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Brief Report

EValuation of Acute and Early Phase P2Y12 Inhibitor DE-escalation After PerCutaneous Intervention (EVADE PCI)

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ABSTRACT

Introduction. Aspirin and an oral P2Y12 inhibitor are recommended for one year after percutaneous coronary intervention (PCI) in patients with acute coronary syndromes. While ticagrelor or prasugrel, more potent P2Y12 inhibitors, are preferred over clopidogrel, de-escalation often is based on provider judgment. This study compared cardiovascular outcomes and bleeding risks between patients who remained on ticagrelor or prasugrel (unchanged group) and those de-escalated to clopidogrel within 30 days of PCI.

Methods. The authors analyzed data from patients admitted between June 2014 and December 2022 for acute coronary syndromes requiring PCI who received an oral P2Y12 inhibitor within 72 hours of admission. The primary outcome was a composite of all-cause mortality, urgent revascularization, stent thrombosis, stroke, and major bleeding at one year. Secondary outcomes included the individual components of the composite outcome. Statistical analyses included chi-square tests, Student's t-tests, or non-parametric equivalents, as appropriate.

Results. A total of 210 patients met the inclusion criteria, with 149 remaining on unchanged P2Y12 therapy and 61 undergoing de-escalation. There was no statistically significant difference in the composite outcome between the unchanged and de-escalated groups (n [%]: 25 [17] vs. 6 [10]; χ^2 [1, N = 210] = 1.658, p = 0.198). Additionally, secondary outcomes, including all-cause mortality, urgent revascularization, stent thrombosis, stroke, and major bleeding, did not differ significantly between groups.

Conclusions. A composite outcome of all-cause mortality, urgent revascularization, stent thrombosis, stroke, and major bleeding at one year was similar between patients who continued ticagrelor or prasugrel and those de-escalated to clopidogrel within 30 days of PCI. Larger studies are needed to confirm these findings and assess the optimal timing for therapy adjustments.

INTRODUCTION

An oral purinergic receptor type Y subtype 12 (P2Y12) inhibitor is recommended in combination with aspirin for one year after percutaneous coronary intervention (PCI) in patients with acute coronary syndromes.[1,2] Studies comparing the efficacy of oral P2Y12 inhibitors suggest that ticagrelor or prasugrel provides better outcomes than clopidogrel, as clopidogrel undergoes extensive first-pass metabolism, exhibits greater pharmacokinetic and pharmacodynamic variability, and provides less platelet inhibition.[3-7] Despite these findings, clopidogrel often is prescribed due to cost, adherence concerns, or an increased risk of bleeding.[8-14]

De-escalation of P2Y12 inhibitor therapy occurs when a patient initially receives ticagrelor or prasugrel after PCI and later is switched to clopidogrel. The timing of de-escalation requires balancing ischemic and hemorrhagic risks. Current expert consensus defines de-escalation timing as acute (<24 hours), early (1-30 days), and late (>30 days).[8] Previous trials indicate that late-phase de-escalation to clopidogrel does not adversely affect clinical outcomes one-year post-PCI.[15-22]

Studies report an in-hospital P2Y12 inhibitor de-escalation rate of 5-23% among patients with acute coronary syndromes undergoing PCI.[13,23-29] This suggests a preference for ticagrelor or prasugrel at initial treatment, with de-escalation occurring post-discharge once patient factors such as cost, adherence, or bleeding risk are identified.[8-14] However, there is limited published outcome data on in-hospital de-escalation. One expert panel provides guidance on how to de-escalate P2Y12 therapy but does not specify timing,[8] while two consensus statements classify de-escalation as potentially safe and effective but acknowledge limited supporting data.[30,31] Various guidelines differ on guided versus unguided de-escalation, with some suggesting platelet function testing for select patients, though it is not routinely recommended.[31]

We designed a retrospective cohort study to compare acute and early-phase P2Y12 inhibitor de-escalation to unchanged therapy following PCI in patients with acute coronary syndromes.

METHODS

Study Design. This retrospective cohort study, conducted at a comprehensive cardiac hospital, compared cardiovascular outcomes and bleeding risks between patients de-escalated to clopidogrel within 30 days of PCI and those who remained on their initial P2Y12 inhibitor therapy. The study was approved by the hospital's Institutional Review Board (IRB) and classified as minimal risk.

