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Original Research

Utilization and Predictors of PPI Co-Prescription in Warfarin-Treated Patients: Opportunities for Clinical Pharmacy Intervention

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Abstract

Background: Warfarin is recommended for several diseases, but it may cause bleeding particularly gastrointestinal bleeding. Proton pump inhibitor (PPI) is recommended in five conditions such as history of peptic ulcer disease, co-administration of antiplatelet, NSAIDs, or corticosteroids. There is limited data on PPI prophylaxis in patients with warfarin treatment with these five conditions. **Objective:** This study aimed to find additional predictors for PPI prophylaxis in patients who received warfarin therapy with any other recommended factors. **Methods:** This study was a retrospective cohort study conducted on hospital database of Khon Kaen University, Thailand. The inclusion criteria were adult patients who received warfarin therapy with any indications and were indicated for PPI prophylaxis by presence of one of any recommended factors mentioned above. Rates of PPI prophylaxis in the five conditions and clinical factor predictive PPI prescription were analyzed. **Results:** There were 1,789 patients who required PPI prevention while taking warfarin. The mean age of all patients was 70.45 year with a proportion of male patient of 51.87%. Of those, 611 patients (34.15%) received PPI prevention. According to the recommended factors, the PPI group had higher proportions of patients with age of more than 65 years (80.36% vs 73.60%), uncomplicated peptic ulcer disease (2.95% vs 0.68%), and concomitant corticosteroid (27.66% vs 12.31%) than the non-PPI group significantly. Concomitant antiplatelet and NSAIDs were not significant (p value = 0.665 and 0.458). Several predictors for PPI prophylaxis were identified such as diabetes, ischemic heart disease, treatment with clopidogrel, or internists as a primary physician. **Conclusions:** PPI prophylaxis in patients treated with warfarin was low at 34.15%. Predictors both positively and negatively of PPI prophylaxis were identified in five categories. Physicians who treat patients with warfarin therapy should be acknowledged on PPI prophylaxis appropriately. Additionally, these findings highlight the need for pharmacy-led interventions, such as clinical audits or risk assessment tools, to ensure appropriate gastroprotection in patients on warfarin.

Keywords: diabetes, ischemic heart disease, clopidogrel

INTRODUCTION

Warfarin is recommended for several diseases such as atrial fibrillation, acute coronary syndrome, or venous thromboembolism[1]. It is widely used in clinical practice due to its low cost with plenty of clinical evidence. A systematic review of 14,423 patients found that warfarin significantly lower risk of stroke and systemic embolism compared with aspirin by 41%[2]. But, it increased risk of bleeding by 2.88 times[1]. Severe bleeding incidence rate was 37 per 1000 person-year with slightly higher rate in men (38 vs 35). Additionally, the incidence rate of upper gastrointestinal (GI) bleeding with hospitalization from warfarin was 127/10,000 person-year[3].

Proton pump inhibitor (PPI) is effective and recommended in patients receiving warfarin therapy[4,5]. A probability of GI bleeding in five years was 12.6% which leading to higher incidence of all-cause mortality by 2.9 times ($p < 0.001$)[6]. Risk of hospitalized upper GI bleeding was decreasing by 24% in patients received warfarin and PPI co-therapy and 45% if antiplatelet or NSAIDs were used concomitantly[3,7]. It is recommended that PPI should be prescribed in patients receiving warfarin with an age of 65 years, history of peptic ulcer disease, co-administration of antiplatelet, NSAIDs, or corticosteroids[8]. Several risk factors for GI bleeding from warfarin were identified such as age, being hypertension, or alcohol dependence[1]. However, only 42.2% of patients received any anticoagulation with aspirin were prescribed PPI[9]. Only age and preadmission PPI use were significant predictors for PPI prophylaxis. Note that the previous study included patients who received warfarin only 56.6%. This study aimed to find additional predictors for PPI prophylaxis in patients who received warfarin therapy with any other recommended factors.

