EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 6
48-53
Year: 2022

SINGLE VS. DUAL ANTIPLATELET THERAPY IN POST-TAVR PATIENTS: A SYSTEMATIC REVIEW

Benish Alam*[1], Iqra Mukhtar[2], Maryam Ahmed[3], Muhammad Idrees[4], Mohammed Numaan Ahmed[5], Danish Waqar[6], Shilpa Rai[7], Shaffiq Yusuf[8], Olubukola Oloniyo[9], Sally Fouda[10], Uyi Osunde[11], Ademidun O. Ayoade[12], Stephen Dada[9], Mayowa Stephen Apata[9] and Frederick Ferguson[13]

[1]Karachi Medical and Dental College (KMDC), Pakistan.
[2]Al-Nafees Medical College and Hospital, Pakistan.
[3]Punjab Medical College (PMC), Pakistan.
[4]Ayub Medical College, Pakistan.
[5]Al Ameen Medical College and Hospital, India.
[6]Wuhan University School of Medicine, China.
[7]Isra University, Hyderabad , Pakistan.
[8]Washington university of Health and Science, Belize.
[9]Windsor University School of Medicine, St Kitts and Nevis.
[10]Mansoura university College of Medicine.
[11]All Saints University, St Vincent and Grenadines.
[12]Benjamin S. Carson College of Health and Medical Sciences, Nigeria.
[13]Caribbean Medical University, Curaçao.

***Corresponding Author: Benish Alam**
Karachi Medical and Dental College (KMDC), Pakistan.

Article Received on 15/04/2022 **Article Revised on 06/05/2022** **Article Accepted on 27/05/2022**

ABSTRACT

Introduction: Transcatheter aortic valve replacement (TAVR) is provided to patients with severe symptomatic aortic valve stenosis who are considered high risk candidates for surgical aortic valve replacement (SAVR). We compared the efficacy and safety of TAVR with single vs dual antiplatelet therapy. **Methods:** The systematic review was performed as per the Cochrane methods. We searched relevant databases until December 27, 2021. We chose studies as per the inclusion criteria and used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. **Results:** A total of 4 RCTs were included with 1,086 patients and an average follow-up of 9.2 months. The baseline clinical characteristics were comparable in either group receiving single vs. dual antiplatelet therapy. There was a lower incidence of life-threatening bleeding and myocardial infarction in the SAPT group. Conclusion: The incidence of bleeding was significantly reduced with SAPT with no major increase in stroke risk demonstrating the lack of inferiority with SAPT regimen post-TAVR.

KEYWORDS: Single antiplatelet therapy, dual antiplatelet therapy, aspirin, clopidogrel, TAVR.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) is a therapeutic modality provided to patients with severe symptomatic aortic valve stenosis, specifically to patients who have contraindications to surgical aortic valve replacement (SAVR).[1] The modality is less invasive than SAVR and has a high success rate. However, TAVR has been associated with two common complications, including stroke and life-threatening bleeding, whereas vascular complications, myocardial infarctions, and mortality are less frequently observed.[2,3] Two key trials explored the incidence rates of cerebral ischemia and life-threatening bleeding until 30 days after TAVR, noting it to be 5% and 10%, respectively, among patients at intermediate risk for surgery.[4,5] To minimize the risk of embolism, the American Heart Association/American College of Cardiology (AHA/ACC) endorsed three- to six-months dual antiplatelet therapy (DAPT) with clopidogrel and aspirin or to continue using oral anticoagulant agents (OAC) if already indicated before the procedure.[6] With no other indication to receive OAC, DAPT with clopidogrel for 3-6 months and lifelong aspirin is considered the most used strategy.[7] Theoretically, DAPT has a lower risk of thrombotic events, but there is a higher risk of bleeding than single antiplatelet therapy (SAPT). Overall, the optimal regimen following TAVR remains inconclusive. Therefore, we conducted a systematic review of the recent studies to identify the safety and efficacy of either DAPT or SAPT in patients undergoing TAVR.

METHODS

Search Strategy and Selection

We conducted a systematic search with keywords including "Single," "Dual," "antiplatelet," "therapy," and "TAVR." The databases searched included MEDLINE, Clinical Key, and Cochrane Library. Two independent reviewers conducted screening and selection. First, the reviewers independently screened the title and abstract. If there were discrepancies between the first and second reviewers, the third reviewers solved these. The next step was to finalize the screening after reviewing the full text of the articles for eligibility. There were no restrictions to time or language. All papers from inception until December 27, 2021, were reviewed. We included only randomized controlled trials (RCTs). Duplicates were removed using the software Endnote X9.

