Effects of single versus dual antiplatelet therapy on the adverse events after transcatheter aortic valve implantation: A meta-analysis

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Abstract

Dual antiplatelet therapy (DAPT) was currently recommended for transcatheter aortic valve implantation (TAVI) postoperative management in clinical application. However, POPular-TAVI trial showed DAPT increased the incidence of adverse events compared to single antiplatelet therapy (SAPT). Herein, we performed a meta-analysis to investigate the effect of SAPT versus DAPT on the adverse events after TAVI. Eleven studies were available from PubMed, Embase, Cochrane Library, and Web of Science from inception to April 1, 2021. The pooled effect size was presented as relative risk (RR) with 95% confidence intervals (CIs). The sensitivity analysis was used to assess the stability of analysis results, and Begg's test was applied to evaluate the publication bias. The Cochran Q test and the $I^2$ statistic were used to evaluate the heterogeneity, and the source of heterogeneity was explored by meta-regression. A total of 4804 patients were obtained, with 2257 in SAPT group and 2547 in DAPT group. Compared to the DAPT, SAPT was associated with the decreased risk of all-cause bleeding (RR: 0.51, 95% CI: 0.44–0.61), major bleeding (RR: 0.53, 95% CI: 0.32–0.86), and minor bleeding (RR: 0.58, 95% CI: 0.34–0.98). There were no significant differences in mortality and myocardial infarction events, stroke events, and acute kidney injury between the two groups. SAPT was superior to DAPT in decreasing all-cause bleeding, major bleeding, and minor bleeding, suggesting that SAPT could be preferentially recommended for TAVI postoperative management in most patients without another indication for DAPT and oral anticoagulation.

KEYWORDS
DAPT, meta-analysis, SAPT, TAVI

1 | INTRODUCTION

Aortic stenosis is a common kind of valvular heart disease, affecting 2%–7% of older population.1,2 Currently, transcatheter aortic valve implantation (TAVI) has been proved as an effective therapy to replace the conventional surgery for patients with severe aortic stenosis.3 However, some postoperative adverse events of TAVI cannot be ignored. Especially, thrombotic events commonly occur, with 1% being myocardial infarction (MI) and 3% being ischemic stroke, which lead to a high mortality.4,5 Therefore, more attention should be paid to the thrombotic events after TAVI for the improvement of prognosis.
The American College of Cardiology/American Heart Association (ACC/AHA) guidelines suggest dual antiplatelet therapy (DAPT) for thrombotic events.6 Patients are recommended with aspirin and clopidogrel for the first 3–6 months after TAVI; however, this therapy is lack of clear clinical evidence. Currently, single antiplatelet therapy (SAPT) that use aspirin alone is applied as an alternative antithrombotic treatment regimen after TAVI.7 Previous studies have compared the effects of SAPT and DAPT on the adverse events after TAVI, but the results remained controversial.6,9 Hu et al. and Ahmad et al. reported that DAPT reduced the risk of thrombotic events and helped to mitigate stoke.10,11 POPular-TAVI trial assessed the safety between SAPT and DAPT, and results indicated DAPT was associated with a higher incidence of bleeding events.12 Ichibori et al. reported the similar finding that DAPT increased the risk of SAPT compared to DAPT.7 Rodés-Cabau et al found that SAPT deceased the occurrence of major adverse events compared to the DAPT.13 Ussia et al. reported that there was no significant difference between SAPT and DAPT in death, transient ischemic attack, and bleeding events.14

Given that there is no consensus now, we perform a meta-analysis to compare the effects of SAPT and DAPT on the postoperative adverse events after TAVI. Meta-regression to explore source of heterogeneity and subgroup analysis based on study design and follow-up time are also performed.

