ORIGINAL ARTICLE

JIACM 2026; 27 (2): 94-99

Proton Pump Inhibitors and Gastrointestinal Bleeding in Patients Taking Oral Dual Antiplatelet Therapy

Desai Jay, Subhendu Mohanty**, Deepak Sharma***, Abhishek Deepak**, Pokala Sai Badrinath*, Sanket Pale**

Abstract

Background: Dual antiplatelet therapy (DAPT) increases the risk of gastrointestinal (GI) bleeding. Proton pump inhibitors (PPIs) are commonly prescribed for gastroprotection, but real-world prescribing practices and their impact on bleeding outcomes in Indian settings remain unclear.

Objectives: To evaluate PPI prescribing patterns in adults receiving DAPT and to determine the association between PPI use and GI bleeding.

Material and Methods: This cross-sectional observational study was conducted at a tertiary care centre in North India. A total of 150 adults on DAPT for ≥6 months were enrolled. Data on demographics, clinical profile, DAPT duration, and PPI use (type and duration) were collected. GI bleeding was assessed using clinical history, faecal occult blood test (FOBT), and endoscopy where indicated. Statistical analysis included chi-squared test, Fisher's exact test, and Welch's t-test, with $p < 0.05$ considered significant.

Results: The mean age was 59.50 ± 9.74 years, and 56% were males. GI bleeding was observed in 10.7% of patients. PPIs were prescribed in 51.3% of patients, with Pantoprazole being the most common agent. No significant association was found between PPI use and overall GI bleeding ($p = 0.600$). However, PPI use was significantly associated with a lower incidence of clinically significant haemoglobin drop (>3 g/dL) (2.6% versus 11%; $p = 0.016$). Shorter PPI duration was associated with greater haemoglobin decline ($p < 0.001$). Increasing age was a significant risk factor for GI bleeding ($p = 0.027$), while other baseline variables were not significantly associated.

Conclusion: PPI co-prescription in patients on DAPT was associated with reduced clinically significant haemoglobin decline, suggesting a protective effect against meaningful bleeding. Although no association was observed with test-defined GI bleeding, haemoglobin-based outcomes provided additional clinical insight. Targeted and sustained PPI use in high-risk patients, particularly older individuals, appears justified. Further prospective studies are needed to confirm these findings.

Key words: Dual antiplatelet therapy; proton pump inhibitors; gastrointestinal bleeding; haemoglobin decline; pantoprazole; risk factors.

Introduction

Gastrointestinal (GI) Bleeding is a serious medical event with direct clinical and public health consequences. It is a leading cause of hospital admissions and can result in prolonged stays, transfusions and increased mortality. In patients receiving Dual Antiplatelet Therapy (DAPT), the risk of GI Bleeding rises further. DAPT is essential in managing Cardiovascular Disease, yet it carries well-known risks to Gastrointestinal safety[1-3].

DAPT involves the combination of Aspirin and a P2Y12 receptor antagonist such as Clopidogrel, Prasugrel, or Ticagrelor. This combination reduces Platelet Aggregation and prevents thrombotic events in patients with Acute Coronary Syndromes or those who undergo Percutaneous Coronary Intervention. It is a widely accepted therapy based on strong clinical evidence. Despite proven benefits - DAPT increases the risk of Upper Gastrointestinal mucosal injury, Ulcer formation and Bleeding[3-5].

Proton Pump Inhibitors (PPIs) are the most commonly used agents to reduce gastric acid secretion. By increasing gastric pH, they help preserve mucosal integrity and reduce the risk of acid-related injury. Clinical trials have shown that PPIs can significantly lower the risk of Upper GI Bleeding in patients on Antiplatelet therapy. Based on the existing evidence major cardiology and gastroenterology guidelines recommend co-prescribing PPIs for high-risk patients receiving DAPT[6].