OBJECTIVES

The primary objective was to summarize outcomes of key RCTs for single vs. dual antiplatelet therapy among patients receiving TAVR. The secondary objective was to explore the safety of single vs. dual antiplatelet treatment and provide recommendations for patients receiving TAVR.

Data analysis

Three reviewers extracted data on a customized datasheet in Excel. The variables were tabulated, including trial characteristics, baseline clinical characteristics of the patients, and outcomes of the patients. The trial characteristics included author-year, selection criteria, dosing of DAPT and SAPT group, follow-up time point, the primary endpoint, TAVR device. The baseline clinical characteristics of the patients were age, gender, hypertension, diabetes, chronic kidney disease (CKD), coronary artery disease (CAD), previous percutaneous coronary intervention (PCI), previous myocardial infarction (MI), permanent atrial fibrillation (AF), left ventricular ejection fraction (EF), and New York Heart Association (NYHA) class III or IV. All three reviewers utilized the Cochrane Risk of Bias (ROB) tool. We conducted a qualitative analysis to analyze the current evidence regarding single vs. dual antiplatelet therapy for post-TAVR care.

RESULTS

The search process is shown in figure 1. The first phase of the screening yielded 423 results. After removing duplicates, 385 results were screened for titles and abstracts. In the second phase, we removed 312 results as they did not meet the eligibility criteria. Next, we reviewed 54 full texts. A total of four studies were included in the qualitative analysis during the third phase.

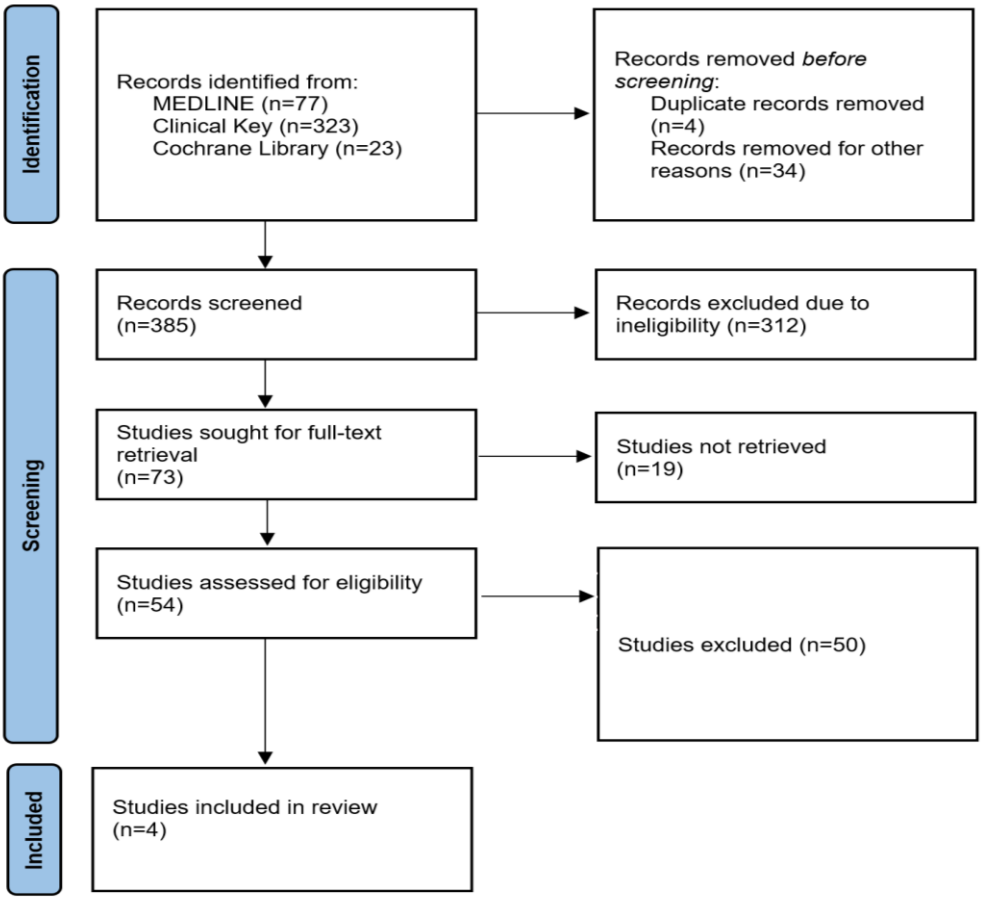

Figure 1: PRISMA Flowchart.