METHODS

This study was a retrospective cohort study conducted on hospital database of Khon Kaen University, Thailand. The inclusion criteria were adult patients who received warfarin

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therapy with any indications and were indicated for PPI prophylaxis by presence of any recommended factors mentioned above at the outpatient department. Eligible patients were followed for two consecutive time frames of 180 days or 360 days. This study was a part of the warfarin project of Khon Kaen University and conducted between January 2018 and December 2023. The study protocol was approved by the ethics committee in human research, Khon Kaen University (HE 661254) and compiled with the principles of the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines.

Eligible patients were identified from the hospital database and the pharmacy database by searching on patients who received warfarin. The hospital database was used to evaluate the baseline characteristics and comorbid diseases, while the pharmacy database was used to collect data of concomitant medications, and refill data. Eligible patients were evaluated for baseline characteristics (age, and sex) and six categories including recommended factors for PPI prophylaxis, comorbidities, indications for warfarin, associated GI diseases, antiplatelet, and primary physicians. The indications for warfarin treatment were one of the seven diseases: atrial fibrillation, valvular heart disease, venous thromboembolism, ischemic stroke, ischemic heart disease, cardiomyopathy, and antiphospholipid syndrome. The associated gastrointestinal diseases were gastroesophageal reflux disease, dyspepsia, gastritis/ duodenitis, uncomplicated peptic ulcer disease, and bleeding peptic ulcer disease. Those with gastritis/ duodenitis, uncomplicated peptic ulcer disease, and bleeding peptic ulcer disease were categorized as peptic ulcer disease. PPI prescription was defined by presence of PPI prescription with warfarin and warfarin refills. The partial PPI prescription was considered as non-PPI group.

Statistical analyses. Patients were categorized into two groups: non-PPI and PPI group. Descriptive statistics were used to summarize studied variables. Factors in the six categories were compared between non-PPI and PPI group using Chi square or Fisher Exact test where appropriate. Clinical factor predictive models for PPI prescription of the six categories except recommended factors were performed by using a stepwise multivariable logistic regression analysis. All factors in each category were put in the stepwise multivariable logistic regression model. Factors with a p value of less than 0.20 remained in the model. Unadjusted and adjusted odds ratio with 95% confidence intervals for factors in each model were reported. All analyses were computed by using STATA software version 18.0 (College Station, Texas, USA).

RESULTS

There were 1,789 patients who required PPI prevention while taking warfarin. The mean age of all patients was 70.45 year (SD 13.26) with a proportion of male patient of 51.87% (928 patients). Of those, 611 patients (34.15%) received PPI prevention.

According to the recommended factors (Table 1), the PPI group had higher proportions of patients with age of more than 65 years (80.36% vs 73.60%), uncomplicated peptic ulcer disease (2.95% vs 0.68%), and concomitant corticosteroid (27.66% vs 12.31%) than the non-PPI group significantly. Concomitant antiplatelet and NSAIDs were not significant (p value = 0.665 and 0.458). The PPI group had significantly higher proportions of three comorbidities including diabetes, chronic kidney disease, and heart failure than the non-PPI group. Additionally, the proportions of the following factors were significantly higher in the PPI group than non-PPI group: indications for warfarin (ischemic heart disease); associated GI diseases (gastroesophageal reflux disease, dyspepsia, gastritis/ duodenitis, and uncomplicated peptic ulcer); antiplatelet (clopidogrel); and primary physicians (cardiologist, nephrologist, and rheumatologist). The non-PPI group had significantly higher proportions of patients with valvular heart disease (32.09% vs 16.04%; p value < 0.001), and cardiovascular thoracic surgeon (28.27% vs 12.93%; p value < 0.001) than the PPI group (Table 1).