Patient Selection. Patients were included if they were ≥18 years old, admitted to a comprehensive cardiac hospital for an acute coronary syndrome requiring PCI between June 2014 and December 2021, received an oral P2Y12 inhibitor within 72 hours of admission, and continued dual antiplatelet therapy (DAPT) at discharge.

Exclusion criteria included initial P2Y12 therapy with clopidogrel; thrombocytopenia on admission (platelet count $<50\times10^9$/L); death within 24 hours of admission; pre-admission DAPT or chronic anticoagulation therapy; allergy to clopidogrel, prasugrel, ticagrelor, or aspirin; history of intracranial or gastrointestinal bleeding within the past year and planned coronary artery bypass graft within 30 days post-PCI.

Patients in the de-escalated group received at least one dose of ticagrelor or prasugrel and were switched to clopidogrel within 30 days post-PCI. The unchanged group remained on ticagrelor or prasugrel throughout treatment.

Outcomes. The primary outcome was a composite of all-cause mortality, urgent revascularization, stent thrombosis, stroke, and major bleeding at one-year post-acute coronary syndrome. Secondary outcomes included the individual components of this composite measure.

Data Collection. Collected data included:

- Patient demographics (name, age, sex, weight)
- Hospital admissions (June 2014-December 2022)
- Medical history (hypertension, diabetes, dyslipidemia, smoking, myocardial infarction, prior coronary artery bypass graft)
- Diagnosis codes for unstable angina, ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, stent thrombosis, and stroke
- Baseline clinical characteristics (ejection fraction, initial platelet count, allergies to P2Y12 inhibitors or aspirin, culprit lesions, number of vessels treated, stent type)
- P2Y12 inhibitor therapy details (name, dose, route, frequency, administration date/time, therapy changes)
- Mortality data and transfused packed red blood cells
- Major bleeding events (defined as transfusion of ≥2 units of packed red blood cells within 24 hours)

Because the hospital's standard protocol includes aspirin 81 mg with a P2Y12 inhibitor, aspirin administration was not specifically recorded.

Standard Hospital Procedures. During the study period, patients received a loading dose of prasugrel or ticagrelor once their coronary anatomy was confirmed, followed by maintenance therapy. No standardized protocol existed for de-escalation timing, so patients could have been switched to clopidogrel at any point during their admission.

Data Analysis. A power calculation was performed based on a prior study evaluating a composite outcome of cardiovascular death, urgent revascularization, stroke, and bleeding, which reported event rates of 13.4% in patients who switched DAPT after 30 days and 26.3% in those who remained on unchanged DAPT.[15] Assuming similar event rates, a sample size of 298 patients was required to achieve 80% power with an alpha of 0.05.

Patients were selected in reverse chronological order until the target sample size was met. Discrete variables were analyzed using the Chi-squared or Fisher's exact test, as appropriate, while continuous variables were assessed using a Student's t-test or Wilcoxon rank sum test, depending on data distribution. Statistical analyses were conducted using SigmaPlot 14.5®.

RESULTS

Of the 313 patients screened, 210 met the inclusion criteria for analysis (unchanged DAPT: n = 149; de-escalated DAPT: n = 61; Figure 1). The study population was predominantly male (131/210, 62%) with a median age of 62.5 years (interquartile range [IQR]: 54-69.25). At presentation, 53% (112/210) of patients had a non-ST-elevation myocardial infarction (NSTEMI), and 95% received ticagrelor as the initial P2Y12 inhibitor.

In the de-escalation group, there was a significantly higher proportion of smokers (n [%]: 30 [49] vs. 50 [34]; χ^2[1, N = 210] = 4.48, p = 0.034) and patients with diabetes (n [%]: 29 [47] vs. 47 [32]; χ^2[1, N = 210] = 4.796, p = 0.029) compared to the unchanged DAPT group. Additionally, the de-escalation group had a significantly longer hospital stay (median [IQR]: 3.2 [2.5-4.6] vs. 2.7 [2.1-4.1] days; p <0.023). No other baseline characteristics differed significantly between groups (Table 1).

Among the 61 patients in the de-escalation group, therapy de-escalation occurred at a median of 1.26 days (IQR: 0.73-2.6) post-PCI.