A total of four RCTs were included in the systematic review[8–11], with 1,086 patients. The average follow-up was 9.2 months. The most commonly used access was trans-femoral. The therapy used for SAPT was aspirin, whereas aspirin plus clopidogrel was used as DAPT except for Stabile et al.[11], where ticlodipine was also offered. Brouwer et al.[10] administered both balloon-expandable and self-expandable TAVR valves, whereas Ussia et al.[8] allowed only self-expandable TAVR valves. Two trials[9,11] administered only balloon-expandable TAVR valves. Overall, the RCTs were open-label except for Stabile et al.[11] The baseline characteristics of the trials are summarized in table 1.

Table 1: Baseline characteristics of the included trials.

Author-year	Ussia et al. (2011)	Stabile et al. (2014)	Rodes-Cacau et al. (2017)	Brouwer et al. (2020)
Selection criteria	Severe symptomatic AS with AVA < 1cm^2	Severe AS; echocardiographically derived AVA <0.8 cm^2 peak jet velocity >4.0 m/s; NYHA functional class II; predicted operative mortality 15% or STS score 10%	Clinical indication for TAVR with a ballon-expandable Edwards SAPIEN XT or SAPIEN 3 valve	TAVI population at high-risk for surgery
DAPT group	Aspirin 100 mg/day; Clopidogrel 300 mg loading followed by 75 mg/day for 3 months	Aspirin 80 mg/day; Clopidogrel 75 mg/day or ticlodipine BID for 6 months	Aspirin 80-100 mg/day for 6 months; Clopidogrel 75 mg/day for 3 months	Aspirin 80-100 mg for 3 months; Clopidogrel 75 mg/day for 3 months
SAPT group	Aspirin 100 mg/day for 3 months	Aspirin 75-160 mg/day for 6 months	Aspirin 80-100 mg/day for 6 months	Aspirin 80-100 mg/day for 3 months
Follow-up time points	6 months	30 days, 6 months	1, 2, 3 months	1, 2, 6 months, 1 year
Primary endpoint	Composite of death from any cause, MI, major stroke, LTB, and urgent or emergency conversion to surgery	Composite of a major stroke, acute coronary event, acute coronary event, all-cause mortality, major and lethal bleeding	Mortality, MI, ischemic stroke or TIA, LTB, major bleed at three months follow-up	All bleeding and non-procedure-related bleeding at 12 months
TAVR device	CoreValve	SAPIEN	SAPIEN XT or SAPIEN 3	NA

AS: Aortic stenosis; AVA: Aortic valve area; BID: two times a day; LTB: Life-threatening bleed; DAPT: Dual antiplatelet therapy; MI: Myocardial infarction; NYHA: New York Heart Association; SAPT: Single antiplatelet therapy; STS: Society of Thoracic Surgeones; TIA; Transient ischemic attack.

Patients in both groups were elderly and had multiple comorbidities. Both the groups had comparable rates of previous percutaneous coronary intervention (PCI), myocardial infarction (MI), and coronary artery disease (CAD). The baseline clinical characteristics across the patients in each group were comparable. Key features are summarized in table 2.

Table 2. Baseline characteristics of the patients in the trials.

Author-year	Ussia et al. (2011)	Stabile et al. (2014)	Rodes-Cabau et al. (2017)	Brouwer et al. (2020)
Number of patients in either group (n)	DAPT (n=40); SAPT (n=39)	DAPT (n=60); SAPT (n=60)	DAPT (n=111); SAPT (n=111)	DAPT (n=334); SAPT (n=331)
Age (years)	80 ± 6; 81 ± 4	80.2 ± 5.7; 81.1 ± 4.8	79 ± 9; 79 ± 9	79.5 ± 6.4; 80.4 ± 6.2
Female (n,%)	20 (50%); 23 (59%)	44 (73.3%); 36 (60%)	41 (36.9%); 52 (46.8%)	NA
Hypertension (n,%)	35 (87.5%); 31 (79.5%)	57 (95%); 57 (95%)	86 (77.5%); 87 (73%)	255 (76.3%); 243 (73.4%)
Diabetes (n,%)	13 (32.5%); 8 (20.5%)	15 (25%); 17 (28.3%)	41 (36.9%); 36 (32.4%)	85 (25.4%); 78 (23.6%)
CKD (n,%)	NA	NA	NA	NA
CAD (n,%)	NA	NA	NA	138 (41.3%); 134 (40.5%)
Previous PCI (n,%)	12 (30%); 9	NA	NA	NA

