Submitted: 23 June, 2024 Accepted: 28 November, 2024 Published: 08 March, 2025 DOI:10.22514/sv.2025.044

Open Access
Signa Vitae

CASE REPORT

Personalized antiplatelet therapy in a post-PCI patient with high bleeding risk

Jamilya Mansurova[1], Assel Kassymova[1,*], Anar Kozhabayeva[1], Lyudmila Karazhanova[1]

[1]Semey Medical University, 071400 Semey, AR, Kazakhstan

***Correspondence**
assel.kassymova@smu.edu.kz
(Assel Kassymova)

Abstract

Background: Therapeutic de-escalation involving P2Y12 receptor inhibitors, such as transitioning from prasugrel or ticagrelor to clopidogrel or reducing the dose of prasugrel or ticagrelor, has been proposed as an alternative strategy for dual antiplatelet therapy (DAPT) in patients with acute coronary syndrome (ACS). This approach is particularly relevant for patients at high bleeding risk who are unsuitable for potent P2Y12 receptor inhibitors. However, de-escalation within the first 30 days following the ACS index event is associated with an increased risk of ischemic events and is generally not recommended. **Case**: We present a clinical case of a post-percutaneous coronary intervention (PCI) patient with a high risk of bleeding who underwent de-escalation of DAPT. The approach involved reducing the dose of ticagrelor, a potent P2Y12 receptor inhibitor, guided by platelet function testing and genetic analysis. A transition to clopidogrel, a less potent P2Y12 receptor inhibitor, was not feasible due to prior stent thrombosis while the patient was on clopidogrel. **Conclusions**: This case highlights the importance of individualized antithrombotic strategies in high-risk patients. Prospective evaluation of de-escalation strategies using platelet function testing or genetic analysis is recommended to optimize therapy while minimizing both bleeding and ischemic risks.

Keywords

Percutaneous coronary intervention; P2Y12 receptor inhibitor; Residual platelet reactivity; Bleeding; De-escalation

1. Introduction

The advent of advanced-generation drug-eluting stents and the increased use of potent P2Y12 receptor inhibitors have significantly reduced thrombotic events, shifting the primary focus to the prevention of hemorrhagic complications. While PCI outcomes have improved in patients with coronary heart disease (CHD), DAPT-related bleeding remains a critical determinant of poor post-PCI prognosis. The importance of reducing bleeding risk is further underscored by its prognostic impact, including mortality [1]. Consequently, DAPT de-escalation of P2Y12 receptor inhibitors has emerged as a potential strategy to mitigate bleeding in patients with reduced thrombotic risk but ongoing hemorrhagic concerns.

According to the 2019 consensus expert report, two approaches to DAPT de-escalation are recommended: platelet function testing (PFT) and genetic testing [2]. Studies such as PHILO (Study to Assess Safety and Efficacy of Ticagrelor (AZD6140) Versus Clopidogrel in Asian/Japanese Patients With Non-ST or ST Elevation Acute Coronary Syndromes) and TICAKOREA (Ticagrelor Versus Clopidogrel in Asian/Korean Patients with ACS Intended for Invasive Management; URL: https://www.clinicaltrials.gov; unique identifier: NCT02094963) demonstrated that, compared to clopidogrel, standard-dose ticagrelor was associated with an increased risk of adverse outcomes, including major bleeding, cardiovascular death and stroke [3].

However, pharmacodynamic and pharmacokinetic responses to potent P2Y12 receptor inhibitors vary across ethnicities; Asian populations demonstrate approximately 30% higher exposure to the active metabolite of ticagrelor compared to Europeans, even after adjusting for body weight [4, 5]. Thus, balancing ischemic and hemorrhagic risks has become a critical consideration in prescribing DAPT, with safety and efficacy requiring careful, individualized assessment.

2. Case description

A 59-year-old Asian male of Kazakh descent was admitted to the urology department with complaints of macrohematuria, difficulty urinating, and general weakness.