Table 2-6 showed predictive model for PPI prescription in patients who received warfarin treatment by comorbidities, indications for warfarin, associated gastrointestinal diseases, antiplatelet therapy, and primary physicians. Among the six comorbidities (Table 2), four factors remained in the model; three factors were significant. Chronic kidney disease had the highest adjusted odds ratio at 2.03 (Table 2). For indications for warfarin model (Table 3), there were five factors remaining in the model. Of those, two factors were significant including ischemic heart disease (highest adjusted odds ratio of 3.64), and valvular heart disease (adjusted odds ratio of 0.37). The model for associated gastrointestinal diseases had four remaining factors with three significant factors including gastroesophageal reflux disease (highest adjusted odds ratio of 6.56, dyspepsia, and uncomplicated peptic ulcer disease (Table 4). Clopidogrel was a significant factor in the antiplatelet category with the adjusted odds ratio of 5.15 (95% confidence interval of 3.30, 8.04), while aspirin was negatively related with PPI prophylaxis with adjusted odds ratio of 0.74 (95% confidence interval of 0.59, 0.93) as shown in Table 5. There were seven primary physicians remaining in the model with one negative factor: cardiovascular thoracic surgeon (adjusted odds ratio of 0.66) and five positive factors: internists, cardiologists, hematologists, rheumatologists, and nephrologists. The rheumatologists had the highest adjusted odds ratio of 4.50 (Table 6).

DISCUSSION

This study found that the PPI prophylaxis in patients who received warfarin therapy was 34.15%. The highest PPI prophylaxis rate was given in the setting of age of 65 years or more (80.36%) as shown in Table 1, while PPI prophylaxis was given with low rate in the setting of gastritis/ duodenitis (1.15%), general surgeon (1.15%) and ticagrelor (0.16%). These data may indicate that attending physicians may not be acknowledged for PPI prophylaxis in patients with warfarin therapy. Even though this study was conducted in the university hospital, the overall rate was somewhat lower than the previous report from New York (34.15% vs 42.2%).[9] But this rate was higher than a study from

Table 1. Clinical factors of proton pump inhibitor prescription in patients who received warfarin treatment by clinical category.

Factors	No PPI (n = 1,178)	PPI (n = 611)	p value
1. Recommended factors			
> 65 years	867 (73.60)	491 (80.36)	0.002
Peptic ulcer disease	29 (2.46)	36 (5.89)	< 0.001
Concomitant antiplatelet	368 (31.24)	197 (32.24)	0.665
Concomitant corticosteroid	145 (12.31)	169 (27.66)	< 0.001
Concomitant NSAIDs	94 (7.98)	55 (9.00)	0.458
2. Comorbidities			
Hypertension	303 (25.72)	173 (28.31)	0.239
Diabetes mellitus	178 (15.11)	117 (19.15)	0.029
Chronic kidney disease	96 (8.15)	99 (16.20)	< 0.001
Active malignancy	52 (4.41)	28 (4.58)	0.87
Heart failure	36 (3.06)	38 (6.22)	0.001
Cirrhosis	18 (1.53)	16 (2.62)	0.109
3. Indications for warfarin			
Atrial fibrillation	486 (41.26)	243 (39.77)	0.544
Valvular heart disease	378 (32.09)	98 (16.04)	< 0.001
Venous thromboembolism	152 (12.90)	77 (12.60)	0.857
Ischemic stroke	131 (11.12)	85 (13.91)	0.086
Ischemic heart disease	53 (4.50)	95 (15.55)	< 0.001
Cardiomyopathy	34 (2.89)	25 (4.09)	0.176
Antiphospholipid syndrome	23 (1.95)	21 (3.44)	0.055
4. Associated GI diseases			
Gastroesophageal reflux disease	6 (0.51)	19 (3.11)	< 0.001
Dyspepsia	5 (0.42)	10 (1.64)	0.012
Gastritis / Duodenitis	6 (0.51)	7 (1.15)	0.133
Uncomplicated peptic ulcer disease	8 (0.68)	18 (2.95)	< 0.001
Bleeding peptic ulcer disease	15 (1.27)	11 (1.80)	0.377
5. Antiplatelet			
Aspirin	352 (29.88)	156 (25.53)	0.053
Clopidogrel	30 (2.55)	69 (11.29)	< 0.001
Cilostazol	9 (0.76)	9 (1.47)	0.154
Ticagrelor	0	1 (0.16)	0.165
Dual antiplatelet	368 (31.24)	196 (32.08)	0.717
Any antiplatelet	368 (31.24)	197 (32.24)	0.665
6. Primary physicians			
Cardiovascular thoracic surgeons	333 (28.27)	79 (12.93)	< 0.001
Internists	218 (18.51)	122 (19.97)	0.455
Cardiologists	180 (15.28)	135 (22.09)	< 0.001
Neurologists	139 (11.08)	72 (11.78)	0.992
Hematologists	56 (4.75)	37 (6.06)	0.239
Nephrologists	36 (3.06)	54 (8.84)	< 0.001
General practitioners	55 (4.67)	21 (3.44)	0.221
Rheumatologists	28 (2.38)	45 (7.36)	< 0.001