	(23.1%)			
Previous MI (n,%)	7 (17.5%); 4 (10.3%)	NA	26 (23.4%); 20 (18%)	31 (9.3%); 28 (8.5%)
Permanent AF (n,%)	4 (10%); 6 (15%)	NA	NA	NA
Left ventricular EF (%)	51 ± 12; 54 ± 8	52.4 ± 14.4; 51.3 ± 11	55 ± 12; 54 ± 13	NA
NYHA class III or IV (n,%)	26 (65%); 23 (59%)	54 (90%); 53 (88.3%)	NA	NA

AF: Atrial fibrillation; CAD: Coronary artery disease; CKD: Chronic kidney disease; DAPT: Dual antiplatelet therapy; EF: Ejection fraction; MI: Myocardial infarction; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention; SAPT: Single antiplatelet therapy

There was a lower incidence of LTB or major bleeding in the SAPT group (5.4% vs. 10.6%). The incidence of any bleeding was also lower in the SAPT group (14.7% vs. 24.2%). The all-cause mortality was similar across both the SAPT and DAPT groups (6.1% vs. 6.1%). The incidence of MI was lower in the SAPT group (0.9% vs. 2%). The incidence of major stroke was higher in the SAPT group (1.8% vs. 1.5%). Key findings are summarized in table 3.

Table 3. Outcomes of the patients in the trials.

Author-year	Ussia et al. (2011)	Stabile et al. (2014)	Rodes-Cabau et al. (2017)	Brouwer et al. (2020)
Follow-up time point	6 months	30 days	3 months	12 months
Number of patients in either group (n)	DAPT (n=40); SAPT (n=39)	DAPT (n=60); SAPT (n=60)	DAPT (n=110); SAPT (n=109)	DAPT (n=334); SAPT (331)
All-cause death (n,%)	4 (10%); 4 (10%)	NA	7 (6.4%); 4 (3.7%)	21 (6.3%); 19 (5.7%)
Cardiovascular death (n,%)	1 (3%); 0	2 (3.3%); 1 (1.7%)	NA	14 (4.2%); 13 (3.9%)
Major stroke (n,%)	1 (3%); 2 (5%)	1 (1.7%); 1 (1.7%)	1 (0.9%); 1 (0.9%)	5 (1.5%); 6 (1.8%)
Minor stroke (n,%)	0; 0	1 (1.7); 0	3 (2.7%); 1 (0.9%)	11 (3.3%); 13 (3.9%)
Transient ischemic attack (n,%)	1 (3%); 1 (3%)	NA	0; 0	NA
Spontaneous MI (n,%)	1 (3%); 0	NA	4 (3.6%); 1 (0.9%)	6 (1.8%); 4 (1.2%)
Conversion to open heart surgery (n,%)	0; 0	NA	NA	NA
Life-threatening bleeding (n,%)	2 (5%); 2 (5%)	NA	12 (10.9%); 4 (3.7%)	11 (3.3%); 9 (2.7%)
Major bleeding (n,%)	2 (5%); 1 (3%)	0; 3 (5%)	5 (4.6%); 3 (2.8%)	25 (7.5%); 8 (2.4%)
Minor bleeding (n,%)	3 (8%); 4 (10%)	3 (5%); 5 (8.3%)	NA	53 (15.9%); 33 (10%)

DAPT: Dual antiplatelet therapy; MI: Myocardial infarction; SAPT: Single antiplatelet therapy

DISCUSSION

Different protocols have been evaluated in post-TAVR patients to minimize complications in these patients. The European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EATCS) guidelines do not currently recommend antiplatelet therapy for the TAVR.[12] However, the ACC/AHA guidelines do recommend DAPT based on empirical evidence.[1] The current evidence level C recommendations by the ACC/AHA for DAPT post TAVR are specifically for patients without other indications for OAC.[1] Antiplatelet therapy is often challenging in dosing due to the risk of ischemic strokes and bleeding events in the postoperative period.[13] While DAPT has comparable efficacy with SAPT for the prevention of ischemic stroke, the risk of bleeding is mechanistically and clinically higher with DAPT.[14] Thus, the use of DAPT in the early setting after TAVR should take into consideration the increased risk of major bleeding e.g. intracranial hemorrhage.