2 | METHODS

2.1 | Literature search strategy

We searched for available literatures from PubMed, Embase, Cochrane Library and Web of Science, and the deadline for searching studies was April 1, 2021. The literature retrieval was independently conducted by two researchers (S. Q. Y. and S. Y. Z.). Search strategies included: “Transcatheter Aortic Valve Implantation” OR “Transcatheter Aortic Valve Replacement” AND “single antiplatelet therapy” OR “dual antiplatelet therapy” OR “Dual Anti-Platelet Therapy” OR “Anti-Platelet Therapies, Dual” OR “Anti-Platelet Therapy, Dual” OR “Dual Anti Platelet Therapy” OR “Dual Anti-Platelet Therapies” OR “Aspirin” OR “Acetylsalicylic Acid” OR “Acid, Acetylsalicylic” OR “2-(Acetyloxy)benzoic Acid” OR “Aclyprin” OR “Aloxipirum” OR “Colfarit” OR “Dispril” OR “Easprin” OR “Ecostrin” OR “Endosprin” OR “Magencyl” OR “Micristin” OR “Polopirina” OR “Polopiryn” OR “Solprin” OR “Solupsan” OR “Zorprin” OR “Acetylsal” OR “Clopidogrel” OR “SC 25989C” OR “SC 25990C” OR “SR 25989” OR “Clopidogrel-Mepha” OR “Clopidogrel Metha” OR “Clopidogrel Sandox” OR “Iscover” OR “Clopidogrel Napadisilate” OR “Clopidogrel Hydrochloride” OR “PCR 4099” OR “PCR-4099” OR “Clopidogrel Besylate” OR “Clopidogrel Besilate” OR “Clopidogrel, (S)-isomer” OR “Plavix” OR “Clopidogrel Bisulfate” OR “Hydrochloride, Prasugrel” OR “Prasugrel HCl” OR “HCl, Prasugrel” OR “CS 747” OR “747, CS” OR “CS-747” OR “CS747” OR “Prasugrel” OR “Efient” OR “Effient” OR “LY 640315” OR “640 315, LY” OR “LY640315” OR “LY-640315” OR “Ticagrelor” OR “Brilique” OR “AZD 6140” OR “AZD6140” OR “AZD-6140” OR “Brillinta” OR “3-(7-[2-(3,4-difluorophenyl)cyclopropyl]amino)-5-(propylthio)-3H-(1,3)-triazolo[4,5-d]pyrimidin-3-yl]-5-(2-hydroxyethoxy) cyclopentane-1,2-diol”.

2.2 | Inclusion and exclusion criteria

Studies were included based on the following criteria: (1) severe aortic stenosis patients undergoing TAVI; (2) the experimental group receiving SAPT (aspirin) and the control group receiving DAPT (aspirin plus clopidogrel); (4) randomized controlled trials (RCTs) or cohort studies; (5) studies published in English.

Studies were excluded according to the following criteria: (1) animal experiments; (2) studies without complete data; (3) conference reports, case reports, editorial materials, letters, protocols, meta-analyses, and reviews.

2.3 | Data extraction

Data from the eligible studies were independently extracted by two investigators (S. Q. Y. and S. Y. Z.), and a third investigator (C. L. Y.) participated to resolve disagreements. The data requested to be extracted were name of the first author, year of publication, country, study design, groups, total number of participants, age, sex, follow-up time and outcomes.

2.4 | Outcome variable measurement

2.4.1 | Primary outcomes

1. Mortality and myocardial infarction (MI) events: all-cause death, cardiovascular death, and MI.
2. Stroke events: all stroke, disabling stroke, minor stroke, and transient ischemic attack.
3. Bleeding events: all-cause bleeding, life-threatening bleeding, major bleeding, and minor bleeding.

2.4.2 | Secondary outcomes

1. Acute kidney injury.

2.5 | Methodological quality appraisal

Two independent investigators (S. Q. Y. and S. Y. Z.) were responsible for quality assessment. Jadad scale15 and revised Newcastle-Ottawa Scale (NOS)16 were separately used to assess the quality of RCTs and cohort studies. The total score of Jadad scale was 7, and studies with 1–3 points were considered as low quality and 4–7 points were considered as high quality. The total score of NOS was 10, and studies were divided into low quality (<5 points) and high quality (≥5 points).
2.6 | Statistical analysis

Stata 15.1 (Stata Corporation, College Station, TX) was applied for statistical analysis, and \( p < .05 \) was considered as statistical significance. The relative risk (RR) with 95% confidence intervals (CIs) was calculated to analyze the binary outcome. The Cochran Q test and the \( I^2 \) statistic were used to assess between-study heterogeneity for each outcome effect size. To combine the effect amount, the fixed-effect model was used when the heterogeneity was low (\( I^2 < 50\% \)), and the random-effect model was used when the heterogeneity was high (\( I^2 \geq 50\% \)). Based on study design and follow-up time, subgroup analysis was used to assess the incidence of major bleeding and minor bleeding in SAPT and DAPT groups. Meta-regression was performed to explore sources of inconsistency (\( I^2 \geq 50\% \)). Sensitivity analysis was performed for all outcomes and publication bias was assessed by Begg’s test.