Medical History: Two months prior, the patient underwent elective PCI with stent placement in the right coronary

artery (RCA). In alignment with ESC/EACTS (European Society of Cardiology)/(European Association for Cardio-Thoracic Surgery) myocardial revascularization guidelines, the patient was initiated on DAPT with acetylsalicylic acid (ASA) and clopidogrel [6, 7]. Despite adherence to the medication regimen, five days post-discharge, the patient experienced a myocardial infarction (MI) with ST-segment elevation affecting the inferior wall of the left ventricle (MI type 4b), requiring emergency readmission. Coronary angiography revealed stent thrombosis in the RCA, which was successfully managed with mechanical thrombus aspiration, balloon dilation, and additional stenting. The patient's comorbidities included diabetes mellitus and dyscirculatory encephalopathy.

Given the occurrence of stent thrombosis, the patient was transitioned to ticagrelor 90 mg twice daily alongside ASA 100 mg. However, a week after initiating DAPT with ticagrelor, the patient developed hematuria, which progressively worsened. One month later, he was readmitted with macrohematuria. Laboratory tests revealed decreased hemoglobin and hematocrit. Leukocytes, platelets, and erythrocytes were within normal ranges. Biochemical analysis showed normal levels of urea, creatinine, glucose, Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and glomerular filtration rate (GFR). Coagulation parameters were within normal limits, while urinalysis confirmed significant proteinuria and macrohematuria (Table 1). Echocardiography demonstrated reduced left ventricular (LV) function with an ejection fraction of 49%.

Urethrocystoscopy Results: A pale gray, villous bladder tumor, approximately 4.5 cm in size, was identified along the right side wall and lower wall. Histopathological evaluation revealed a papillary urothelial tumor of low malignancy.

Given the presence of BARC (Bleeding Academic Research Consortium) type 3 bleeding associated with DAPT, a strategy of antiplatelet therapy de-escalation was pursued, guided by PFT and genetic testing [8]. Platelet function was assessed using an AggRAM Helena aggregometer, with stimulation by (adenosine diphosphate) ADP (10.0 mcg/mL) and epinephrine. The maximum residual platelet reactivity (RPR) was 14.3%, and the area under the area under the curve (AUC) curve was 0.46, indicating significant platelet inhibition (Fig. 1). Pharmacogenetic testing using polymerase chain reaction (PCR) analysis revealed no significant (cytochrome P450 2C19) *CYP2C19* polymorphism in the DNA sample. Two days after discontinuing DAPT, the patient underwent bipolar transurethral resection of the bladder tumor. According to 2020 ESC guidelines, DAPT was held for five days with PFT monitoring [9].

Subsequent antithrombotic therapy was managed with PFT oversight, and after five days, the maximum percentage of platelet aggregation was 62.3% (Fig. 2). Based on the observed positive clinical course, absence of hemorrhagic events, and PFT data, ticagrelor therapy was resumed at a reduced dose of 60 mg twice daily on the sixth day, achieving optimal platelet activity suppression (RPR 58.0%) (Fig. 3).

The patient was discharged in satisfactory condition on dual antiplatelet therapy (DAPT) consisting of ticagrelor 60 mg twice daily and ASA 100 mg. During a 6-month follow-up period, the patient showed no recurrence of bleeding or ischemic events.

3. Discussion

According to the 2023 ESC recommendations, patients with ACS who undergo PCI are advised to receive ASA in combination with next-generation P2Y12 receptor inhibitors, such as prasugrel or ticagrelor, due to their superior efficacy. For patients at high bleeding risk, transitioning from potent P2Y12 in-

TABLE 1. Characteristics of the presented clinical case report.