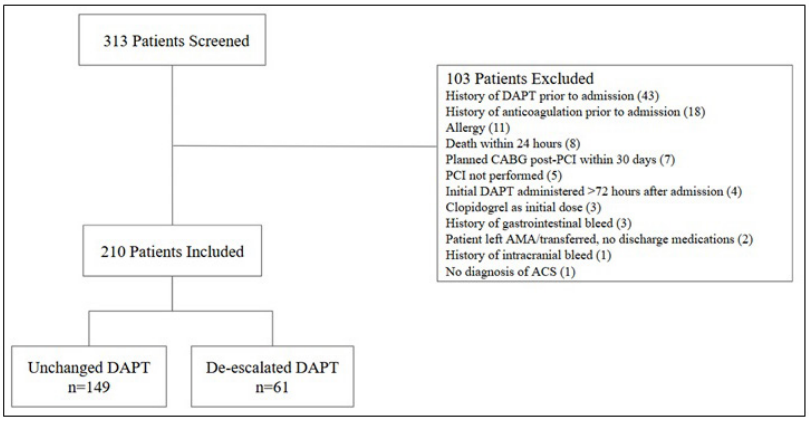

Figure 1. Patient criteria. DAPT, dual antiplatelet therapy; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention, AMA, against medical advice; ACS, acute coronary syndrome.

In patients presenting with acute coronary syndrome and undergoing PCI, there was a composite outcome rate of 14.8%, with no significant difference between the de-escalated and unchanged DAPT groups (n [%]: 6 [9.8] vs. 25 [16.8]; χ^2[1, N = 210] = 1.658, p = 0.198).

Although there was a numerical decrease in all-cause mortality (1 [2%] vs. 13 [9%]; χ^2[1, N = 210] = 3.492, p = 0.062) and major bleeding (1 [2%] vs. 8 [5%]; χ^2[1, N = 210] = 1.468, p = 0.226) in the de-escalation group, these differences were not statistically significant.

Similarly, there were no significant differences between the de-escalated and unchanged DAPT groups in stent thrombosis (0 [0%] vs. 1 [1%]; χ^2[1, N = 210] = 0.411, p = 0.521), urgent revascularization (4 [7%] vs. 11 [7%]; χ^2[1, N = 210] = 0.044, p = 0.833), or stroke (0 [0%] vs. 1 [1%]; χ^2[1, N = 210] = 0.411, p = 0.521).

DISCUSSION

There was a 14.8% risk of major adverse cardiovascular events, with no statistically significant difference between patients receiving de-escalated and unchanged DAPT. Compared to unchanged DAPT, the de-escalation group showed a trend toward lower all-cause mortality and major bleeding. To the authors' knowledge, this is the first study to evaluate the one-year risk of major adverse cardiovascular events following in-hospital, acute-phase P2Y12 inhibitor therapy de-escalation after PCI without platelet function testing guidance.

Previous studies assessing P2Y12 inhibitor de-escalation at or after discharge found similar rates of major adverse cardiovascular events compared to no de-escalation, with most patients in these studies receiving prasugrel post-PCI.[13,26,32,33] Our study, which primarily evaluated ticagrelor as the initial antiplatelet therapy, found no difference in major adverse cardiovascular events. Unlike prior trials, we excluded patients on chronic anticoagulation or pre-admission DAPT to better isolate the effects of de-escalation.[33] Despite differences in study populations and designs, our findings reinforce that early de-escalation to clopidogrel may be a safe alternative to more potent P2Y12 inhibitors.[13,26,32-34]

Table 1. Clinical characteristics.

Characteristic	De-escalated DAPT N = 61	Unchanged DAPT N = 149
Age, mean (SD)	60 (13)	63 (11)
Sex, male	32 (52)	99 (66)
Medical history		
Hypertension	44 (72)	98 (66)
Diabetes*	29 (47)	47 (32)
Dyslipidemia	46 (75)	102 (69)
Current smoker*	30 (49)	50 (34)
History of CABG	3 (5)	8 (5)
EF, median (IQR)	55 (45-60) N = 39	44 (40-55) N = 99
Presenting condition		
Unstable angina	1 (2)	1 (<1)
NSTEMI	38 (62)	74 (50)
STEMI	22 (36)	74 (50)
Initial antiplatelet, Ticagrelor*	58 (95)	142 (95)
Hospital LOS, median (IQR)*	3.2 (2.5-4.6)	2.7 (2.1-4.1)
In-hospital mortality	0 (0)	5 (3)
Culprit lesion		
Left main	0 (0)	8 (5)
Left anterior descending	0 (0)	8 (5)
Left circumflex	17 (28)	29 (19)
Right coronary artery	23 (38)	63 (43)
Venous graft	1 (2)	3 (2)
Number of vessels treated		
1	50 (82)	120 (81)
2	11 (18)	25 (17)
3	0 (0)	4 (3)
Stent type		
Drug-eluting stent	60 (98)	149 (100)

