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ORIGINAL RESEARCH

Proton Pump Inhibitors Use in Patients With Ischemic Stroke on Dual Antiplatelet Therapy at Low Risk of Upper Gastrointestinal Bleeding

Minyoul Baik, MD; Jimin Jeon, MS; Seok-Jae Heo, PhD; Jinkwon Kim, MD, PhD; Joonsang Yoo, MD, PhD

BACKGROUND: Current guidelines lack recommendations regarding the use of proton pump inhibitors (PPIs) for preventing upper gastrointestinal bleeding (UGIB) among patients at low risk for UGIB treated with dual antiplatelet therapy for ischemic stroke (IS). Our objective was to assess the effectiveness of PPIs in lowering the risk of significant UGIB in this patient group.

METHODS AND RESULTS: A retrospective cohort study was conducted involving patients at low risk for UGIB admitted for IS between 2014 and 2018 and treated with dual antiplatelet therapy. The study used a nationwide claims database in Korea. The primary end point was significant UGIB during 12 months after IS. To evaluate the risk of significant UGIB based on PPI use, we performed a multivariable Cox regression analysis. Subgroup analyses and propensity score matching analysis were conducted for validation. Among 96 722 patients with IS at low risk for UGIB who were on dual antiplatelet therapy (mean age, 67.0 years; men: 63.0%), 16 084 (16.6%) were treated with PPIs. During 12 months of follow-up, 325 patients experienced significant UGIB, and 479 experienced any UGIB. PPI use was associated with a reduced risk of significant UGIB (hazard ratio, 0.63 [95% CI, 0.45–0.89]; *P*=0.009). This association was consistent in the subgroup and propensity score matching analyses.

CONCLUSIONS: In patients with IS receiving dual antiplatelet therapy, PPI use reduced the risk of significant UGIB by 37% on average, even among low-risk patients. However, the use of PPIs in this patient group was limited, highlighting the need for additional prospective studies.

Key Words: dual antiplatelet therapy ■ ischemic stroke ■ proton pump inhibitor ■ upper gastrointestinal bleeding

Dual antiplatelet therapy (DAPT) is recommended to reduce recurrent ischemic stroke (IS) risk in the acute period after minor non-cardioembolic IS, high-risk transient ischemic attack, and symptomatic major intracranial arterial stenosis.[1–5] Although DAPT effectively reduces the recurrence of IS, it concurrently increases the risk of major bleeding, especially upper gastrointestinal bleeding (UGIB), which is a life-threatening complication.[2,6–8] Consequently, continuous endeavors are directed toward a more precise assessment of the UGIB risk and formulation of effective prevention strategies tailored to individual risk profiles.[9]

Proton pump inhibitors (PPIs) reduce the risk of UGIB in patients on DAPT,[10,11] and their use in patients at a high risk of UGIB is recommended by guidelines on coronary artery disease to avoid UGIB.[12,13] Furthermore, some guidelines advocate routine PPI use for all patients with coronary artery disease on DAPT, regardless of their bleeding risk.[14,15] Although DAPT is also associated with an increased UGIB risk, even in patients with IS at low risk for bleeding,[2,6–8]

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CLINICAL PERSPECTIVE

What Is New?

- Proton pump inhibitor use is associated with a reduced risk of significant upper gastrointestinal bleeding in patients with ischemic stroke and a low risk of bleeding who are receiving dual antiplatelet therapy.

What Are the Clinical Implications?

- Given the absence of specific guidelines for preventing bleeding in patients with ischemic stroke on dual-antiplatelet therapy, proton pump inhibitor use may be considered an effective preventive strategy against significant upper gastrointestinal bleeding until updated guidelines become available.
- The benefit of proton pump inhibitors in patients with a low-risk for bleeding highlights the need for an improved risk stratification system to accurately identify those at high risk for gastrointestinal bleeding in patients with ischemic stroke.

Nonstandard Abbreviations and Acronyms

DAPT	dual antiplatelet therapy
HIRA	Health Insurance Review and Assessment Service
IS	ischemic stroke
UGIB	upper gastrointestinal bleeding

research on the specific benefits of PPIs in this group is limited. Current stroke guidelines do not provide recommendations for preventing UGIB, including the use of PPIs in patients with IS receiving DAPT.[4,16]

We hypothesized that PPI use will reduce the occurrence of UGIB in patients with IS, including those at low risk for bleeding, aligning with the findings from coronary studies.[10,11,14,15] Hence, we sought to explore practical use of PPIs in patients with IS on DAPT, specifically those at low risk for bleeding. Additionally, we aimed to evaluate the efficacy of PPIs in reducing significant UGIB in these patients, using data from a nationwide database.