Beginning	14 January 2024; 8:30 AM
Main Complaint	For macrohematuria, difficulty urinating, general weakness.
Case record	Two months prior, the patient underwent elective percutaneous coronary intervention (PCI) with stent placement in the right coronary artery. Following the procedure, dual antiplatelet therapy (DAPT) was initiated with acetylsalicylic acid (ASA) and clopidogrel. Five days post-PCI, stent thrombosis occurred despite DAPT administration. Consequently, repeat PCI with stent placement was performed. The patient was subsequently prescribed ticagrelor 90 mg twice daily in combination with ASA 100 mg daily. One week following the initiation of DAPT with ticagrelor, the patient developed hematuria. Approximately one month later, the patient was admitted to the urology department with macrohematuria and a significant decline in hemoglobin levels. During the bleeding episode, DAPT was interrupted for five days under the guidance of platelet function testing (PFT).
Process of diagnostic	Urethrocystoscopy, medical history, pharmacogenetics of clopidogrel, platelet function test.
Laboratory results	
Hemoglobin	Hemoglobin level: 96.0 g/L (reference range for men: 135–160 g/L).
Hematocrit	Hematocrit: 31% (reference range for men: 40–48%).
Urine analysis	Red blood cells in urine: Complete field of view (reference range: 0–1 per high power field). Proteinuria: 9.9 g/L (reference range: up to 0.033 g/L).

Chnl	Reag	Lot No.	Conc.	Units	PPP	PRP	Max%	TMax
1	AdenosineDiphosphate		10	µM	0.128	0.776	14.3	22
2	AdenosineDiphosphate		5	µM	0.143	0.740	9.4	21
3	Epinephrine		2.5	µM	0.101	0.764	1.3	45
4	Epinephrine		10	ug/mL	0.103	0.845	15.5	595

Chnl	Slope	Slope2	Lag	AreaUndCrv
1	70.5	3.2	4.7	0.46
2	61.0	1.2	5.7	0.26
3	3.0		597.2	0.16
4	6.3		28.1	9.56

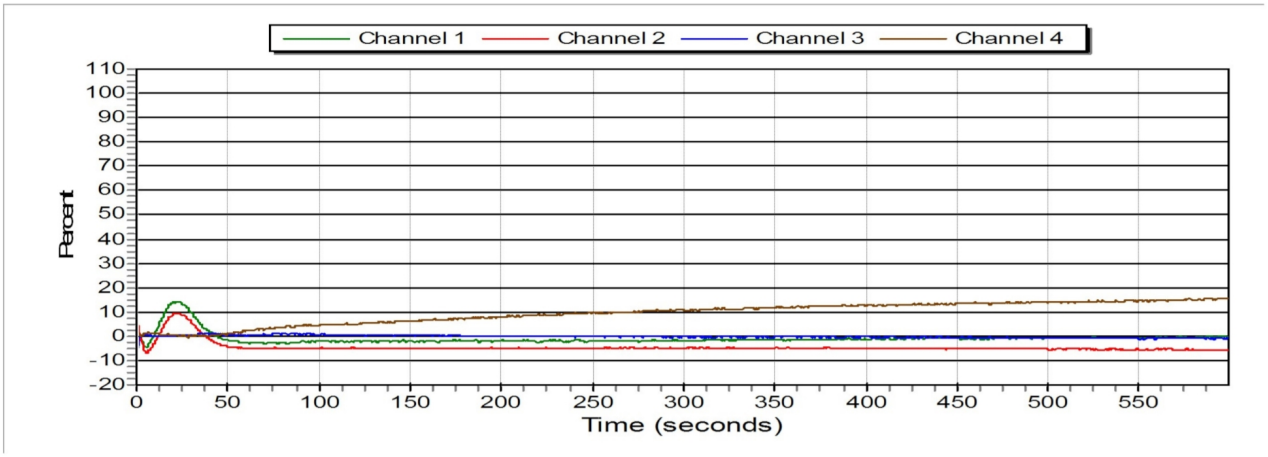

FIGURE 1. Aggregatogram with 10 mcg/mL of ADP. Residual platelet reactivity against the background of a standard dose of ticagrelor. PPP: platelet-poor plasma; PRP: platelet-rich plasma; TMax: time to maximum concentration; Chnl: channel; Lot No.: Lot Number; Conc.: concentration; AreaUndCrv: area under the curve.