**Junior Resident, **Associate Professor, ***Professor, Department of Medicine, Sharda Hospital and School of Medical Sciences and Research, Greater Noida - 201 310, Uttar Pradesh.*

Corresponding Author: Dr Subhendu Mohanty, Associate Professor, Department of Medicine, Sharda Hospital and School of Medical Sciences and Research, Greater Noida - 201 310, Uttar Pradesh. Tel: 9871983939, E-mail: subhendu.mohanty@sharda.ac.in

Real world practice often does not align with guideline-based care. Some patients are prescribed PPIs without a clear indication. Others do not receive any gastroprotective therapy even with obvious risk factors. This inconsistency can lead to both over-treatment and under-treatment. The overuse of PPIs also comes with consequences. Long term PPI therapy has been linked to increased risk of *Clostridium difficile* infections, bone fractures, magnesium deficiency and potential interactions with Clopidogrel due to shared metabolic pathways[8]. This creates a dilemma for physicians. The decision to prescribe a PPI along with DAPT must balance protection from GI Bleeding with the potential harms of chronic acid suppression. The challenge lies in identifying which patients truly benefit from PPI use and ensuring they receive appropriate care[7,8].

In India, cardiovascular disease is the leading cause of death and disability. The use of DAPT is widespread in tertiary care centres and in smaller hospitals. Limited research exists on how PPIs are used in patients receiving DAPT in the Indian setting. Most studies are from Western countries with different prescribing patterns, healthcare access and patient risk profiles. Applying these findings to India without local data may result in poor decisions being made[9,10].

Data on the prevalence of GI Bleeding in Indian patients receiving DAPT are also scarce. Most evidence is limited to small hospital-based studies or retrospective chart reviews. These often lack detailed risk assessment or standardised reporting. As a result - there is not a clear understanding of how often GI Bleeding occurs in this population or whether it could be prevented with more appropriate use of PPIs. Hence, this study was planned to address these knowledge gaps. The objectives of the study were as follows:-

- To determine the association between concomitant PPI prescription and the occurrence of GI Bleeding in patients on DAPT.
- To describe PPI prescribing patterns in DAPT patients (agent, dose, frequency, timing relative to DAPT initiation, and duration).
- To estimate the occurrence of GI bleeding (overall and classified as upper vs. lower GI where ascertainable) among patients on DAPT.

Material and Methods

This cross-sectional observational study was conducted in the Department of General Medicine, School of Medical Sciences and Research, Sharda Hospital, Greater Noida, Uttar Pradesh during April 2024 – November 2025. The study commenced after Institutional Ethics Committee approval. Participants were recruited from the Cardiology OPD, Gastroenterology OPD, and Medicine OPD. Adults (≥18 years), either sex, on Dual Antiplatelet Therapy (DAPT) and willing to participate after informed consent. This includes patients on DAPT with CAD and intervention.

Inclusion Criteria

- Patients on DAPT for at least 6 months with CAD and intervention
- Patients with stroke on DAPT
- Age >18 years
- Both sexes
- Willing to participate (informed consent).

Exclusion Criteria

- Concomitant NSAIDs or corticosteroids
- Patients on newer oral anticoagulants
- Known bleeding disorders
- Severe liver disease
- Severe kidney disease.

Sample Size

The sample size is estimated for a single-proportion (prevalence) objective using:-

$$\frac{Z^2 P(1-P)}{d^2}$$

Where (Z) is the standard normal deviate (1.96 for 95% CI), (P) is the expected prevalence, and (d) is the absolute precision.

The protocol assumed P = 56% (Jinadu *et al*[11]) for Co-prescription of DAPT with PPI and d = 8%. Substituting values:-

$$n = \frac{1.96 \times 0.56 \times (1 - 0.56)}{0.08^2} \sim 147.9 \Rightarrow 148$$

Final sample size (rounded): 150.

Variables and Operational Definitions

1. Exposure: PPI Co-prescription among patients receiving DAPT (agent, dose, timing *versus* DAPT start, and duration) was captured via history and drug chart/ records in the case record form (CRF).
2. Outcomes: Gastrointestinal (GI) bleeding was ascertained clinically and by investigations as available:

history of melena/hematemesis, new anaemia on CBC, FOBT, and Upper GI endoscopy where indicated. When feasible, classify as upper *versus* lower GI bleeding.