METHODS

Data Availability Statement

The data used in the study are accessible from the Health Insurance Review and Assessment Service (HIRA), but there are restrictions requiring approval. Researchers can request access to the database for this study through the Korean Health Insurance Review Health Big Data Hub (https://opendata.hira.or.kr).

Ethical Statement

This study received approval from the Institutional Review Board of Yongin Severance Hospital (no. 9-2021-0025). This study was conducted in accordance with the Helsinki Declaration. The requirement for informed consent was waived owing to the retrospective nature of the study and use of an anonymous health insurance claims database. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Study Design and Population

A retrospective cohort study was conducted using data from the nationwide Korean medical claims database. The National Health Insurance Service provides health insurance benefits to the entire Korean population,[17] whereas the HIRA reviews all National Health Insurance Service claims and performs quality evaluations. From the HIRA database, we identified patients who were newly diagnosed with acute IS from January 2014 to December 2018. Patients with acute IS were identified as those hospitalized with a primary diagnosis of IS based on the *International Classification of Diseases, Tenth Revision* (*ICD-10*) code of I63 and who underwent brain computed tomography or magnetic resonance imaging examination. DAPT use was identified as the administration of medications for a minimum of 21 days within 30 days following an index IS and was limited to the administration of aspirin along with other antiplatelet agents, including clopidogrel, ticlopidine, prasugrel, ticagrelor, cilostazol, or triflusal, as approved by the HIRA in Korea. The index date was defined as the date of IS admission. To specifically assess the benefits of PPIs in low-risk patients on DAPT, we excluded patients without DAPT, those considered high risk for UGIB, those receiving concurrent anticoagulant therapy, those with a follow-up period of <1 month, and those whose hospitalization for IS lasted >1 month after the index date. Detailed information based on the claims data are provided in Data S1 and Table S1.

Covariates

We extracted information on the comorbid conditions and medications from the medical claims data using the *ICD-10* diagnosis codes and Anatomical Therapeutic Chemical Classification System codes (Table S1). In the main analyses, the use of a particular medication was identified as receiving it for a minimum of 21 days within a 1-month window after the index IS. Considering the dynamic changes in medication use, especially in antiplatelet therapy and PPIs, we additionally investigated

medication use during the study period in time-varying variables and presented descriptive data regarding medication usage patterns. We assessed the daily use of these medications based on whether the prescriptions covered each day after IS.

Bleeding Risk Assessment

To assess the benefit of PPIs in low-risk patients, we excluded those at elevated risk for UGIB based on the 2010 American guidelines.[18] These guidelines recommend PPIs for patients on antiplatelet therapy with a history of UGIB or multiple risk factors, such as older age; simultaneous use of nonsteroidal anti-inflammatory drugs, corticosteroids, and anticoagulants; or the presence of *Helicobacter pylori* infection.[18] Nevertheless, in our study, patients receiving anticoagulants were already excluded, and the determination of patients with *H pylori* infection was challenging owing to the lack of precise identification in the Korean HIRA database. Lastly, patients with a history of recent UGIB or those with 2 risk factors (age 65 or older, or nonsteroidal anti-inflammatory drugs users or corticosteroids users) were classified as elevated risk and subsequently excluded, whereas the others were classified as low risk and included in the current study (Table S1).

Outcomes and Follow-Ups

The primary end point was the occurrence of significant UGIB during 12 months post-IS. Significant UGIB was identified upon hospitalization based on the assigned *ICD-10* codes and the claim of red blood cell transfusions during hospitalization (Table S1). The secondary end point was any UGIB, identified as hospitalization with a relevant diagnostic code regardless of the presence or absence of transfusion (Table S1). After the index IS, the patients were followed up until the development of the primary outcome, loss of National Health Insurance Service eligibility owing to emigration, death, or until 12 months from the index date, whichever happened first.