Chnl	Reag	Lot No.	Conc.	Units	PPP	PRP	Max%	TMax
1	AdenosineDiphosphate		10	µM	0.088	0.687	62.3	138
2	AdenosineDiphosphate		5	µM	0.120	0.701	46.6	77
3	Epinephrine		2.5	µM	0.100	0.669	32.8	588
4	Epinephrine		10	ug/mL	0.111	0.657	49.1	597

Chnl	Slope	Slope2	Lag	AreaUndCrv
1	107.5	17.5	5.2	50.6
2	99.1	5.1	6.2	35.84
3	14.8		12.9	22.19
4	26.5		10.5	35.63

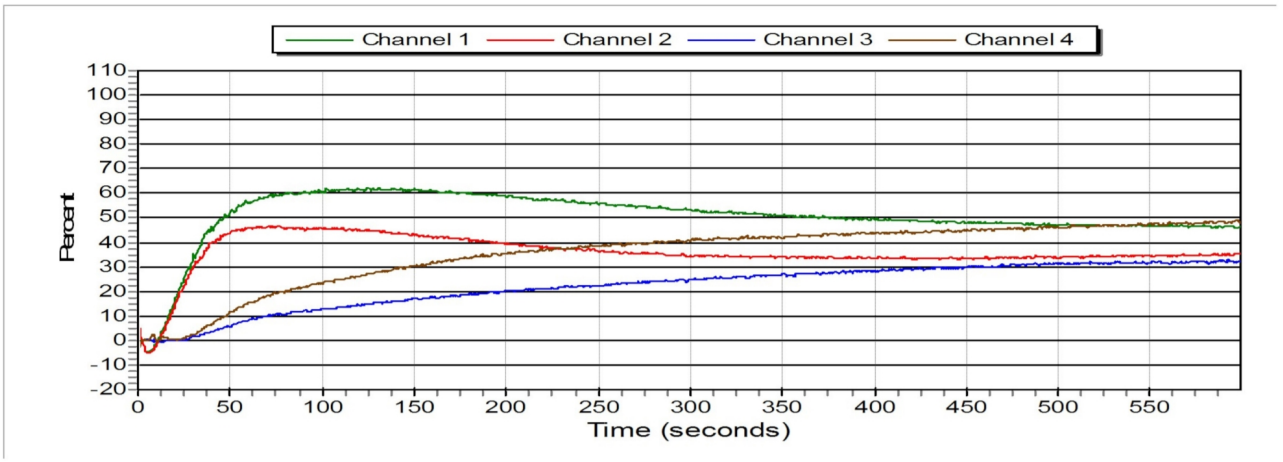

FIGURE 2. Aggregatogram at the interruption of antithrombotic therapy. PPP: platelet-poor plasma; PRP: platelet-rich plasma; TMax: time to maximum concentration; Chnl: channel; Lot No.: Lot Number; Conc.: concentration; AreaUndCrv: area under the curve.

Chnl	Reag	Lot No.	Conc.	Units	PPP	PRP	Max%	TMax
1	AdenosineDiphosphate		10	µM	0.234	0.508	58.0	49
2	AdenosineDiphosphate		5	µM	0.266	0.589	31.7	35
3	Epinephrine		2.5	µM	0.239	0.532	27.4	242
4	Epinephrine		10	ug/mL	0.232	0.522	38.0	592

Chnl	Slope	Slope2	Lag	AreaUndCrv
1	142.1	1.5	5.8	20.71
2	104.2	10	5.2	1.65
3	26.5		19.0	21.49
4	33.4		19.0	30.21