General surgeons	25 (2.12)	7 (1.15)	0.139
Gastroenterologists	16 (1.36)	8 (1.31)	0.932

Note. Data presented as number (percentage); NSAIDs: nonsteroidal anti-inflammatory drugs.

Table 2. Predictive model of proton pump inhibitor prescription in patients who received warfarin treatment by comorbidities.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Diabetes Mellitus	1.33 (1.03, 1.72)	1.94 (1.21, 3.13)
Chronic kidney disease	2.17 (1.61, 2.94)	2.03 (1.49, 2.75)
Cirrhosis	1.73 (0.88, 3.42)	1.67 (0.84, 3.33)
Heart failure	2.10 (1.31, 3.36)	1.94 (1.21, 3.13)

Table 3. Predictive model of proton pump inhibitor prescription in patients who received warfarin treatment by indications for warfarin.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Atrial fibrillation	0.94 (0.77, 1.15)	0.80 (0.64, 1.00)
Valvular heart disease	0.40 (0.32, 0.52)	0.37 (0.29, 0.49)
Venous thromboembolism	0.97 (0.73, 1.31)	0.76 (0.55, 1.05)
Antiphospholipid syndrome	1.79 (0.98, 3.26)	1.50 (0.81, 2.76)
Ischemic heart disease	3.91 (2.75, 5.56)	3.64 (2.53, 5.23)

Table 4. Predictive model of proton pump inhibitor prescription in patients who received warfarin treatment by associated gastrointestinal diseases.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Gastroesophageal reflux disease	6.27 (2.49, 15.78)	6.56 (2.60, 16.50)
Dyspepsia	3.90 (1.33, 11.47)	4.14 (1.41, 12.17)
Gastritis / Duodenitis	2.26 (0.76, 6.77)	2.42 (0.81, 7.22)
Uncomplicated peptic ulcer disease	1.42 (0.65, 3.11)	4.66 (2.01, 10.78)

Table 5. Predictive model of proton pump inhibitor prescription in patients who received warfarin treatment by antiplatelet therapy.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Aspirin	0.80 (0.65, 1.00)	0.74 (0.59, 0.93)
Clopidogrel	4.87 (3.13, 7.57)	5.15 (3.30, 8.04)

Table 6. Predictive model of proton pump inhibitor prescription in patients who received warfarin treatment by primary physicians.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Cardiovascular thoracic surgeons	0.38 (0.29, 0.49)	0.66 (0.46, 0.97)
Internists	1.10 (0.86, 1.41)	1.57 (1.10, 2.24)
Cardiologists	1.57 (1.23, 2.02)	2.10 (1.47, 3.01)
Neurologists	0.99 (0.74, 1.35)	1.45 (0.98, 2.16)
Hematologists	1.29 (0.84, 1.98)	1.85 (1.12, 3.06)

Rheumatologists	3.26 (2.02, 5.29)	4.50 (2.61, 7.80)
Nephrologists	3.08 (1.99, 4.75)	4.20 (2.53, 6.97)

University of Michigan (8.9%)[10]. Note that this study included only patients receiving warfarin with various indications, while the New York study was conducted in patients with various anticoagulation combination with aspirin; 56.5% took warfarin. The PPI prophylaxis rate in patients treated with warfarin and aspirin was even lower in this study at 25.53%. The low PPI prophylaxis rate was similar to a previous study of PPI prophylaxis in patients receiving low dose aspirin (46% of PPI prophylaxis) or dual antiplatelet therapy (32% of PPI prophylaxis)[11,12].