Variables and Parameters: Demographics (age, sex, address, education), lifestyle (smoking/alcohol), clinical profile, vitals, general/systemic examination, and relevant investigations (CBC with haemoglobin/PCV/platelets, lipid profile, RBS, ECG, 2D echo).

Data Collection Procedures: After institutional ethics committee approval and written informed consent, eligible patients were enrolled consecutively. A structured case-record form was used to capture demographics, clinical examination, DAPT duration, PPI intake, and GI-bleeding assessments (melena, hematemesis, anaemia); FOBT and endoscopy were performed where indicated.

Statistical Analysis: Continuous variables were summarised as mean ± SD with minima and maxima, and categorical variables as counts and percentages. Age was banded into four groups and GI-bleeding proportions across bands were compared using the chi-squared test. Binary associations in 2 × 2 Tables (e.g., PPI use *versus* significant haemoglobin fall >3 g/dL; bleeding-consistent endoscopy by PPI use) were evaluated with Fisher's exact test. Group differences for continuous exposures (e.g., PPI duration among users by bleeding status; DAPT duration by haemoglobin-drop status) were assessed using Welch's t-tests to accommodate unequal variances. GI-bleeding period prevalence was calculated from the FOBT/endoscopy-based definition, and two-sided p-values were reported with a significance threshold of <0.05.

Results

The mean age of the study population was 59.50 ± 9.74 years, with majority of patients belonging to the 50 - 59 years age group (35.3%), followed by 60 - 69 years (32.7%). Males constituted 56% of the study population. A history of smoking and alcohol use was present in 25.3% and 17.3% of patients, respectively. The mean body mass index (BMI) was 25.81 ± 5.23 kg/m^2, and the mean blood pressure was 132.55 ± 15.27/82.91 ± 9.76 mmHg. Gastrointestinal (GI) bleeding was observed in 16 patients, yielding a prevalence of 10.7%, while 89.3% of patients did not experience any bleeding episode (Table I).

The mean duration of DAPT was 8.37 ± 3.63 months. Proton pump inhibitors (PPIs) were prescribed in 51.3% of patients. Among these, pantoprazole was the most commonly used PPI (27.3%), followed by rabeprazole (18.7%) and esomeprazole (5.3%). The mean duration of PPI therapy was 7.44 ± 2.30 months (Table II).

Table I: Baseline demographic, clinical characteristics and prevalence of gastrointestinal bleeding (n = 150).

Variable	Value
Age (years), mean ± SD	59.50 ± 9.74
Age group, n (%)	<50: 25 (16.7)
	50 - 59: 53 (35.3)
	60 - 69: 49 (32.7)
	≥70: 23 (15.3)
Gender, n (%)	Male: 84 (56.0)
	Female: 66 (44.0)
Smoking, n (%)	Yes: 38 (25.3)
	No: 112 (74.7)
Alcohol use, n (%)	Yes: 26 (17.3)
	No: 124 (82.7)
Past illness, n (%)	Present: 115 (76.7)
Family history, n (%)	Present: 45 (30.0)
BMI (kg/m^2), mean ± SD	25.81 ± 5.23
SBP/DBP (mmHg), mean ± SD	132.55 ± 15.27/82.91 ± 9.76
Prevalence of gastrointestinal bleeding, n (%)	16 (10.7)

Table II: DAPT characteristics and PPI prescribing pattern.

Variable	Value
DAPT duration (months), mean ± SD	8.37 ± 3.63
PPI use, n (%)	Yes: 77 (51.3)
	No: 73 (48.7)
PPI type, n (%)	Pantoprazole: 41 (27.3)
	Rabeprazole: 28 (18.7)
	Esomeprazole: 8 (5.3)
	None: 73 (48.7)
PPI duration (months), mean ± SD	8.81 ± 2.54

A statistically significant association was observed between PPI use and reduction in significant haemoglobin (Hb) drop (>3 g/dL). Patients receiving PPI had a lower incidence of Hb drop (2.6%) compared to those not receiving PPI (11%), and this difference was statistically significant (p = 0.016). However, when different types of PPIs were compared, no statistically significant association was found with the occurrence of GI bleeding (p = 0.600) (Table III).

Table III: Association between PPI use and bleeding outcomes.