3 | RESULTS

3.1 | Study selection and baseline characteristics

A total of 5008 studies were identified using the four English databases. Among which, 401 studies were eliminated as duplicates. After evaluating titles and abstracts, 4581 studies were excluded. The residual 26 texts were further assessed; of these, 15 texts were removed because of the incomplete data (\( n = 10 \)) and control groups not meeting the requirements (\( n = 5 \)). Finally, 11 studies (4 RCTs and 7 cohort studies)\(^{7,12,14,17–24}\) were included, and the flow chart of study selection was shown in Figure 1. Totally, 4804 patients were enrolled, including 2257 patients in SAPT group and 2547 patients in DAPT group. Moreover, according to the evaluation results of Jadad and revised NOS, 9 studies were of high quality and 2 studies were of low quality. Table 1 summarizes the baseline characteristics and quality assessment score of included studies.

![Flow chart of study selection](image)
| Author                | Year of publication | Country | Study design | Groups | Total | Age (years) | Male/female | Follow-up (months) | Quality of literatures | Outcomes         |
|-----------------------|---------------------|---------|--------------|--------|-------|-------------|-------------|---------------------|----------------------|---------------------|
| Ussia                 | 2011                | Italy   | RCT          | SAPT   | 39    | 81 ± 4      | 16/23       | 6                   | 4                    | a, b, c, e, f, g, i, j, k |
|                       |                     |         |              | DAPT   | 40    | 80 ± 6      | 20/20       |                     |                      |                    |
| Poliacikova           | 2013                | UK      | Cohort       | SAPT   | 91    | 82          | 49/42       | 6                   | 4                    | a, c, d, h         |
|                       |                     |         |              | DAPT   | 58    | 81.6        | 32/26       |                     |                      |                    |
| Durand                | 2013                | France  | Cohort       | SAPT   | 164   | 82.7 ± 6.3  | 90/74       | 6                   | 5                    | a, c, d, e, f, g, h, i, j, k, l |
|                       |                     |         |              | DAPT   | 128   | 84.6 ± 5.8  | 50/78       |                     |                      |                    |
| Stabile               | 2014                | Italy   | RCT          | SAPT   | 60    | 81.1 ± 4.8  | 24/36       | 6                   | 6                    | a, b, c, e, f, j, k, l |
|                       |                     |         |              | DAPT   | 60    | 80.2 ± 5.7  | 16/44       |                     |                      |                    |
| Czerwińska-Jelonkiewicz| 2016               | Poland  | Cohort       | SAPT   | 124   | 79.14 ± 7.39| 56/68       | 12                  | 6                    | c, i               |
|                       |                     |         |              | DAPT   | 352   | 78.92 ± 7.24| NA          |                     |                      |                    |
| D’Ascenzo             | 2017                | Italy   | Cohort       | SAPT   | 605   | 81 ± 4      | 256/349     | 12                  | 4                    | a, d, h, i, j, k   |
|                       |                     |         |              | DAPT   | 605   | 81 ± 5      | 269/336     |                     |                      |                    |
| Ichibori              | 2017                | Japan   | Cohort       | SAPT   | 78    | 83 ± 6      | 28/50       | 12                  | 5                    | i, l               |
|                       |                     |         |              | DAPT   | 66    | 84 ± 6      | 24/42       |                     |                      |                    |
| Mangieri              | 2017                | Italy   | Cohort       | SAPT   | 108   | 84.3 ± 7.1  | 46/62       | 12                  | 6                    | a, b, c, d, i, j, k, l |
|                       |                     |         |              | DAPT   | 331   | 82.9 ± 8.2  | 117/214     |                     |                      |                    |
| Rodés-Cabau           | 2017                | Canada  | RCT          | SAPT   | 111   | 79 ± 9      | 59/52       | 3                   | 4                    | a, c, d, e, f, g, i, j |
|                       |                     |         |              | DAPT   | 111   | 79 ± 9      | 70/41       |                     |                      |                    |
| Brouwer               | 2020                | Netherlands | RCT     | SAPT   | 331   | 80.4 ± 6.2  | 167/164     | 12                  | 5                    | a, b, c, d, e, f, h, i, j, k |
|                       |                     |         |              | DAPT   | 334   | 79.5 ± 6.4  | 174/160     |                     |                      |                    |
| Hioki                 | 2021                | Japan   | Cohort       | SAPT   | 546   | 85 (81–88)  | 151/395     | 12                  | 5                    | a, b               |
|                       |                     |         |              | DAPT   | 462   | 84 (81–87)  | 147/315     |                     |                      |                    |