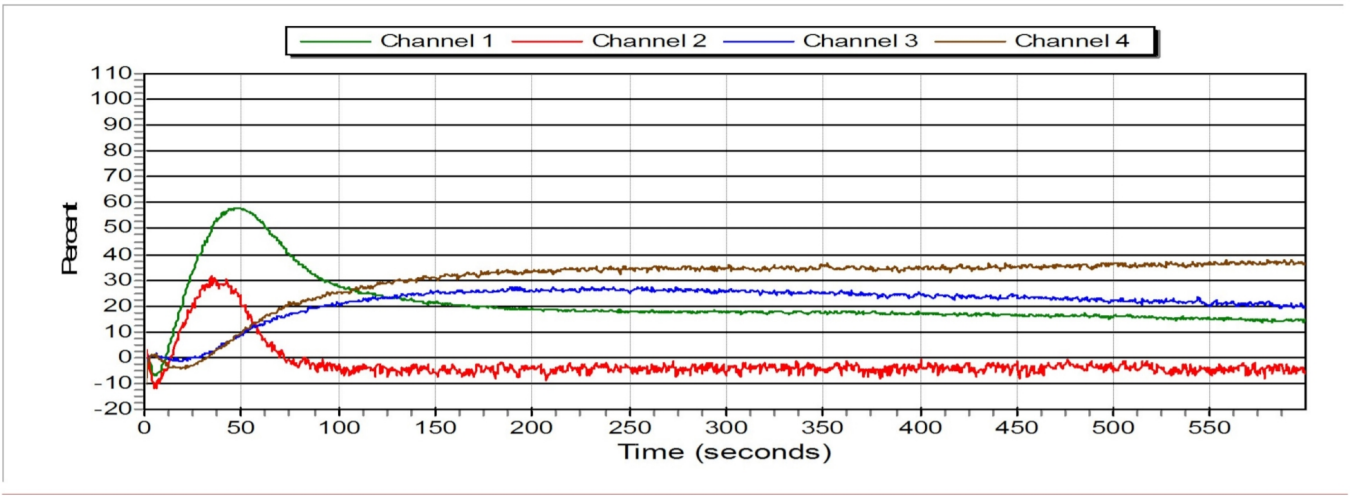

FIGURE 3. Aggregatogram with 10 mcg/mL of ADP. Residual platelet reactivity on the background of a reduced dose of ticagrelor. PPP: platelet-poor plasma; PRP: platelet-rich plasma; TMax: time to maximum concentration; Chnl: channel; Lot No.: Lot Number; Conc.: concentration; AreaUndCrv: area under the curve.

hibitors (prasugrel/ticagrelor) to a less potent agent like clopidogrel, or opting for a reduced dose of potent inhibitors under the guidance of platelet function testing PFT and *CYP2C19* genotyping, is recommended as an alternative DAPT strategy [10].

The approach to both escalation and de-escalation of DAPT is therefore based on PFT and genotyping of *CYP2C19* receptors, tailored according to patient risk profiles and the availability of appropriate diagnostic methods. In this study, platelet function was assessed using an adenosine diphosphate (ADP) inducer and epinephrine at 10.0 mcg/mL, for which established reference intervals are available [11, 12].

While multiple tests are available to assess platelet function, the effectiveness of antiplatelet therapy remains challenging to monitor [11]. Optical aggregometry remains the "gold standard" for evaluating platelet function, based on the turbidimetric method originally developed by G. Born in the 1960s [13].

To date, there is limited comparative pharmacodynamic data on dose-reduction strategies for potent P2Y12 inhibitors. However, the Heart Outcomes Prevention Evaluation - Tailored Approaches for Personalized Outcomes (HOPE-TAILOR) study, conducted in Korean patients with ACS, demonstrated that a de-escalation strategy using half doses of ticagrelor and prasugrel significantly increased optimal platelet reactivity without serious bleeding or ischemic complications over a 9-month observation period, compared to standard dosing [14, 15].

The safety and efficacy of DAPT de-escalation have been explored in numerous recent randomized controlled trials (RCTs). A meta-analysis [16] of 16 studies, including 1629 ACS patients on DAPT, showed that among the 756 patients who received low-dose ticagrelor, 484 received 90 mg once daily, 240 received 45 mg twice daily, and 32 received 60 mg twice daily. Compared to clopidogrel at 75 mg once daily, lower doses of ticagrelor significantly reduced cardiovascular death, myocardial infarction, or stroke OR (odds ratio) = 0.39, 95% CI (confidence interval) = 0.26–0.58, $p < 0.01$).