PPI use	Hb drop n (%)	No drop n (%)	p-value
Yes (n = 77)	2 (2.6)	75 (97.4)	**0.016**
No (n = 73)	8 (11.0)	65 (89.0)	
PPI type	GI bleed n (%)	No bleed n (%)	
Esomeprazole (n = 8)	0 (0)	8 (100)	0.600
Pantoprazole (n = 41)	3 (7.3)	38 (92.7)	
Rabeprazole (n = 28)	3 (10.7)	25 (89.3)	

No significant association was observed between duration of PPI therapy and occurrence of GI bleeding (p = 0.532). However, shorter duration of PPI therapy was significantly associated with greater risk of significant Hb drop (p <0.001). Additionally, DAPT duration showed a borderline association with Hb drop (p = 0.05) as shown in Table IV.

Table IV: Effect of therapy duration on bleeding outcomes.

PPI use	Hb drop n (%)	No drop n (%)	p-value
PPI duration (months)	8.33 ± 1.75	8.85 ± 2.61	0.532
PPI duration vs Hb drop	6.11 ± 0.33	7.52 ± 2.34	**<0.001**
DAPT duration (months)	12.89 ± 1.96	14.47 ± 3.69	0.05

We compared select baseline characteristics between those with and without GI Bleeding using Welch's t-tests for continuous variables and Fisher's exact tests for binary variables. Those with GI Bleeding were older on average (64.75 ± 9.25 *versus* 58.87 ± 9.64 years; p = 0.027). Differences in BMI, DAPT duration, baseline haemoglobin and platelets were not statistically significant (all p ≥0.20). Categorical comparisons for gender, smoking, alcohol and past illness (present/absent) showed no significant differences (all p ≥0.30) as shown in Table V.

Table V: Potential risk indicators.

Variable	Group	N	Min	Mean ± SD	Max	p value
Age (years)	GI bleed = Yes	16	47	64.75 ± 9.25	83	
	GI bleed = No	134	37	58.87 ± 9.64	82	**0.027**
BMI (Kg/m^2)	GI bleed = Yes	16	18.6	27.80 ± 6.47	41.7	
	GI bleed = No	134	13.9	25.57 ± 5.04	43.9	0.201
DAPT Duration (months)	GI bleed = Yes	16	10	14.31 ± 3.74	21	
	GI bleed = No	134	9	14.38 ± 3.62	27	0.892
Haemoglobin (g/dL)	GI bleed = Yes	16	10.8	12.97 ± 1.41	15.5	
	GI bleed = No	134	9	12.60 ± 1.42	16.3	0.341
Platelet Count (x10^9/L)	GI bleed = Yes	16	146	231.13 ± 66.14	351	
	GI bleed = No	134	116	251.94 ± 56.48	389	0.243
Gender	GI bleed = Yes (M)	11				
	GI bleed = Yes (F)	5				0.303
Smoking Y/N	GI bleed = Yes (Y)	2				
	GI bleed = No (N)	2				0.76
Alcohol Y/N	GI bleed = Yes (Y)	10				
	GI bleed = No (N)	6				0.48
Past Illness	GI bleed = Yes (Present)	12				
	GI bleed = No(Absent)	4				1

Discussion

We set out to evaluate prescribing patterns of proton pump inhibitors among adults receiving Dual Antiplatelet Therapy; we aimed to determine whether PPI prescription correlated with gastrointestinal bleeding in this population. The primary objective focused on any correlation between PPI use and GI bleeding while on DAPT; secondary objectives addressed how PPIs were being prescribed in routine practice and the incidence of GI bleeding among patients on DAPT at our centre.

In this study, the prevalence of GI bleeding among patients on DAPT was 10.7%, which is higher than the incidence reported in several international studies (1 - 2.5%) but comparable to observations in real-world and high-risk populations[3,12]. This variation may be attributed to differences in patient demographics, comorbidity burden, and variability in adherence to risk stratification protocols, particularly in the Indian healthcare setting[9,10].