Note: Data presented as mean ± SD or n. RCT, randomized control trial; SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy; a, all-cause death; b, cardiovascular death; c, myocardial infarction; d, all stroke; e, disabling stroke; f, minor stroke; g, transient ischemic attack; h, all-cause bleeding; i, life-threatening bleeding; j, major bleeding; k, minor bleeding; l, acute kidney injury.
3.2 | Mortality and MI events

Table 2 shows no significant difference in all-cause death between
the two groups (RR: 0.90, 95% CI: 0.77–1.05, p = .183) (Figure 2A).
The cardiovascular death of the two groups was not statistically sig-
nificant (RR: 0.71, 95% CI: 0.45 to 1.11, p = .132) (Figure 2B). Also,
the incidence of MI in SAPT group showed no statistical difference
from DAPT group (RR: 0.70, 95% CI: 0.35–1.39, p = .306) (Figure 2C).

3.3 | Stroke events

For stroke events, results were shown in Table 2, indicating that no
statistical significance was found between the two groups in the inci-
dence of all stroke (RR: 0.69, 95% CI: 0.45–1.08, p = .102)
(Figure 3A), disabling stroke (RR: 0.88, 95% CI: 0.39–1.99, p = .763)
(Figure 3B), minor stroke (RR: 0.73, 95% CI: 0.37–1.43, p = .354)
(Figure 3C), and transient ischemic attack (RR: 0.90, 95% CI: 0.13–
6.23, p = .911) (Figure 3D).

TABLE 2  Meta-analysis results of outcomes between SAPT and DAPT

| Outcomes                 | RR (95% CI)       | p    | I²   |
|--------------------------|-------------------|------|------|
| **Mortality and MI events** |                   |      |      |
| All-cause death          | 0.90 (0.77, 1.05) | .183 | 30.4 |
| Cardiovascular death     | 0.71 (0.45, 1.11) | .132 | 43.3 |
| Myocardial infarction    | 0.70 (0.35, 1.39) | .306 | 0.0  |
| **Stroke events**        |                   |      |      |
| All stroke               | 0.69 (0.45, 1.08) | .102 | 0.0  |
| Disabling stroke         | 0.88 (0.39, 1.99) | .763 | 0.0  |
| Minor stroke             | 0.73 (0.37, 1.43) | .354 | 0.0  |
| Transient ischemic attack| 0.90 (0.13, 6.23) | .911 | 0.0  |
| **Bleeding events**      |                   |      |      |
| All-cause bleeding       | 0.51 (0.44, 0.61) | <.001 | 47.5 |
| Life-threatening bleeding| 0.55 (0.28, 1.08) | .083 | 73.8 |
| Major bleeding           | 0.53 (0.32, 0.86) | .011 | 58.7 |
| Minor bleeding           | 0.58 (0.34, 0.98) | .044 | 63.3 |

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy; MI, myocardial infarction; RR, relative risk; SAPT, single antiplatelet therapy.

FIGURE 2  Forrest plots of all-cause death (A), cardiovascular death (B), and myocardial infarction (C)
3.4 | Bleeding events

Table 2 displays the analysis results of bleeding events between the two groups. Compared to DAPT, SAPT group showed a 49% reduction in all-cause bleeding (RR: 0.51, 95% CI: 0.44–0.61, p < .001) (Figure 4A), while it was not significantly correlated with the decreased risk of life-threatening bleeding (RR: 0.55, 95% CI: 0.28–1.08, p = .083) (Figure 4B). Moreover, patients accepting SAPT had a lower incidence of major bleeding (RR: 0.53, 95% CI: 0.32–0.86, p = .011) (Figure 4C). Similarly, SAPT decreased the risk of minor bleeding compared with DAPT (RR: 0.58, 95% CI: 0.34–0.98, p = .044) (Figure 4D).