Regarding predictors for PPI prophylaxis in patients with warfarin treatment (Table 2-6), several factors were significant additional to the previous study[9] including comorbidities, indications for warfarin, associated GI diseases, antiplatelet therapy, and primary physicians. Chronic kidney disease was previously reported to be a significant predictor for GI bleeding in patients with anticoagulant therapy either warfarin or direct oral anticoagulants with adjusted odds ratio of 6.7 (95% confidence interval of 2.3-19.6), this finding may remind physicians to prescribe PPI prophylaxis in patients receiving warfarin in this study with the highest adjusted odds ratio (2.03) in the comorbidities category[6]. Other studies also confirmed that chronic kidney disease was associated with GI bleeding by 1.72 times ($p < 0.0010$) and mortality from major bleeding by 8.24 times: 95% confidence interval of 6.76, 10.04[13,14]. Most comorbidities and indications for warfarin therapy are at risk of GI bleeding resulting in more PPI prescription rates such as diabetes, cirrhosis, heart failure or ischemic heart disease (Table 2, 3). Patients with acute coronary syndrome with GI bleeding was associated with mortality with adjusted hazard ratio of 4.87 (95% confidence interval of 2.61, 9.08)[15]. Valvular heart disease was associated with lower rates of PPI prophylaxis (Table 3). Using PPI may be related with increasing risk of cardiovascular surgery by 5.77 times ($p < 0.001$) or atrial fibrillation by 1.87 times ($p = 0.025$) in patients with ischemic and valvular heart disease[16]. These may prevent using PPI in patients with valvular heart disease but not patients with ischemic heart disease in this study.

A study in patients with low dose aspirin treatment found that those with duodenal ulcer or peptic ulcer but not heart burn are at risk of GI complications significantly (1.1% vs 0.1% for peptic ulcer; $p < 0.0001$)[11]. The history of peptic ulcer disease was more common in patients treated with warfarin with GI bleeding than those without GI bleeding (12.9% vs 5.7%; $p = 0.048$)[14]. In this study, gastroesophageal reflux disease was related to PPI prophylaxis as well as dyspepsia, and uncomplicated peptic ulcer disease. These findings may be explained by these conditions were treated with PPI as the main treatment. However, the PPI prophylaxis prescription in this category was still low (1.15%-3.11%) as shown in Table 1. Surprisingly, bleeding peptic ulcer disease was not a significant predictor for PPI prophylaxis and did not remain in the predictive model. A previous study found that prior history of GI bleeding was related to GI bleeding in patients with warfarin therapy ($p < 0.001$)[14]. But it was not significant in this study after adjusted by other GI conditions. These may imply that previous GI bleeding may not be a strong indicator of PPI prophylaxis compared to other conditions of peptic ulcer disease (Table 4).

Regarding antiplatelet therapy, only two factors remained in the model and both aspirin and clopidogrel were associated with PPI prophylaxis significantly (Table 5). These findings may indicate that physicians may believe that clopidogrel had higher risk of GI bleeding than aspirin in patients receiving warfarin therapy. Additionally, clopidogrel and PPI combination was the common regimen in patients with vascular ischemic events[17]. As previously reported, PPI prophylaxis was low in patients with aspirin therapy (46%) and even lower in this study (25.53%) resulting in negative adjusted odds ratio of aspirin in this study[11]. Note that though triple therapy with warfarin, aspirin, and clopidogrel was associated with fatal or nonfatal bleeding (hazard ratio of 3.70; 95% confidence interval of 2.89, 4.76), it was not significant in this study ($p = 0.717$; table 1) and was not remaining in the predictive model (Table 5). These results may indicate that attending physicians may not acknowledge this risk. Among primary physicians, internists, cardiologists, hematologists, rheumatologists, and nephrologists were likely to prescribe PPI prophylaxis in patients with received warfarin as these physicians see patients with high risk of GI bleeding. Therefore, the rate of PPI prophylaxis was significantly higher than others. In contrast, cardiovascular thoracic surgeons tended to not prescribe PPI prophylaxis. Several studies showed that inappropriate PPI prophylaxis was common during perioperative period[18-20]. An inappropriate PPI prescription was high at 42.4% in surgical inpatients and 9.3% of under prescription[18].