The current guidelines consider DAPT for the first 3-6 months following TAVR, primarily to mitigate thromboembolization risk caused by the prosthetic valve before the endothelialization occurs.[15] Patients who have undergone TAVR have been noted to develop valve thrombosis, with an incidence of 7-40%.[16,17] Valve thrombosis is characterized by reduced leaflet motion, increased mean pressure gradient, and imaging abnormalities.[18–20] These studies demonstrate that OAC has a protective effect against valve thrombosis. The risk of valve thrombosis is higher with TAVR compared to surgical methods.[19] Certain factors that have been attributed to the development of valve thrombosis include inadequate antiplatelet therapy, the underlying risk for hypercoagulability, atrial fibrillation, endothelial injury during balloon placement, and valve malposition

as well as others.[16] With subclinical leaflet thrombosis post-TAVR, there is an increased risk of stroke or TIAs which leads to a worse prognosis.[17] It is recommended that a tailored approach be considered for patients as per their valve function to determine the need for OAC.[21] There is a need to examine appropriate anti-thrombotic data to identify evidence of outcomes for patients after TAVR.[21]

Bleeding complications is another common factor associated with high mortality and worse prognosis following TAVR. Catheter-associated damage to access sites and arteries is a common underlying etiology for bleeding.[13] With certain diseases, including arterial calcification, anemia, and gastrointestinal disease, the prognosis of TAVR is variable.[22] TAVR-associated bleeding occurs during the procedure or in the early post-procedural period.[23] Therefore, the antithrombotic use following TAVR needs to be carefully initiated and monitored.[21] While antithrombotic therapy is essential to manage ischemic events, it comes at the cost of increased risk of bleeding.[21]

In the current systematic review, we identified relevant RCTs to compare the benefits and safety of DAPT vs. SAPT following TAVR. DAPT was inferior to SAPT due to an increased risk of major bleeding and MI. There were no differences in all-cause mortality and comparable burden of major stroke with both SAPT and DAPT. The comparison of single vs. dual antiplatelet therapy has been conducted across a few quantitative analyses. The balance of ischemic and bleeding events is still unclear when considering SAPT and DAPT. However, these studies have demonstrated the lack of inferiority of SAPT to DAPT for all-cause mortality without increased bleeding episodes observed in DAPT.[24,25] Our findings support SAPT in the reduction of bleeding and MI.

RECOMMENDATIONS

As the current recommendation by ACC/AHA is to administer DAPT following TAVR in patients not already on OAC e.g., patients with atrial fibrillation, it is of considerable importance to explore the balance of ischemic and bleeding events for optimization. Patients who present with severe aortic valve stenosis are usually elderly with associated comorbidities such as atrial fibrillation or hypertension, which increases the complexity of antiplatelet therapy. It is also pertinent to explore valve thrombosis following TAVR, which is better managed with adequate antithrombotic therapy. A tailored approach with proper evaluation of the patients and their valve function is another strategy that may be considered to determine the required dose for antithrombotics. There is a need to further explore these outcomes with SAPT and DAPT to expand the anticoagulation data following TAVR. Future trials may focus on ischemic and bleeding events with either SAPT or DAPT to clarify and establish a clear balance for improved prognosis.

LIMITATIONS

There are a few limitations of our study. We compared RCT data only as these trials have a limited risk of bias. However, this renders our sample size fairly small to moderate. The studies' follow-up periods were not uniform, which may lead to a discrepancy in the outcomes.

CONCLUSION

In conclusion, our results suggest no differences in mortality following TAVR with either SAPT or DAPT. However, bleeding is significantly reduced with SAPT with no major increase in stroke risk. We recommend further large-scale randomized trials that explore the optimal antiplatelet regimen following TAVR to balance the incidence of ischemia and bleeding without compromising the mortality risk in patients.

REFERENCES

1. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin III JP, Gentile F, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol, 2021; 77(4): 450–500.
2. van Baal JWPM, Roszek B, van Elk M, Geertsma RE. Transcatheter aortic valve replacement: clinical safety and performance data. Expert Rev Med Devices, 2019; 16(10): 899–911.
3. Sattar Y, Rauf H, Bareeqa SB, Ullah W, Myla M. Transcatheter aortic valve replacement versus surgical aortic valve replacement: a review of aortic stenosis management. Cureus, 2019; 11(12).
4. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med., 2016; 374(17): 1609–20.
5. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med., 2017; 376(14): 1321–31.
6. Members WC, Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin III JP, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol, 2021; 77(4): e25–197.
7. Ferlini M, Mauri S, Rossini R. Dual antiplatelet therapy after TAVR: A drop in the bucket? Int J Cardiol, 2019; 280: 46–8.
8. Ussia GP, Scarabelli M, Mulè M, Barbanti M, Sarkar K, Cammalleri V, et al. Dual antiplatelet therapy versus aspirin alone in patients undergoing transcatheter aortic valve implantation. Am J Cardiol, 2011; 108(12): 1772–6.