3.5 | Acute kidney injury

The results of meta-analysis were summarized in Table 2. Four studies were included to compare the effect of SAPT and DAPT on acute kidney injury, and random-effect model was used. The pooling data suggested that no remarkable significance was observed between the two groups in the occurrence of acute kidney injury (RR: 0.83, 95% CI: 0.32–2.15, p = .699) (Figure 5).

3.6 | Meta-regression and subgroup analysis

To explore the source of heterogeneity among studies for life-threatening bleeding, major bleeding and minor bleeding, meta-regression analysis was performed based on study design and follow-up time. The results showed that heterogeneity among the studies was not associated with study design and follow-up time (Table 3). Results of SAPT versus DAPT on adverse outcomes in different subgroups were shown in Table 4. SAPT decreased the risk of major bleeding compared to DAPT in RCT articles (RR: 0.42, 95% CI: 0.23–0.79, p = .007), while cohort studies presented no differences.
FIGURE 4  Forrest plots of all-cause bleeding (A), life-threatening bleeding (B), major bleeding (C), and minor bleeding (D)

FIGURE 5  Forrest plot of acute kidney injury
between the two groups (RR: 0.54, 95% CI: 0.26–1.13, p = .100) (Figure 6A). Our findings also showed that the incidence of major bleeding was lower in SAPT group at 6 months follow-up (RR: 0.33, 95% CI: 0.12–0.96, p = .041), but no significance at 3 months (RR: 0.60, 95% CI: 0.15–2.45, p = .477) and 12 months (RR: 0.60, 95% CI: 0.33–1.09, p = .096) (Figure 6B). Either cohort studies (RR: 0.52, 95% CI: 0.19–1.41, p = .198) or RCTs (RR: 0.64, 95% CI: 0.39–1.07, p = .087) did not show the significance between the two groups regarding to minor bleeding (Figure 6C). Similarly, the difference was not found at follow-up of 6 months (RR: 0.57, 95% CI: 0.22–1.49, p = .250) or 12 months (RR: 0.58, 95% CI: 0.29–1.16, p = .123) (Figure 6D).

3.7 | Sensitivity analysis and publication bias

Sensitivity analysis was implemented via sequentially removed single study and reanalyzing the remaining dataset to test the strength of results. The stability and reliability of this meta-analysis were confirmed by the similar heterogeneity before and after the study removal (Table 2). In addition, the result of Begg’s test showed no publication bias in the analysis of all-cause death (Z = −0.10, p = 1.000).

4 | DISCUSSION

Our meta-analysis included 11 studies comparing the effects of SAPT and DAPT on the adverse events in severe aortic stenosis patients who underwent TAVI. Overall results presented that SAPT was superior to DAPT in decreasing all-cause bleeding, major bleeding, and minor bleeding. Either SAPT or DAPT did not show better efficacy in all-cause death, cardiovascular death, MI, all stroke, disabling stroke, minor stroke, transient ischemic attack, life-threatening bleeding, and acute kidney injury. Considering the higher bleeding risk and drug abuse problem of DAPT, our results suggested SAPT as the appropriate antiplatelet therapy for most patients who did not have the indication for DAPT or oral anticoagulation after TAVI.

The successful clinical introduction of TAVI is of great importance in the treatment of severe aortic stenosis.25 Because of the frequent transcatheter heart valve thrombosis, concern for antithrombotic therapy after TAVI has been increasingly important. Current clinical practice of post-TAVI antithrombotic therapy is still based on
experience and/or authority. Despite the lack of evidence, ACC/AHA guidelines recommend DAPT that used clopidogrel in addition to aspirin for 3–6 months after TAVI according to the clinical experience of coronary stents. Aspirin, an antiplatelet drug, has been used to inhibit platelet aggregation and prevent the formation of thrombosis after transient ischemic attack, MI, artificial heart valve or other operations. Clopidogrel is also an antiplatelet drug and used to prevent and treat heart, brain and other arterial circulation disorders caused by high platelet aggregation, such as stroke, MI and confirmed peripheral artery disease. Prior to the completion of valve endothelialization, a temporary enhanced antiplatelet regimen over one drug is considered to reduce the risk of stent-mediated thromboembolism. Sharma et al. reported that postoperative thromboembolic events and risk of bleeding were still the significant challenge for patients undergoing TAVI. After TAVI, up to 15% of patients occurred major bleeding at 1 year, and DAPT was found to result in an increased bleeding risk compared to SAPT. Also, the ARTE trial presented a lower incidence of bleeding correlated with SAPT than with DAPT. Similarly, our meta-analysis showed SAPT decreased the risk of all-cause bleeding, major bleeding and minor bleeding compared to DAPT.