*Statistically significant p <.05
Data presented as numbers (%), unless otherwise stated.
DAPT, dual antiplatelet therapy; SD, standard deviation; CABG, coronary artery bypass graft; EF, ejection fraction; LOS, length of stay; IQR, interquartile range; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

Current guidelines recommend aspirin with a potent P2Y12 inhibitor after coronary stent placement while suggesting de-escalation for patients at increased bleeding risk.[1,2] However, the safety of de-escalation in the acute early phase remains uncertain. Prior studies have assessed de-escalation after 30 days post-PCI and found no significant difference in ischemic events. Our study is unique in evaluating the safety and efficacy of de-escalation within 30 days of stent placement, providing updated evidence on early de-escalation strategies in acute coronary syndrome patients post-PCI.[13,33,34]

Patients with diabetes and a history of smoking have an increased risk of platelet hyperreactivity and thrombotic events.[35-37] Previous studies have found no significant difference in outcomes between de-escalation and standard P2Y12 inhibitor therapy in diabetic patients.[38,39] Additionally, smoking may influence the pharmacokinetics and pharmacodynamics of clopidogrel.[40] In our study, 47% (29/61) of patients in the de-escalated group and 32% (47/149) in the unchanged group had diabetes, while 49% (30/61) and 34% (50/149), respectively, were current smokers. Notably, our study found a trend toward improved composite outcomes in the de-escalation group. This hypothesis-generating subgroup analysis raises questions about the influence of social history and comorbidities on platelet hyperreactivity post-PCI.

Limitations. Due to the retrospective nature of this study, the sample size was small and did not achieve the calculated power, increasing the risk of a type II error. A larger sample size would be needed to draw more definitive conclusions. The study also is limited by the assumption of aspirin administration and adherence to P2Y12 inhibitor therapy, as compliance was not directly assessed.

Additionally, the reasons for de-escalation remain unknown, and data on de-escalation after hospital discharge were not collected. No platelet function assays were performed, as they are not guideline-recommended.[31] As a result, patients who were non-responders to clopidogrel could not be identified, limiting the study's external validity.

Furthermore, outcomes for patients who were readmitted to outside hospitals were not captured. While some studies have used more comprehensive bleeding definitions, this study defined major bleeding as requiring transfusion of two or more units of packed red blood cells within 24 hours.

CONCLUSIONS

De-escalation of P2Y12 therapy from prasugrel or ticagrelor to clopidogrel within 30 days of PCI did not statistically impact one-year outcomes of all-cause mortality, urgent revascularization, stent thrombosis, stroke, and major bleeding. Further randomized controlled trials are needed to strengthen these findings.

REFERENCES

[1] Writing Committee Members, Lawton JS, Tamis-Holland JE, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. J Am Coll Cardiol 2022; 79(2):e21-e129. PMID: 34895950.
[2] Steinhubl SR, Berger PB, Mann JT 3rd, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: A randomized controlled trial. JAMA 2002; 288(19):2411-2420. PMID: 12435254.
[3] Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009; 361(11):1045-1057. PMID: 19717846.
[4] Cannon CP, Harrington RA, James S, et al. Comparison of ticagrelor with clopidogrel in patients with a planned invasive strategy for acute coronary syndromes (PLATO): A randomised double-blind study. Lancet 2010; 375(9711):283-293. PMID: 20079528.
[5] Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2007; 357(20):2001-2015. PMID: 17982182.
[6] Montalescot G, Wiviott SD, Braunwald E, et al. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): Double-blind, randomised controlled trial. Lancet 2009; 373(9665):723-731. PMID: 19249633.
[7] Xu J, Lo S, Mussap CJ, et al. Impact of ticagrelor versus clopidogrel on coronary microvascular function after non-st-segment-elevation acute coronary syndrome. Circ Cardiovasc Interv 2022; 15(4):e011419. PMID: 35369712.

