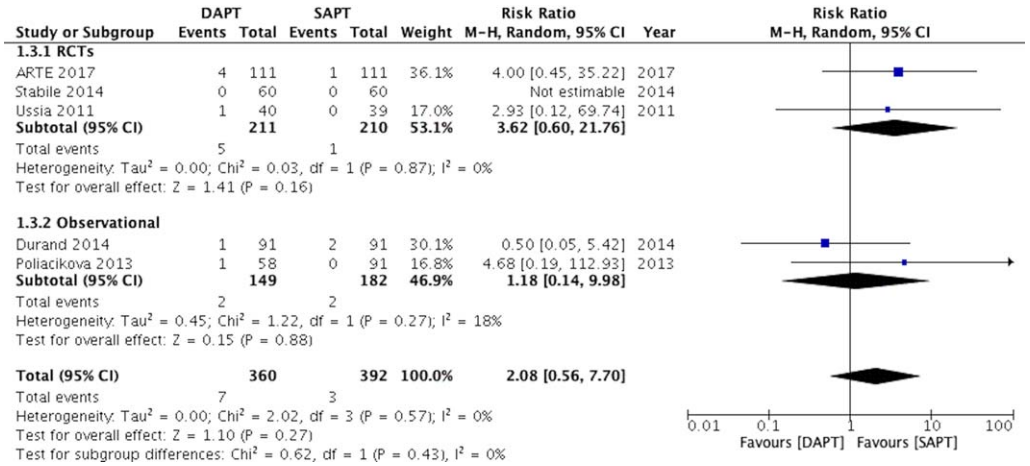

FIGURE 4 Forrest plot showing meta-analysis of myocardial infarction comparing dual versus single antiplatelet therapy [Color figure can be viewed at wileyonlinelibrary.com]

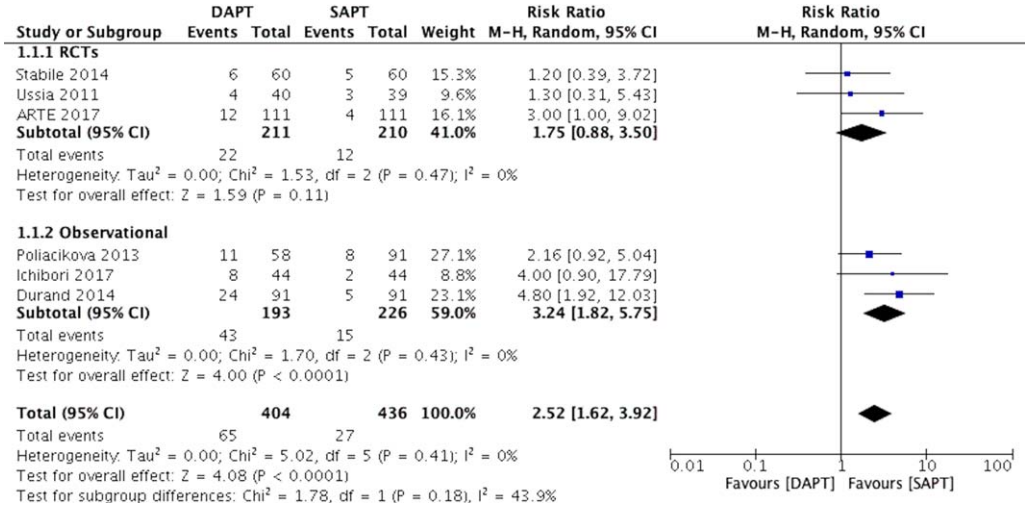

FIGURE 5 Forrest plot showing meta-analysis of major/life threatening bleed comparing dual versus single antiplatelet therapy [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

In this meta-analysis comparing DAPT versus SAPT after TAVR, DAPT did not prevent stroke, MI or mortality when compared with SAPT. Whereas, DAPT was associated with an increased risk of major and life-threatening bleeding as compared to SAPT. The outcomes of 30-day analysis were similar to that of the longest follow up period suggesting a consistent pattern over time.

The rationale for post-TAVR anti-thrombotic therapy stems from potential risk of thromboembolic events after TAVR. It has been shown that the risk of neurological events is highest in the first 3 months after TAVR [22]. While factors related to device implantation such as aorta manipulation and embolization of debris are the likely causative factor for stroke in immediate post-intervention period, valve thrombosis has been speculated in the later period. However, a recently published trial reported no benefit of DAPT in leaflet thrombosis prevention compared to SAPT, hence the role of DAPT after TAVR is questionable [23].