Age was found to be a significant predictor of GI bleeding, with affected patients being older than those without bleeding (64.75 ± 9.25 *versus* 58.87 ± 9.64 years; p = 0.027). This finding is consistent with previous studies demonstrating that advanced age is an independent risk factor due to impaired mucosal defence, polypharmacy, and increased comorbidities[13,14]. Elderly patients on prolonged antiplatelet therapy are particularly vulnerable and require careful monitoring and preventive strategies.

PPI co-prescription was observed in 51.3% of patients, indicating moderate adherence to gastroprotective strategies. This is lower than rates reported in Western populations (60 - 80%) but comparable to data from other Asian and Indian studies, where prescribing patterns remain inconsistent[15-18]. Pantoprazole was the most commonly prescribed PPI, followed by rabeprazole and esomeprazole. This preference aligns with pharmacological evidence suggesting lower CYP2C19 inhibition and reduced interaction with clopidogrel[19-21].

A statistically significant association was observed between PPI use and reduction in clinically significant haemoglobin

drop (>3 g/dL), with lower incidence in PPI users (2.6% *versus* 11%; p = 0.016). This supports the protective role of PPIs in reducing the severity of bleeding events. Similar findings have been reported in multiple meta-analyses, where PPI co-therapy significantly reduced upper GI bleeding risk in patients receiving antiplatelet therapy[22,23]. However, no statistically significant association was found between PPI use and overall GI bleeding incidence (p = 0.600). This finding is consistent with studies suggesting that while PPIs reduce the severity and complications of bleeding, they may not completely prevent bleeding events, particularly in patients with multiple risk factors[13,22]. This highlights the multifactorial nature of GI bleeding in patients on DAPT.

The duration of PPI therapy showed important clinical relevance. Although no direct association was observed between PPI duration and GI bleeding, shorter duration of therapy was significantly associated with higher haemoglobin drop (p <0.001). This finding suggests that continuous and adequate duration of gastroprotection is essential, especially in patients receiving prolonged DAPT. Similar observations have been reported in studies emphasising sustained acid suppression to prevent mucosal injury[24,25].

The mean duration of DAPT in this study was 8.37 ± 3.63 months, and a borderline association was observed between longer DAPT duration and haemoglobin drop (p = 0.05). This aligns with previous evidence demonstrating that prolonged antiplatelet therapy increases bleeding risk, necessitating individualised duration based on risk-benefit assessment[4,26].

Interestingly, traditional risk factors such as smoking, alcohol use, BMI, and baseline laboratory parameters did not show statistically significant association with GI bleeding in this study. This may reflect the cumulative and multifactorial nature of bleeding risk, where individual factors alone may not be predictive without comprehensive risk assessment tools[27,28].

The study also highlights a significant gap between guideline recommendations and clinical practice. While international guidelines recommend PPI co-prescription in high-risk patients on DAPT, real-world adherence remains inconsistent, with both underuse in high-risk patients and overuse in low-risk individuals[15,16]. Similar discrepancies have been reported globally and are often attributed to lack of awareness, absence of standardised protocols, and variability in physician practice patterns[15,29].

The potential interaction between PPIs and clopidogrel remains a topic of debate. Although pharmacokinetic studies suggest reduced activation of clopidogrel due to CYP2C19 inhibition, clinical evidence has not consistently demonstrated adverse cardiovascular outcomes[30,31]. Current evidence supports the use of PPIs, particularly pantoprazole and rabeprazole, in patients at high risk of GI bleeding, as the benefits outweigh theoretical risks[32].

Overall, the findings of this study are consistent with existing literature in demonstrating that PPIs play a significant role in reducing the severity of bleeding in patients on DAPT. However, variability in prescribing patterns underscores the need for improved implementation of guideline-directed therapy.

Strengths and Limitations: This study provides valuable real-world data from an Indian tertiary care setting, addressing a gap in regional literature. However, the cross-sectional design limits causal inference. The relatively small sample size and lack of universal endoscopic confirmation may affect the generalisability and accuracy of bleeding classification.