Some observational studies have indicated that DAPT lacks any beneficial effects to prevent cardiovascular and cerebrovascular events after TAVI compared to SAPT. Two RCTs have also showed the similar results. Ussia et al. found that no differences in the major ischemic stroke between the two groups. Similarly, our results showed no differences between the groups in the stroke events, including all stroke, disabling stroke, minor stroke, and transient ischemic attack. A retrospective review from a
dedicated TAVI database of a single high-volume center in Milan reported that no significant difference was found in all-cause mortality and cardiovascular mortality between DAPT and SAPT. Moreover, the incidence of thromboembolic events of MI in the two groups showed no significant difference. Accordingly, our results found that the incidence of all-cause death, cardiovascular death and MI was not significantly different in the two groups. Moreover, the significance in life-threatening bleeding between the two groups was not found in our meta-analysis, which was in accordance with the studies from D’Ascenzo et al. and Ullah et al. Also, our study found the similar result as the reports of Durand et al. and Stabile et al. that DAPT was not superior to SAPT in acute kidney injury.

Although SAPT was not superior to DAPT in decreasing the risk of mortality and MI events, stroke events, life-threatening bleeding, and acute kidney injury, the use of SAPT avoided drug abuse and mitigated the economic burden of patients and their families. In addition, clopidogrel caused more damage to patients’ body with a higher risk of diarrhea and rash than aspirin, supporting that DAPT with clopidogrel plus aspirin brought more toxicity than SAPT with aspirin alone.

Our meta-analysis showed a clear benefit of SAPT for TAVI post-operative management. In addition, meta-regression based on study design and follow-up time was performed to explore the heterogeneity. However, some limitations were existed. First, our study combined RCTs and cohort studies, and the heterogeneity might exist among the included studies. Second, our study was lack of adjustment for confounders in baseline characteristics and comorbidities of the included patients across groups.

In conclusion, our meta-analysis indicated that SAPT decreased the incidence of all-cause bleeding, major bleeding and minor bleeding. Although SAPT was not superior to DAPT in life-threatening bleeding, mortality and MI events, stroke events, and acute kidney injury, it avoided the drug abuse, and mitigated the damage to patients’ bodies and the economic burden to their family members. Based on available data, SAPT was preferred after TAVI for most patients who were absent another indication for DAPT or oral anticoagulation.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES
1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet. 2006;368:1005-1011.
2. Jung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: the euro heart survey on Valvular heart disease. Eur Heart J. 2003;24:1231-1243.
3. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016;374:1609-1620.
4. Khatri PJ, Webb JG, Rodés-Cabau J, et al. Adverse effects associated with transcatheter aortic valve implantation: a meta-analysis of contemporary studies. Ann Intern Med. 2013;158:35-46.
5. Généreux P, Cohen DJ, Williams MR, et al. Bleeding complications after surgical aortic valve replacement compared with transcatheter aortic valve replacement: insights from the PARTNER I trial (placement of aortic transcatheter valve). J Am Coll Cardiol. 2014;63:1100-1109.
6. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the Management of Patients with Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol. 2017;70:252-289.
7. Ichihori Y, Mizote I, Maeda K, et al. Clinical outcomes and bioprosthetic valve function after Transcatheter aortic valve implantation under dual antiplatelet therapy vs. aspirin alone. Circ J. 2017;81:397-404.
8. Gargiulo G, Collet JP, Valgimigli M. Antiplatelet therapy in TAVI patients: changing concepts. EuroIntervention. 2015;11(suppl W):W92-W95.
9. Hassell ME, Hildick-Smith D, Durand E, et al. Antiplatelet therapy following transcatheter aortic valve implantation. Heart. 2015;101:1118-1125.
10. Hu X, Yang FY, Wang Y, Zhang Y, Chen M. Single versus dual antiplatelet therapy after transcatheter aortic valve implantation: a systematic review and meta-analysis. Cardiology. 2018;141:52-65.
11. Ahmad Y, Demir O, Rajkumar C, et al. Optimal antiplatelet strategy after transcatheter aortic valve implantation: a meta-analysis. Open Heart. 2018;5:e000748.
12. Brouwer J, Nijenhuis VJ, Delewi R, et al. Aspirin with or without clopidogrel after transcatheter aortic-valve implantation. N Engl J Med. 2020;383:1447-1457.
13. Rodés-Cabau J, Masson JB, Welsh RC, et al. Aspirin versus aspirin plus clopidogrel as antiplatelet treatment following transcatheter aortic valve replacement with a balloon-expandable valve: the ARTE (aspirin versus aspirin + clopidogrel following transcatheter aortic valve implantation) randomized clinical trial. JACC Cardiovasc Interv. 2017;10:1357-1365.
14. Ussia GP, Scabellini M, Mul M, et al. Dual antiplatelet therapy versus aspirin alone in patients undergoing transcatheter aortic valve implantation. Am J Cardiol. 2011;108(12):1772-1776.
15. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17:1-12.
16. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed April 16, 2021.
17. Hioki H, Watanabe Y, Kozuma K, et al. Short-term dual anti-platelet therapy decreases long-term cardiovascular mortality after transcatheter aortic valve replacement. Heart Vessels. 2021;36:252-259.
18. Rodes-Cabau J, Masson JB, Welsh RC, et al. Aspirin versus aspirin plus clopidogrel as anti thrombotic treatment following transcatheter aortic valve replacement with a balloon-expandable valve the ARTE (aspirin versus aspirin plus clopidogrel following transcatheter aortic valve implantation) randomized clinical trial. JACC Cardiovasc Interv. 2017;10:1357-1365.
19. Mangieri A, Jabbour RJ, Montalto C, et al. Single-antiplatelet therapy in patients with contraindication to dual-antiplatelet therapy after Transcatheter aortic valve implantation. Am J Cardiol. 2017;119:1088-1093.
20. D’Ascenzo F, Benedetto U, Bianco M, et al. Which is the best anti-aggregant or anticoagulant therapy after TAVI? A propensity-matched analysis from the ITER registry the management of DAPT after TAVI. EuroIntervention. 2017;13:e1392-e1400.