Statistical Analysis

Group differences were assessed by applying the independent *t* test to continuous variables and the chi-square test to categorical variables, where appropriate. To evaluate the pattern of PPI use among the patients during the study period (2014–2018), the Cochran–Armitage test was applied. Cumulative incidence curves for significant UGIB were plotted according to the assessed bleeding risk group for all patients with stroke and the PPI treatment used for patients at low risk for UGIB. The differences in cumulative incidence curves were assessed using the log-rank test. To examine the impact of PPIs in lowering the risk of significant UGIB, we performed a multivariable Cox regression analysis to calculate the adjusted hazard ratio (aHR) and 95% CI. The following variables were adjusted: year of admission; sex; age; hypertension; diabetes; renal disease; hepatic disease; cancer; functional dyspepsia; and the use of statins, nonsteroidal anti-inflammatory drugs, corticosteroids, and other gastrointestinal protectors. In the analysis of secondary outcome, we generated additional Cox regression model for any UGIB and evaluated the risk of any UGIB according to the PPI used.

We performed subgroup analyses to confirm the association between PPI use and significant UGIB risk according to sex, age, and simultaneous use of other gastrointestinal protectors. The proportional hazard assumption was confirmed using correlation testing based on Schoenfeld residuals, and it was not violated. To address the potential confounding effects of different baseline characteristics, a 1:2 propensity score matching analysis was performed as a sensitivity analysis (Data S2). After propensity score matching, stratified Cox regression analysis was conducted on the selected patients with and without PPI use. Statistical analyses were performed using SAS (version 9.4.2; SAS Institute) and R (version 3.5.1; R Foundation for Statistical Computing). A P value of <0.05 was considered significant.

RESULTS

Study Population and Baseline Characteristics

In total, 333 916 patients with newly diagnosed IS between January 2014 and December 2018 were screened, and 135 042 were treated with DAPT (Figure 1). After exclusion, 96 722 patients with IS at low risk for UGIB treated with DAPT were included in the final analysis (mean age±SD, 67.0±12.6 years; 60 896 [63.0%] were men). Significant UGIB was more prevalent in the high-risk groups compared with the low-risk groups, indicating the appropriate inclusion of patients at low risk for UGIB in this study (log-rank test, P<0.001; Figure S1). There was no difference in the risk of significant UGIB according to the use of PPIs in the high-risk groups (P>0.05, Table S2). Among the included patients (with low risk of UGIB and DAPT), 16 084 (16.6%) were treated with PPIs. When evaluating medication use as a time-varying variable (Figure S2 and Table S3), all patients were treated with DAPT at 1 month, according to the inclusion criteria of this study, and 18.2% of them were treated with PPIs at 1 month. Patients were treated with DAPT in 69.1% of cases at risk at 3 months, 56.6% at 6 months, and 45.0% at 1 year. Of these, PPIs were used in 19.7% of patients with DAPT at 3 months, 19.7% at 6 months, and 20.1% at 12 months. Patients receiving PPIs, compared with those not receiving PPI treatment, were older, less likely to be men, and more likely to