These databases were conducted in many patients with warfarin treatment and showed several additional predictors of PPI prophylaxis. However, PPI prophylaxis rate was still low as previously reported.[9] These results may imply that clinical pharmacists may identify high-risk patients and guide appropriate PPI prophylaxis by using the pharmacy database. The possible interventions by the clinical pharmacists included history taking from the patients at risk, medication reconciliation from the pharmacy database, system alert for the high-risk patients, or multidisciplinary educational initiatives for patients receiving warfarin. There are some limitations in this study. First, the model was computed in each category but not across to other categories. Second, only patients with warfarin therapy were included; direct oral anticoagulants were not studied. Finally, those with partial PPI prophylaxis were defined as incomplete or no PPI prophylaxis.

CONCLUSIONS

PPI prophylaxis in patients treated with warfarin was low at 34.15%. Predictors both positively and negatively of PPI

prophylaxis were identified in five categories. Physicians who treat patients with warfarin therapy should be acknowledged on PPI prophylaxis appropriately. Additionally, these findings highlight the need for pharmacy-led interventions, such as clinical audits or risk assessment tools, to ensure appropriate gastroprotection in patients on warfarin.

AUTHOR CONTRIBUTIONS

Witsarut Manasirisuk: Conceptualization, Methodology, Data collection, Formal analysis, Writing-original draft preparation; Panisa Manasirisuk: Conceptualization, Methodology, Data collection; Sunee Lertsinudom: Validation, Writing-reviewing and editing; Wattana Sukeepaisarnjaroen: Validation, Writing-reviewing and editing; Kittisak Sawanyawisuth: Formal analysis, Writing-reviewing and editing.

CONFLICTS OF INTEREST

All authors declare that they have no conflicts of interest.