[8] Angiolillo DJ, Rollini F, Storey RF, et al. International expert consensus on switching platelet P2Y12 receptor-inhibiting therapies. Circulation 2017; 136(20):1955-1975. PMID: 29084738.
[9] Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: A meta-analysis of prevalence and clinical consequences. Eur Heart J 2013; 34(38):2940-2948. PMID: 23907142.
[10] Dehghani P, Chopra V, Bell A, et al. Southern Saskatchewan Ticagrelor Registry experience. Patient Prefer Adherence 2014; 8:1427-1435. PMID: 25342889.
[11] Harding SA, Holley A, Wilkins B, Fairley S, Simmonds M, Larsen PD. Contemporary antiplatelet therapy in acute coronary syndromes: Are there differences in outcomes and discontinuation between clopidogrel and ticagrelor? Intern Med J 2017; 47(11):1298-1305. PMID: 28857445.
[12] Wang X, Xi S, Liu J, et al. Switching between ticagrelor and clopidogrel in patients who underwent percutaneous coronary intervention: Insight into contemporary practice in Chinese patients. Eur Heart J Suppl 2016; 18(Suppl F):F19-F26. PMID: 28533726.
[13] Biscaglia S, Campo G, Pavasini R, Tebaldi M, Tumscitz C, Ferrari R. Occurrence, causes, and outcome after switching from ticagrelor to clopidogrel in a real-life scenario: Data from a prospective registry. Platelets 2016; 27(5):484-487. PMID: 27050796.
[14] Zettler ME, Peterson ED, McCoy LA, et al. Switching of adenosine diphosphate receptor inhibitor after hospital discharge among myocardial infarction patients: Insights from the Treatment with Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (TRANSLATE-ACS) observational study. Am Heart J 2017; 183:62-68. PMID: 27979043.
[15] Cuisset T, Deharo P, Quilici J, et al. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: The TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. Eur Heart J 2017; 38(41):3070-3078. PMID: 28510646.
[16] Kim HS, Kang J, Hwang D, et al. Prasugrel-based de-escalation of dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (HOST-REDUCE-POLYTECH-ACS): An open-label, multicentre, non-inferiority randomised trial. Lancet 2020; 396(10257):1079-1089. PMID: 32882163.
[17] Zhao Z, Wang J, Lei M, et al. Effectiveness of dual antiplatelet de-escalation therapy on the prognosis of patients with ST segment elevation myocardial infarction undergoing percutaneous coronary intervention. BMC Cardiovasc Disord 2023; 23(1):168. PMID: 36991321.
[18] De Filippo O, Piroli F, Bruno F, et al. De-escalation of dual antiplatelet therapy for patients with acute coronary syndrome after percutaneous coronary intervention: A systematic review and network meta-analysis. BMJ Evid Based Med 2024; 29(3):171-186. PMID: 38242567.
[19] Li Y, Lei M, Yang Y, et al. A novel de-escalation antiplatelet therapy for patients with acute coronary syndrome undergoing percutaneous coronary intervention. Medicine (Baltimore) 2023; 102(27):e34153. PMID: 37417626.
[20] Kuno T, Watanabe A, Shoji S, et al. Short-term DAPT and DAPT de-escalation strategies for patients with acute coronary syndromes: A systematic review and network meta-analysis. Circ Cardiovasc Interv 2023; 16(9):e013242. PMID: 37609850.
[21] Saito T, Fujisaki T, Aikawa T, et al. Strategy of dual antiplatelet therapy for patients with ST-elevation myocardial infarction and non-ST-elevation acute coronary syndromes: A systematic review and network meta-analysis. Int J Cardiol 2023; 389:131157. PMID: 37433404.
[22] Kim CJ, Park MW, Kim MC, et al. Unguided de-escalation from ticagrelor to clopidogrel in stabilised patients with acute myocardial infarction undergoing percutaneous coronary intervention (TALOS-AMI): An investigator-initiated, open-label, multicentre, non-inferiority, randomised trial. Lancet 2021; 398(10308):1305-1316. PMID: 34627490.
[23] Angiolillo DJ, Patti G, Chan KT, et al. De-escalation from ticagrelor to clopidogrel in acute coronary syndrome patients: A systematic review and meta-analysis. J Thromb Thrombolysis 2019; 48(1):1-10. PMID: 31004312.
[24] Alexopoulos D, Xanthopoulou I, Deftereos S, et al. In-hospital switching of oral P2Y12 inhibitor treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention: Prevalence, predictors and short-term outcome. Am Heart J 2014; 167(1):68-76.e2. PMID: 24332144.