Conclusion

PPI co-prescription in patients receiving DAPT was associated with a reduction in clinically significant haemoglobin decline, indicating a protective effect against meaningful bleeding events. Although no clear association was observed with FOBT or endoscopy-defined bleeding, haemoglobin-based outcomes provided important complementary insight into clinically relevant harm. Increasing age emerged as a key risk factor for GI bleeding, underscoring the importance of risk stratification in guiding gastroprotective therapy. Overall, sustained and selective PPI use in higher-risk patients appears justified in routine practice; however, further large-scale prospective and randomised studies are needed to better define optimal prescribing strategies and confirm these associations.

References

1. Acute Upper Gastrointestinal Bleeding and Variceal Bleeding. 2023; 209-16.
2. Mario CD, Mugelli A, Filardi PP. Long-Term Dual Antiplatelet Therapy: Pharmacological and Clinical Implications. *J Cardiovascular Med* 2018; 19 (8): 399-410.
3. Sharma R, Kumar P, Prashanth SP. Dual Antiplatelet Therapy in Coronary Artery Disease. *Cardiol Ther* 2020; 9 (2): 349-61.
4. Degrauwe S, Pilgrim T, Aminian A. Dual Antiplatelet Therapy for Secondary Prevention of Coronary Artery Disease. *Open Heart* 2017; 4 (2): e000651.
5. Xian Y, Xu H, Matsouaka R *et al*. Analysis of Prescriptions for Dual Antiplatelet Therapy After Acute Ischemic Stroke. *JAMA Netw Open* 2022; 5 (7): e2224157.
6. Baik M, Jeon J, Kim J. Proton Pump Inhibitor for Gastrointestinal Bleeding in Patients with Myocardial Infarction on Dual-Antiplatelet Therapy: A Nationwide Cohort Study. *J Epidemiol Glob Health [Internet]* 2024; 14 (3): 1142-51.
7. Saven H, Zhong L, McFarlane IM. Co-prescription of Dual-

Antiplatelet Therapy and Proton Pump Inhibitors: Current Guidelines. *Cureus* 2022.