References

1. Rydberg DM, Linder M, Malmström RE, Andersen M. Risk factors for severe bleeding events during warfarin treatment: the influence of sex, age, comorbidity and co-medication. Eur J Clin Pharmacol. 2020;76(6):867–76. doi: 10.1007/s00228-020-02856-6
2. Lip GYH, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. Thromb Res. 2006;118(3):321–33. doi: 10.1016/j.thromres.2005.08.007
3. Ludden-Schlatter A, Stevermer JJ. PURLs: The benefits--and limits--of PPIs with warfarin regimens. J Fam Pract. 2017;66(11):694–6.
4. Bhatt DL, Scheiman J, Abraham NS, Antman EM, Chan FKL, Furberg CD, et al. ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2008;52(18):1502–17. doi: 10.1016/j.jacc.2008.08.002
5. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008;133(6 Suppl):160S-198S. doi: 10.1378/chest.08-0670
6. Shimomura A, Nagata N, Shimbo T, Sakurai T, Moriyasu S, Okubo H, et al. New predictive model for acute gastrointestinal bleeding in patients taking oral anticoagulants: A cohort study. J Gastroenterol Hepatol. 2018;33(1):164–71. doi: 10.1111/jgh.13830
7. Ray WA, Chung CP, Murray KT, Smalley WE, Daugherty JR, Dupont WD, et al. Association of Proton Pump Inhibitors With Reduced Risk of Warfarin-Related Serious Upper Gastrointestinal Bleeding. Gastroenterology. 2016;151(6):1105-1112.e10. doi: 10.1053/j.gastro.2016.08.054
8. Abrignani MG, Gatta L, Gabrielli D, Milazzo G, De Francesco V, De Luca L, et al. Gastroprotection in patients on antiplatelet and/or anticoagulant therapy: a position paper of National Association of Hospital Cardiologists (ANMCO) and the Italian Association of Hospital Gastroenterologists and Endoscopists (AIGO). Eur J Intern Med. 2021;85:1–13. doi: 10.1016/j.ejim.2020.11.014
9. Sharma R, Roy A, Ramos C, Rosenberg R, Garcia-Carrasquillo R, Lebwohl B. Low adherence to national guidelines for proton-pump inhibitor prescription in patients receiving combination aspirin and anticoagulation. Therap Adv Gastroenterol. 2017;10(5):387–96. doi: 10.1177/1756283X17694807
10. Kurlander JE, Gu X, Scheiman JM, Haymart B, Kline-Rogers E, Saini SD, et al. Missed opportunities to prevent upper GI hemorrhage: The experience of the Michigan Anticoagulation Quality Improvement Initiative. Vasc Med. 2019;24(2):153–5. doi: 10.1177/1358863X18815971
11. de Jong HJI, Korevaar JC, van Dijk L, Voogd E, van Dijk CE, van Oijen MGH. Suboptimal prescribing of proton-pump inhibitors in low-dose aspirin users: a cohort study in primary care. BMJ Open. 2013;3(7):e003044. doi: 10.1136/bmjopen-2013-003044
12. Awaisu A, Hamou F, Mekideche L, El Muabby N, Mahfouz A, Mohammed S, et al. Proton pump inhibitor co-prescription with dual antiplatelet therapy among patients with acute coronary syndrome in Qatar. Int J Clin Pharm. 2016;38(2):353–61. doi: 10.1007/s11096-016-0250-4
13. Bassand J-P, Virdone S, Badoz M, Verheugt FWA, Camm AJ, Cools F, et al. Bleeding and related mortality with NOACs and VKAs in newly diagnosed atrial fibrillation: results from the GARFIELD-AF registry. Blood Adv. 2021;5(4):1081–91. doi: 10.1182/bloodadvances.2020003560
14. Tang J, Sharma U, Desai S, Molnar J, Perlmuter L, Feller A, et al. A Study of Proton Pump Inhibitors and Other Risk Factors in Warfarin-Associated Gastrointestinal Bleeding. Cureus. 2021;13(1):e12624. doi: 10.7759/cureus.12624
15. Nikolsky E, Stone GW, Kirtane AJ, Dangas GD, Lansky AJ, McLaurin B, et al. Gastrointestinal bleeding in patients with acute coronary syndromes: incidence, predictors, and clinical implications: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. J Am Coll Cardiol. 2009;54(14):1293–302. doi: 10.1016/j.jacc.2009.07.019
16. Boban M, Zulj M, Persic V, Medved I, Zekanovic D, Vcev A. Prolonged utilization of proton pump inhibitors in patients with ischemic and valvular heart disease is associated with surgical treatments, weight loss and aggravates anemia. Int J Cardiol.

2016;219:277–81. doi: 10.1016/j.ijcard.2016.06.058
17. Tantry US, Kereiakes DJ, Gurbel PA. Clopidogrel and proton pump inhibitors: influence of pharmacological interactions on clinical outcomes and mechanistic explanations. JACC Cardiovasc Interv. 2011;4(4):365–80. doi: 10.1016/j.jcin.2010.12.009
18. Li H, Li N, Jia X, Zhai Y, Xue X, Qiao Y. Appropriateness and Associated Factors of Stress Ulcer Prophylaxis for Surgical Inpatients of Orthopedics Department in a Tertiary Hospital: A Cross-Sectional Study. Front Pharmacol. 2022;13:881063. doi: 10.3389/fphar.2022.881063
19. Liu P, Li G, Wu Q, Han M, Zhang C. Analysis of inappropriate prophylactic use of proton pump inhibitors during the perioperative period: an observational study. Perioper Med (Lond). 2024;13(1):19. doi: 10.1186/s13741-024-00376-w
20. Panni U, Srivastava R, Bewley A, Williams GA, Fields RC, Sanford DE, et al. Postoperative Proton Pump Inhibitors are associated with a significantly higher rate of delayed gastric emptying after pancreatoduodenectomy. HPB (Oxford). 2023;25(6):659–66. doi: 10.1016/j.hpb.2023.02.015