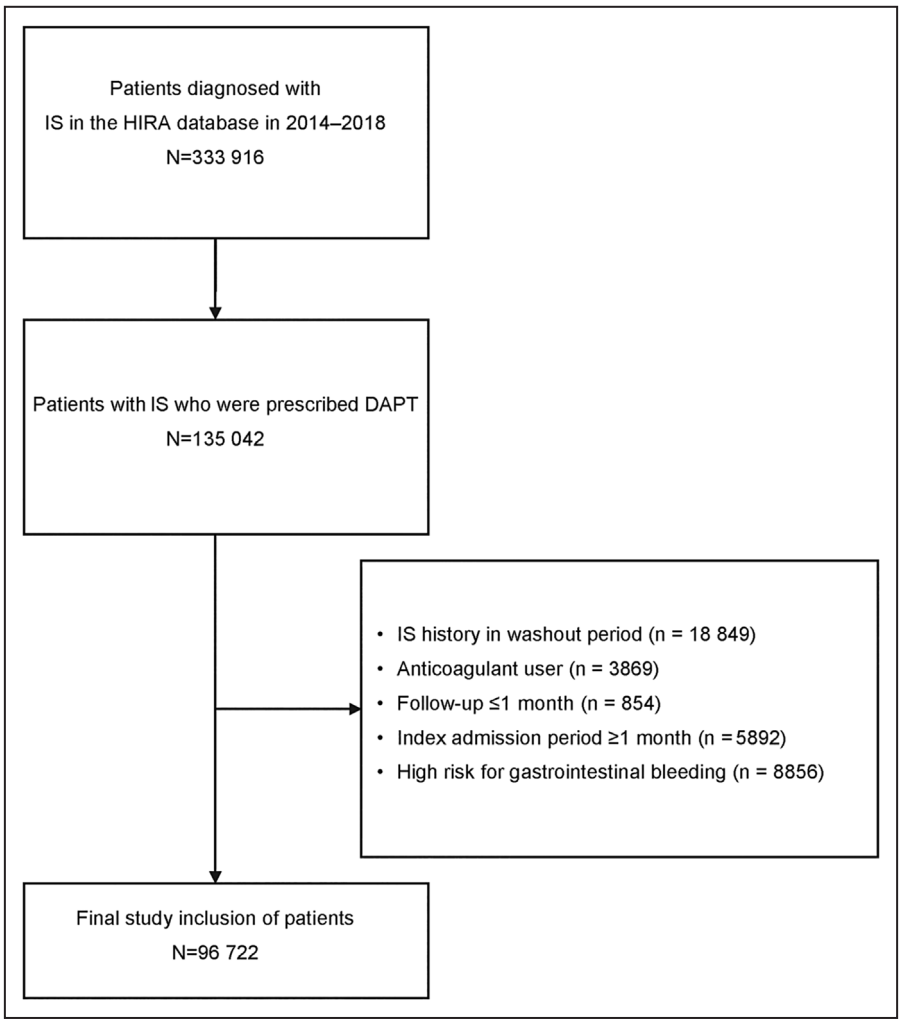

Figure 1. Flow chart of participant inclusion.
DAPT indicates dual-antiplatelet therapy; HIRA, Health Insurance Review and Assessment Service; and IS, ischemic stroke.

have cardiovascular risk factors and functional dyspepsia (Table 1). Throughout the study period, the rate of PPI use significantly increased from 9.4% in 2014 to 22.3% in 2018 (*P* for trend <0.05; Figure 2).

Primary and Secondary End Points

Within the 12 months follow-up after IS, 325 (0.3%) patients experienced significant UGIB. The cumulative incidence curve showed a lower risk of significant UGIB along with PPI use (*P*=0.040; Figure 3). Multivariable Cox regression analysis showed that PPI use was linked to a 36% decreased risk of significant UGIB 12 months after IS (aHR, 0.63 [95% CI, 0.45–0.89]; *P*=0.009; Figure 4). Also, significant UGIB was associated with older age; male sex; and the presence of hypertension, chronic renal disease, and hepatic disease (Table S4).In the secondary end point analysis, 479 (0.5%) patients had any UGIB during 12 months after IS. PPI use was not associated with the risk of any UGIB (aHR, 0.85 [95% CI, 0.66–1.10]; *P*=0.221; Table S5). Analysis of PPI types demonstrated consistent associations between the use of PPI and a decreased risk of significant UGIB, with no significant interaction observed across different PPI types (*P* for interaction >0.999, Table S6).

Subgroup Analysis and Propensity Score Matching Analysis

The associations between PPI use and a decreased risk of significant UGIB were consistent across all subgroups, including age, sex, and use of other gastrointestinal protectors. No significant interaction was found between PPI use and the subgroups (Figure 4).

After implementing a 1:2 propensity score matching, 45 753 patients were selected as the sample cohort (15 251 with PPI use and 30 502 without PPI use).

Table 1. Baseline Characteristics of Patients Treated and Not Treated With PPI Before and After Propensity Score Matching