8. Al-Dosari BS, Binafeef BM, Alsolami SA. Prescribing pattern of Proton Pump Inhibitors among patients admitted to medical ward at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. *Saudi Med J* 2021; 42 (12).
9. Roth GA, Mensah GA, Johnson CO *et al*. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. *J Amer Coll Cardiolo* 2020; Vol 76.
10. Vaduganathan M, Mensah GA, Turco JV. The Global Burden of Cardiovascular Diseases and Risk: A Compass for Future Health. *J Amer Coll Cardiolo* 2022; Vol 80.
11. Jinadu T, Radhakrishnan A, Fan L. Improving use of proton pump inhibitors with dual antiplatelet therapy in patients admitted with acute coronary syndrome. *BMJ Open Quality* 2022; 11: e001956.
12. Taguchi Y, Miura K, Shima Y *et al*. Gastrointestinal and Intracranial Bleeding Events After Second-Generation Drug-Eluting Stent Implantation - Their Association With High Bleeding Risk, Predictors, and Clinical Outcomes. *Circulation J* 2022; 86 (5): 775-83.
13. Li L, Geraghty O, Mehta Z. Age-Specific Risks, Severity, Time Course, and Outcome of Bleeding on Long-Term Antiplatelet Treatment After Vascular Events: A Population-Based Cohort Study. *The Lancet* 2017; 390 (10093): 490-9.
14. Traby L, Kollars M, Kaider A. Effects of P2Y12 Receptor Inhibition With or Without Aspirin on Hemostatic System Activation: A Randomised Trial in Healthy Subjects. *J Thrombo Haemosta* 2016; 14 (2): 273-81.
15. Lee Y, Choi H, Park S. Temporal Trends in Use of Antisecretory Agents Among Patients Administered Clopidogrel based Dual Antiplatelet Therapy After Percutaneous Coronary Intervention. *Pharmacoepidemiol Drug Saf* 2024; 33 (6).
16. Wilairat P, Phrommintikul A, Chotayaporn T *et al*. Trends in Dual Antiplatelet Therapy Regimens and Clinical Outcomes Among Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention With Drug eluting Stents: A Multicenter Real world Study. *Chronic Dis Transl Med* 2024; 11 (1): 57-68.
17. Luo X, Hou M, He S *et al*. Efficacy and Safety of Concomitant Use of Proton Pump Inhibitors With Aspirin-Clopidogrel Dual Antiplatelet Therapy in Coronary Heart Disease: A Systematic Review and Meta-Analysis. *Front Pharmacol* 2023; 13.
18. Vijayakumar TM, Ananthathandavan P, Zago BA. Assessment of prescribing pattern and adverse drug reaction in patients receiving Anticoagulant therapy: A prospective observational study. *Health Sci Rep* 2023; 6 (8).
19. Terry KW, Lam Y, Tan VP. Variability in Response to Clopidogrel: How Important Are Pharmacogenetics and Drug Interactions? *Br J Clin Pharmacol* 2011; 72 (4): 697-706.
20. Mao C, Wei J, Xu Y. A Meta Analysis of Impact of Proton Pump Inhibitors on Antiplatelet Effect of Clopidogrel. *Cardiovasc Ther* 2011; 30 (5).
21. Liu Q, Da-sheng D, Chen Y. The Influence of Omeprazole on Platelet Inhibition of Clopidogrel in Various <i>CYP2C19</I> Mutant Alleles. *Genet Test Mol Biomarkers* 2012; 16 (11): 1293-7.
22. Cardoso R, Benjo A, DiNicolantonio JJ *et al*. Incidence of Cardiovascular Events and Gastrointestinal Bleeding in Patients Receiving Clopidogrel With and Without Proton Pump Inhibitors: An Updated Meta-Analysis. *Open Heart* 2015; 2 (1): e000248.
23. Guo H, Ye Z, Huang R. Clinical Outcomes of Concomitant Use of Proton Pump Inhibitors and Dual Antiplatelet Therapy: A Systematic Review and Meta-Analysis. *Front Pharmacol* 2021; 12.
24. Demcsák A, Lantos T, Bálint ER *et al*. PPIs Are Not Responsible for Elevating Cardiovascular Risk in Patients on Clopidogrel – A Systematic Review and Meta-Analysis. *Front Physiol* 2018; 9.
25. Zhou X, Fang H, Xu J *et al*. Stress Ulcer Prophylaxis With Proton Pump Inhibitors or Histamine 2 Receptor Antagonists in Critically Ill Adults - A Meta-Analysis of Randomised Controlled Trials with Trial Sequential Analysis. *BMC Gastroenterol* 2019; 19 (1).
26. Bonaca MP, Bhatt DL, Cohen M *et al*. Long-Term Use of Ticagrelor in Patients With Prior Myocardial Infarction. *N Eng J Med* 2015; 372 (19): 1791-800.
27. Choi SY, Kim MH, Lee KM *et al*. Comparison of Performance Between ARC-HBR Criteria and PRECISE-DAPT Score in Patients Undergoing Percutaneous Coronary Intervention. *J Clin Med* 2021; 10 (12): 2566.
28. Selcuk M, Cynar T, Paylyk F. The Association of a PRECISE-DAPT Score with No-Reflow in Patients with ST-Segment Elevation Myocardial Infarction. *Angiolo* 2021; 73 (1): 68-72.
29. Che M, Ahmed S, Chan R. Appropriateness of Antiplatelet Therapy and Proton Pump Inhibitor Prescribing in End-Stage Kidney Disease: A Retrospective Quality Investigation Study. *Can J Kidney Health Dis* 2025; 12.
30. Mao C, Wei J, Xu Y. A Meta Analysis of Impact of Proton Pump Inhibitors on Antiplatelet Effect of Clopidogrel. *Cardiovasc Ther* 2011; 30 (5).
31. Liu Q, Da-sheng D, Chen Y. The Influence of Omeprazole on Platelet Inhibition of Clopidogrel in Various <i>CYP2C19</I> Mutant Alleles. *Genet Test Mol Biomarkers* 2012; 16 (11): 1293-7.
32. Goodman SG, Clare RM, Pieper KS *et al*. Association of Proton Pump Inhibitor Use on Cardiovascular Outcomes With Clopidogrel and Ticagrelor. *Circulation* 2012; 125 (8): 978-86.