9. Rodés-Cabau J, Masson J-B, Welsh RC, Garcia del Blanco B, Pelletier M, Webb JG, et al. Aspirin versus aspirin plus clopidogrel as antithrombotic 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(13): 1357–65.
10. Brouwer J, Nijenhuis VJ, Delewi R, Hermanides RS, Holvoet W, Dubois CLF, et al. Aspirin with or without clopidogrel after transcatheter aortic-valve implantation. N Engl J Med., 2020; 383(15): 1447–57.
11. Stabile E, Pucciarelli A, Cota L, Sorropago G, Tesorio T, Salemme 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(3): 624–7.
12. Vahanian A. Task force on the management of valvular hearth disease of the European Society of Cardiology: ESC Committee for Practice Guidelines. Guidelines on the management of valvular heart disease: the Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. Eur Hear J., 2007; 28: 230–68.
13. Rodés-Cabau J, Dauerman HL, Cohen MG, Mehran R, Small EM, Smyth SS, et al. Antithrombotic treatment in transcatheter aortic valve implantation: insights for cerebrovascular and bleeding events. J Am Coll Cardiol, 2013; 62(25): 2349–59.
14. Mackman N, Bergmeier W, Stouffer GA, Weitz JI. Therapeutic strategies for thrombosis: new targets and approaches. Nat Rev Drug Discov, 2020; 19(5): 333–52.
15. Nijenhuis VJ, Bennaghmouch N, Hassell M, Baan Jr J, Van Kuijk JP, Agostoni P, et al. Rationale and design of POPular-TAVI: antiplatelet therapy for patients undergoing transcatheter aortic valve implantation. Am Heart J., 2016; 173: 77–85.
16. Hansson NC, Grove EL, Andersen HR, Leipsic J, Mathiassen ON, Jensen JM, et al. Transcatheter aortic valve thrombosis: incidence, predisposing factors, and clinical implications. J Am Coll Cardiol, 2016; 68(19): 2059–69.
17. Makkar RR, Fontana G, Jilaihawi H, Chakravarty T, Kofoed KF, De Backer O, et al. Possible subclinical leaflet thrombosis in bioprosthetic aortic valves. N Engl J Med., 2015; 373(21): 2015–24.
18. Jose J, Sulimov DS, El-Mawardy M, Sato T, Allali A, Holy EW, et al. Clinical bioprosthetic heart valve thrombosis after transcatheter aortic valve replacement: incidence, characteristics, and treatment outcomes. JACC Cardiovasc Interv, 2017; 10(7): 686–97.
19. Chakravarty T, Søndergaard L, Friedman J, De Backer O, Berman D, Kofoed KF, et al. Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study. Lancet, 2017; 389(10087): 2383–92.
20. De Marchena E, Mesa J, Pomenti S, Marin y Kall C, Marincic X, Yahagi K, et al. Thrombus formation following transcatheter aortic valve replacement. JACC Cardiovasc Interv, 2015; 8(5): 728–39.
21. Hu X, Yang F-Y, 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(1): 52–65.
22. Généreux P, Cohen DJ, Williams MR, Mack M, Kodali SK, Svensson LG, 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(11): 1100–9.
23. Czerwińska-Jelonkiewicz K, Witkowski A, Dąbrowski M, Piotrowski W, Hryniewiecki T, Stępińska J. The role of platelet reactivity assessment in dual antiplatelet prophylaxis after transcatheter aortic valve implantation. Arch Cardiovasc Dis., 2018; 111(4): 233–45.
24. Elbadawi A, Thakker R, Abuzaid AA, Khalife W, Goel SS, Gilani S, et al. Single Anti-platelet Versus Dual Anti-platelet Therapy After Transcatheter Aortic Valve Implantation: A Meta-Analysis of Randomized Trials. Am J Cardiol, 2021; 140: 152–4.
25. Zuo W, Yang M, He Y, Hao C, Chen L, Ma G. Single or dual antiplatelet therapy after transcatheter aortic valve replacement: an updated systemic review and meta-analysis. J Thorac Dis., 2019; 11(3): 959.