[25] Clemmensen P, Grieco N, Ince H, et al. MULTInational non-interventional study of patients with ST-segment elevation myocardial infarction treated with PRimary Angioplasty and Concomitant use of upstream antiplatelet therapy with prasugrel or clopidogrel--the European MULTIPRAC Registry. Eur Heart J Acute Cardiovasc Care 2015; 4(3):220-229. PMID: 25182465.
[26] Bagai A, Peterson ED, Honeycutt E, et al. In-hospital switching between adenosine diphosphate receptor inhibitors in patients with acute myocardial infarction treated with percutaneous coronary intervention: Insights into contemporary practice from the TRANSLATE-ACS study. Eur Heart J Acute Cardiovasc Care 2015; 4(6):499-508. PMID: 25515725.
[27] Schiele F, Puymirat E, Bonello L, et al. Switching between thienopyridines in patients with acute myocardial infarction and quality of care. Open Heart 2016; 3(1):e000384. PMID: 27252877.
[28] De Luca L, Leonardi S, Cavallini C, et al. Contemporary antithrombotic strategies in patients with acute coronary syndrome admitted to cardiac care units in Italy: The EYESHOT Study. Eur Heart J Acute Cardiovasc Care 2015; 4(5):441-452. PMID: 25414322.
[29] Bagai A, Wang Y, Wang TY, et al. In-hospital switching between clopidogrel and prasugrel among patients with acute myocardial infarction treated with percutaneous coronary intervention: Insights into contemporary practice from the national cardiovascular data registry. Circ Cardiovasc Interv 2014; 7(4):585-593. PMID: 25097196.
[30] Gorog DA, Ferreiro JL, Ahrens I, et al. De-escalation or abbreviation of dual antiplatelet therapy in acute coronary syndromes and percutaneous coronary intervention: A consensus statement from an international expert panel on coronary thrombosis. Nat Rev Cardiol 2023; 20(12):830-844. PMID: 37474795.
[31] Sibbing D, Aradi D, Alexopoulos D, et al. Updated expert consensus statement on platelet function and genetic testing for guiding P2Y12 receptor inhibitor treatment in percutaneous coronary intervention. JACC Cardiovasc Interv 2019; 12(16):1521-1537. PMID: 31202949.
[32] Claassens DMF, Vos GJA, Bergmeijer TO, et al. A genotype-guided strategy for oral P2Y12 inhibitors in primary PCI. N Engl J Med 2019; 381(17):1621-1631. PMID: 31479209.
[33] Sibbing D, Aradi D, Jacobshagen C, et al. Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): A randomised, open-label, multicentre trial. Lancet 2017; 390(10104):1747-1757. PMID: 28855078.
[34] Gimbel M, Qaderdan K, Willemsen L, et al. Clopidogrel versus ticagrelor or prasugrel in patients aged 70 years or older with non-ST-elevation acute coronary syndrome (POPular AGE): The randomised, open-label, non-inferiority trial. Lancet 2020; 395(10233):1374-1381. PMID: 32334703.
[35] Galli M, Angiolillo DJ. De-escalation of antiplatelet therapy in acute coronary syndromes: Why, how and when?. Front Cardiovasc Med 2022; 9:975969. PMID: 36093167.
[36] Bray PF. Platelet hyperreactivity: Predictive and intrinsic properties. Hematol Oncol Clin North Am 2007; 21(4):633-645, v-vi. PMID: 17666282.
[37] Centers for Disease Control and Prevention (US); National Center for Chronic Disease Prevention and Health Promotion (US); Office on Smoking and Health (US). How tobacco smoke causes disease: The biology and behavioral basis for smoking-attributable disease: A report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US); 2010. PMID: 21452462.
[38] Kang J, Rizas KD, Park KW, et al. Dual antiplatelet therapy de-escalation in acute coronary syndrome: An individual patient meta-analysis. Eur Heart J 2023; 44(15):1360-1370. PMID: 36883613.
[39] Lee M, Byun S, Lim S, et al. Dual antiplatelet therapy de-escalation in stabilized myocardial infarction with high ischemic risk: Post hoc analysis of the TALOS-AMI Randomized Clinical Trial. JAMA Cardiol 2024; 9(2):125-133. PMID: 38117483.
[40] Gurbel PA, Bliden KP, Logan DK, et al. The influence of smoking status on the pharmacokinetics and pharmacodynamics of clopidogrel and prasugrel: The PARADOX study. J Am Coll Cardiol 2013; 62(6):505-512. PMID: 23602770.

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