	Before propensity score matching				After propensity score matching		
	Without PPI (n=80 638)	With PPI (n=16 084)	*P* value	SMD	Without PPI (n=30 502)	With PPI (n=15 251)	SMD
Year of admission			<0.001	0.337			0.047
2014	14 782 (18.3)	1534 (9.5)			3102 (10.2)	1534 (10.1)	
2015	15 097 (18.7)	2263 (14.1)			4785 (15.7)	2251 (14.8)	
2016	16 422 (20.4)	3224 (20.0)			6642 (21.8)	3164 (20.8)	
2017	17 081 (21.2)	4122 (25.6)			7828 (25.7)	3964 (26.0)	
2018	17 256 (21.4)	4941 (30.7)			8145 (26.7)	4338 (28.4)	
Sex, male	51 069 (63.3)	9827 (61.1)	<0.001	0.046	18 964 (62.2)	9358 (61.4)	0.017
Age, y	66.8±12.6	67.6±12.6	<0.001	0.065	67.5±12.4	67.5±12.6	0.002
Comorbidities							
Hypertension	55 450 (68.8)	11 512 (71.6)	<0.001	0.062	21 623 (70.9)	10 844 (71.1)	0.005
Diabetes	24 926 (30.9)	5418 (33.7)	<0.001	0.059	10 075 (33.0)	5198 (34.1)	0.022
Heart failure	11 376 (14.1)	3402 (21.2)	<0.001	0.186			
Prior myocardial infarction	2753 (3.4)	911 (5.7)	<0.001	0.108			
Prior stroke	13 737 (17.0)	3308 (20.6)	<0.001	0.091			
Renal disease	3950 (4.9)	1206 (7.5)	<0.001	0.108	1880 (6.2)	1043 (6.8)	0.027
Pulmonary disease	9791 (12.1)	2496 (15.5)	<0.001	0.098			
Hepatic disease	2539 (3.2)	646 (4.0)	<0.001	0.047	1104 (3.6)	592 (3.9)	0.014
Cancer, all	3940 (4.9)	979 (6.1)	<0.001	0.053	1660 (5.4)	914 (6.0)	0.024
Gastrointestinal cancer	2666 (3.3)	732 (4.6)	<0.001	0.064			
Functional dyspepsia	3504 (4.4)	937 (5.8)	<0.001	0.067	1589 (5.2)	860 (5.6)	0.019
Cerebrovascular procedure	5164 (6.4)	1248 (7.8)	<0.001	0.053			
Thrombolysis and thrombectomy	2335 (2.9)	599 (3.7)	<0.001	0.046			
Intra/extracranial angioplasty and stent	3466 (4.3)	823 (5.1)	<0.001	0.039			
Concomitant medications							
Statin	67 274 (83.4)	14 123 (87.8)	<0.001	0.1251	26 436 (86.7)	13 297 (87.2)	0.015
Nonsteroidal anti-inflammatory drugs	1105 (1.4)	398 (2.5)	<0.001	0.0805	456 (1.5)	269 (1.8)	0.021
Corticosteroids	169 (0.2)	62 (0.4)	<0.001	0.0323	89 (0.3)	46 (0.3)	0.007
Other gastrointestinal protectors	48 314 (59.9)	3647 (22.7)	<0.001	0.8170	7215 (23.7)	3647 (23.9)	0.006

Data are expressed as numbers (%) or means±SD. PPI indicates proton pump inhibitor; and SMD, standardized mean difference.

PPI users and nonusers demonstrated well-balanced characteristics, with absolute standardized mean differences <0.10 (Table 1). Analysis of the propensity score matching-based samples yielded results consistent with the main findings of our study. A stratified Cox proportional hazard regression analysis indicated that PPI use had consistent association with reduced risk of significant UGIB (HR, 0.68 [95% CI, 0.47–0.98]; *P*=0.040). However, the use of PPI was not linked to the risk of any UGIB (HR, 0.94 [95% CI, 0.71–1.25]; *P*=0.689, Table S5).

DISCUSSION

Using the Korean nationwide database, we investigated the relationship between PPI use and significant UGIB risk in IS patients who were at low risk of UGIB and were treated with DAPT. Despite a notable increase in PPI use during the study period, only approximately one-sixth of Korean patients with IS on DAPT received PPI prescriptions. PPI use demonstrated efficacy in decreasing the risk of significant UGIB, necessitating admission and transfusion in patients receiving DAPT after IS who were at a low risk for UGIB. These results indicate that more proactive use of PPI is a viable approach to prevent significant UGIB, a potentially life-threatening complication, in patients with IS on DAPT.

DAPT effectively reduces the recurrence of IS but increases the risk of major bleeding events, particularly UGIB, even in patients with a low risk for bleeding.[2,6–8] Recent randomized trials comparing the efficacy of DAPT and single antiplatelet therapy for patients with IS have yielded mixed results concerning the