Previous meta-analyses comparing DAPT and SAPT after TAVR have reported conflicting conclusions. Aryal et al. [12] and Gandhi et al. [13] reported increased bleeding risk and no benefit in stroke prevention with DAPT which is consistent with our report. On the contrary, Verdola et al. reported DAPT was better in terms of reduction in mortality and stroke prevention, with no increase in major bleedings as compared with SAPT [24]. Therefore, we performed a more comprehensive analysis which also included the recent ARTE trial. Our analysis is the largest to date comparing DAPT versus SAPT for individual relevant end-points. Further, we restricted our analysis to studies without anti-coagulation, and pooled randomized and observational studies separately to minimize bias. Our findings are concordant with the recently published ARTE (Aspirin Versus Aspirin+ Clopidogrel Following Transcatheter Aortic Valve Implantation) trial in which incidence of major and life-threatening bleeding was significantly higher with DAPT compared to SAPT (10.8% vs. 3.6%, $P = 0.038$), while stroke was not significantly different in two groups (2.7% vs. 0.9%, $P = 0.313$) [18]. Other small RCTs did not reveal a significant higher bleeding risk with DAPT, however stroke risk was similar in DAPT compared with SAPT [10,11]. Similarly, in a prospective observational study by Durand et al, risk of major bleeding was significantly higher in the DAPT group without a decrease in stroke, compared to SAPT [19]. Reconciling these findings, we found an increased risk of bleeding with DAPT compared to SAPT in the cumulative analysis, which however failed to cross the equivalence line when limited to RCTs. A plausible explanation for discrepant results between RCTs and observational studies included in our analysis could be careful selection of patients in RCTs with "less" bleeding risk as well as inadequate power due to low sample size. Our results for other clinical end-points (stroke, MI, mortality) are in agreement with previous RCTs and observational studies. However, it is important to consider that the small sample size in the included studies might not be sufficient to show benefit of stroke prevention

An ongoing large randomized study, POPULAR-TAVI (cohort A) [NCT02247128] comparing DAPT with ASA and clopidogrel versus clopidogrel alone will throw further light on optimal management of patients after TAVR [25]. In the lack of definitive evidence, whether an OAC based approach is superior to SAPT or DAPT in patients otherwise without an indication for anti-coagulation remains unanswered. The announcement of two trials, AUREA (Dual Antiplatelet Therapy Versus Oral Anticoagulation for a Short Time to Prevent Cerebral Embolism After TAVI; NCT01642134) and GALILEO (Global Study Comparing a rivaroxaban based Antithrombotic Strategy to an antiplatelet based Strategy After Transcatheter aortIc valve rEplacement to Optimize Clinical Outcomes; NCT02556203), assessing outcomes with antiplatelet therapy versus OAC in patients undergoing TAVR is timely in this regard.

The findings of our analysis could be inferred to have the following impact. First, the benefits of DAPT after TAVR are not clear but the risk of bleeding is not trivial, so in patients with higher bleeding risk, DAPT could potentially be avoided. Second, since the optimal duration of DAPT after TAVR is not clear, a shorter course of DAPT (1 month) may be acceptable until we get new data from the ongoing randomized trials. There are several lines of evidences suggesting against routine

role of DAPT in preventing thrombo-embolic events after TAVR. First, OAC has been associated with better valvular and clinical outcomes after surgical aortic valve replacement. Secondly, Chakravarty et al. recently reported no differences in rates of subclinical valve thrombosis between DAPT and SAPT, although it was significantly lower in patients who received anticoagulation [23]. Finally, a significant proportion of patients with TAVR suffer from pre-existing or new onset atrial fibrillation which requires use of an OAC. These concerns definitely raise questions against the use of DAPT after TAVR.

There are few limitations of our analysis. First, despite inclusion of all published randomized and non-randomized studies on this topic to date, the sample size of our study was still relatively small with a low event rate. This might have influenced power of our analysis, such as for bleeding risk. Second, studies involved some heterogeneity in terms of duration or type of anti-platelets which might have influenced results, however the influence of such variability is expected to be minimal. Also, we studied outcomes at the longest available follow-up (mean = 4.8 months) which is in line with 3–6 months recommendations for DAPT after TAVR. Finally, due to lack of patient level data, we could not control for potential confounders such as kidney dysfunction, age, and so forth. However, it should be noted that the studies included patients with broad characteristics, and no significant heterogeneity was observed for any end-point in our analysis.

5 | CONCLUSION

Our findings strengthen the previous evidence that DAPT after TAVR does not reduce stroke or mortality compared to SAPT and is associated with higher risk of significant bleeding. Outcomes from ongoing trials will clarify the best approach regarding single antiplatelet or anticoagulation after TAVR.

CONFLICT OF INTEREST

No conflict of interest to disclose.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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