21. Czerwinska-Jelonkiewicz K, Zembala M, Dabrowski M, et al. Can TAVI patients receive aspirin monotherapy as patients after surgical aortic bioprosthesis implantation? Data from the polish registry—POL-TAVI. Int J Cardiol. 2017;227:305-311.

22. Stabile E, Pucciarelli A, Cota L, et al. SAT-TAVI (single antiplatelet therapy for TAVI) study: a pilot randomized study comparing double to single antiplatelet therapy for transcatheter aortic valve implantation. Int J Cardiol. 2014;174:624-627.

23. Durand E, Blanchard D, Chassaing S, et al. Comparison of two antiplatelet therapy strategies in patients undergoing transcatheter aortic valve implantation. Am J Cardiol. 2014;113:355-360.

24. Poliacikova P, Cockburn J, de Belder A, et al. Antiplatelet and antithrombotic treatment after Transcatheter aortic valve implantation—comparison of regimes. J Invasive Cardiol. 2013;25:544-548.

25. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. 2012;33:2451-2496.

26. Tillman H, Johnston SC, Farrant M, et al. Risk for major hemorrhages in patients receiving clopidogrel and aspirin compared with aspirin alone after transient ischemic attack or minor ischemic stroke: a secondary analysis of the POINT randomized clinical trial. JAMA Neurol. 2019;76:774-782.

27. Jneid H, Addison D, Bhatt DL, et al. AHA/ACC clinical performance and quality measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association task force on performance measures. Circ Cardiovasc Qual Outcomes. 2017;10.

28. Sharma A, Goel S, Lavie CJ, Arbab-Zadeh A, Mukherjee D, Lazar J. Antithrombotic therapy before, during and after transcatheter aortic valve replacement (TAVR). J Thromb Thrombolysis. 2015;39(4):467-473.

29. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380:1695-1705.

30. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med. 2019;380:1706-1715.

31. Ullah W, Zghouzi M, Ahmad B, et al. Meta-analysis comparing the safety and efficacy of single vs dual antiplatelet therapy in post Transcatheter aortic valve implantation patients. Am J Cardiol. 2021;145:111-118.

32. Harker LA, Boissel JP, Pilgrim AJ, Gent M. Comparative safety and tolerability of clopidogrel and aspirin: results from CAPRIE. CAPRIE steering committee and investigators. Clopidogrel versus aspirin in patients at risk of ischaemic events. Drug Saf. 1999;21:325-335.

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