Reduced-dose ticagrelor therapy (60 mg twice daily or even 45 mg twice daily) is considered particularly suitable for Asian patients due to its potent, reversible antiplatelet effects and reduced bleeding risk when compared to the standard dose of 90 mg twice daily [15]. Compared to European populations, Asian patients are more likely to exhibit *CYP2C19* mutations, increased platelet reactivity, and higher bleeding risk. Therefore, incorporating bleeding risk assessments, genotyping, PFT, and low-dose ticagrelor therapy could be particularly beneficial in this demographic [17].

This study, however, differs fundamentally from traditional de-escalation strategies. In de-escalation studies, a specific characteristic-such as genetic testing, PFT, or time since stent implantation-triggers the modification of medical therapy, with the risk of events subsequently assessed. Here, the intervention was initiated by a bleeding event, with PFT and

genetic testing used as tools to monitor the impact of the therapeutic adjustment.

This clinical case describes one patient, which limits the possibility of generalizing the obtained results to a wider population. The relatively short observation period (6 months) also limits the possibility of assessing long-term clinical outcomes and the sustainability of the therapeutic effect.

Despite these limitations, the study has a number of strengths. The work uses a comprehensive and personalized approach to the selection and correction of antithrombotic therapy based on genetic testing and functional assessment of platelets, which reflects modern trends in personalized medicine.

The data obtained can form the basis for further large-scale studies and the development of practical recommendations for optimizing antithrombotic therapy in this category of patients.

4. Conclusions

In this clinical case, we assessed the pharmacodynamic effect and clinical outcome of a de-escalation strategy involving a reduced ticagrelor dose of 60 mg in a post-PCI patient with a high bleeding risk. De-escalation to a 60 mg dose of ticagrelor proved effective in optimizing platelet reactivity, as no recurrent bleeding or ischemic events occurred during the 6-month follow-up. Balancing safety and efficacy in dual antiplatelet therapy requires functional testing and *CYP2C19*2* and **3* polymorphism genotyping to guide DAPT de-escalation. Further research is needed to develop optimal dose-reduction strategies for potent P2Y12 inhibitors to achieve a balance between their effectiveness and safety.

ABBREVIATIONS

DAPT, dual antiplatelet therapy; LV, left ventricle; PCI, percutaneous coronary intervention; PCR, polymerase chain reaction; RPR, residual platelet reactivity; PRP, platelet-rich plasma; ACS, acute coronary syndrome; CHD, coronary heart disease; PFT, platelet function testing; RCA, right coronary artery; ESC/EACTS, European Society of Cardiology/European Association for Cardio-Thoracic Surgery; ASA, acetylsalicylic acid; MI, myocardial infarction; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; GFR, glomerular filtration rate; BARC, Bleeding Academic Research Consortium; ADP, adenosine diphosphate; AUC, area under the curve; PFT, platelet function testing.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

AsK—designed the research study, performed the research. JM and AnK—provided help and advice on analysis. LK—analyzed the data. AsK and JM—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study involving human participants was reviewed and approved by the Ethics Committee of Semey Medical University, Kazakhstan. The reference number for this approval is #16, 02 November 2023. Written informed consent was obtained from the patient included in the study.

ACKNOWLEDGMENT

We would like to acknowledge the administrative and technical support provided by Semey Medical University, Kazakhstan, during the course of this study. Additionally, we thank the laboratory staff for their assistance in conducting the platelet function tests and genetic analysis.

FUNDING

The study was funded via a local grant provided by the “SMU” NCJSC (No. 379 dated 12 September 2022).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Sawayama Y, Yamaji K, Kohsaka S, Yamamoto T, Higo Y, Numasawa Y, *et al*. Variation in in-hospital mortality and its association with percutaneous coronary intervention-related bleeding complications: a report from nationwide registry in Japan. PLOS ONE. 2021; 16: e0261371.

[2] Sibbing D, Aradi D, Alexopoulos D, ten Berg J, Bhatt DL, Bonello L, *et al*. Updated expert consensus statement on platelet function and genetic testing for guiding P2Y12 receptor inhibitor treatment in percutaneous coronary intervention. JACC: Cardiovascular Interventions. 2019; 12: 1521–1237.

[3] Park DW, Kwon O, Jang JS, Yun SC, Park H, Kang DY, *et al*. Clinically significant bleeding with ticagrelor versus clopidogrel in korean patients with acute coronary syndromes intended for invasive management: a randomized clinical trial. Circulation. 2019; 140: 1865–1877.

[4] Jeong Y, Tantry US, Omar M, Navarese E, Gorog DA, Gurbel PA. “East Asian Paradox” revisited: precision medicine for antithrombotic strategies tailored to atherothrombotic cardiovascular risks. Journal of Cardiovascular Intervention. 2024; 3: 119–135.

[5] Small DS, Kothare P, Yuen E, Lachno DR, Li YG, Winters KJ, *et al*. The pharmacokinetics and pharmacodynamics of prasugrel in healthy Chinese, Japanese, and Korean subjects compared with healthy Caucasian subjects. European Journal of Clinical Pharmacology. 2010; 66: 127–135.

[6] Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, *et al*. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. European Heart Journal. 2018; 39: 213–260.

[7] Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, *et al*. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal. 2019; 40: 87–165.

[8] Sibbing D, Aradi D, Jacobshagen C, Gross L, Trenk D, Geisler T,

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. The Lancet. 2017; 390: 1747–1757.

[9] Collet JP, Thiele H, Barbato E, Bauersachs J, Dendale P, Edvardsen T, *et al*. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2021; 42: 1289–1367.

[10] Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, *et al*. 2023 ESC Guidelines for the management of acute coronary syndromes. European Heart Journal. 2023; 44: 3720–3826.

[11] Mansurova JA, Karazhanova LK. Independent predictors of adverse cardiovascular events in patients with acute coronary syndrome after percutaneous coronary intervention during hospitalization. Kardiologiya. 2018; 58: 22–29.

[12] Kim MH, Choi SY, An SY, Serebruany V. Validation of three platelet function tests for bleeding risk stratification during dual antiplatelet therapy following coronary interventions. Clinical Cardiology. 2016; 39: 385–390.

[13] Puchinian NF, Furman NV, Malinova LI, Dolotovskaya PV. Monitoring of the effectiveness of antiplatelet therapy in cardiology practice. Rational Pharmacotherapy in Cardiology. 2017; 13: 107–115.

[14] Jin CD, Kim MH, Bang J, Serebruany V. A prospective, randomized, open-label, blinded, endpoint study exploring platelet response to half-dose prasugrel and ticagrelor in patients with the acute coronary syndrome: HOPE-TAILOR study. Cardiology. 2017; 138: 201–206.

[15] Jin CD, Kim MH, Song K, Jin X, Lee KM, Park JS, *et al*. Pharmacodynamics and outcomes of a de-escalation strategy with half-dose prasugrel or ticagrelor in east Asians patients with acute coronary syndrome: results from hope-tailor trial. Journal of Clinical Medicine. 2021; 10: 2699.

[16] Chen Q, Zhang Y, Wang Z, Wang S, Zhang H, Wang Y, *et al*. Efficacy and safety of low dose ticagrelor in patients with acute coronary syndrome: a systematic review and meta-analysis. Postgraduate Medical Journal. 2020; 96: 693–702.

[17] Tam CC, Tse HF. Antiplatelet therapy aims and strategies in Asian patients with acute coronary syndrome or stable coronary artery disease. Journal of Clinical Medicine. 2022; 11: 7440.

How to cite this article: Jamilya Mansurova, Assel Kassymova, Anar Kozhabayeva, Lyudmila Karazhanova. Personalized antiplatelet therapy in a post-PCI patient with high bleeding risk. Signa Vitae. 2025; 21(3): 114-119. doi: 10.22514/sv.2025.044.