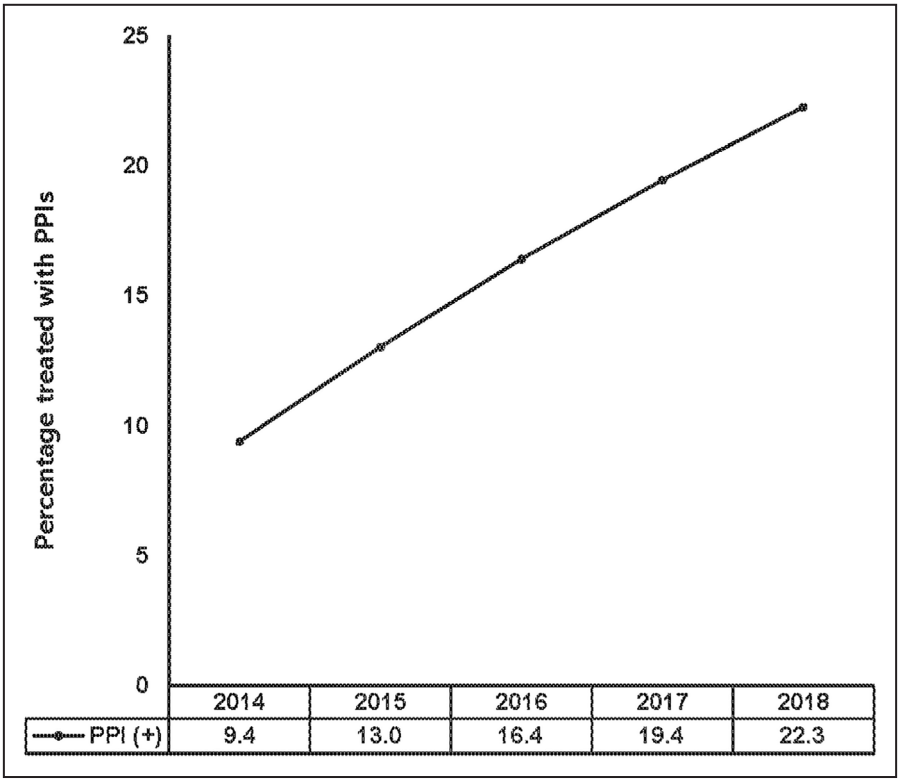

Figure 2. Temporal trends of PPI use.
Number (%) of patients treated with PPI (*P* for trend <0.05). PPI indicates proton pump inhibitor.

association of DAPT with major bleeding.[1–3] The POINT (Platelet-Oriented Inhibition in New TIA [Transient Ischemic Attack] and Minor Ischemic Stroke) trial particularly underscored a notable increase in major non-intracranial bleeding risk, implying a heightened risk of UGIB.[2] The POINT trial protocol, in line with the 2014 stroke guidelines, favored other gastrointestinal protectors and recommended alternatives to esomeprazole if PPIs were deemed necessary.[2,19] By contrast, the CHANCE (Clopidogrel in High-Risk Patients With Acute Nondisabling Cerebrovascular Events) and the THALES (Acute Stroke or Transient Ischemic Attack Treated With Ticagrelor and Aspirin for Prevention of Stroke and Death) trials did not provide specific protocols for gastrointestinal protection.[1,3] The CHANCE trial reported no significant difference in the risk of major bleeding, whereas the THALES trial, without separately analyzing UGIB, found the most severe bleeding to be intracranial.[1,3] Notably, these randomized trials primarily included patients at low risk for gastrointestinal bleeding, by excluding those with recent gastrointestinal bleeding events.[1–3] Other randomized trials that included patients with IS, in which DAPT did not outperform single antiplatelet therapy, highlighted an increased risk of UGIB.[6–8] Our study found that significant UGIB, necessitating transfusion at admission, occurred in 0.3% of patients 1 year after IS onset. This emphasizes the need for careful monitoring of UGIB risk in patients with IS on DAPT.

Current stroke guidelines lack recommendations for preventing UGIB in patients with IS[4]; this contrasts with the more explicit recommendations in coronary guidelines, ranging from universal to targeted PPI prescriptions for patients at elevated risk for UGIB.[12–15] To date, no randomized trials have specifically investigated protective strategies against UGIB in patients with IS on DAPT; however, PPIs have been proven to reduce UGIB risk in patients with coronary artery diseases on DAPT.[10,11] PPIs were reportedly superior to other gastrointestinal protectors in preventing UGIB in patients with coronary artery diseases on DAPT without significant difference in ischemic events.[20,21] Our study, which showed an increasing trend in PPI use despite the absence of clear stroke guidelines,[4] suggests that clinicians may be influenced by the potential benefits of PPI outlined in coronary guidelines.[12–15] Notably, our findings indicate that PPI use could decrease significant UGIB risk, even in low-risk groups. Our study therefore supports the use of PPIs in decreasing significant UGIB in patients with IS on DAPT; however, further prospective trials are needed to confirm this association.

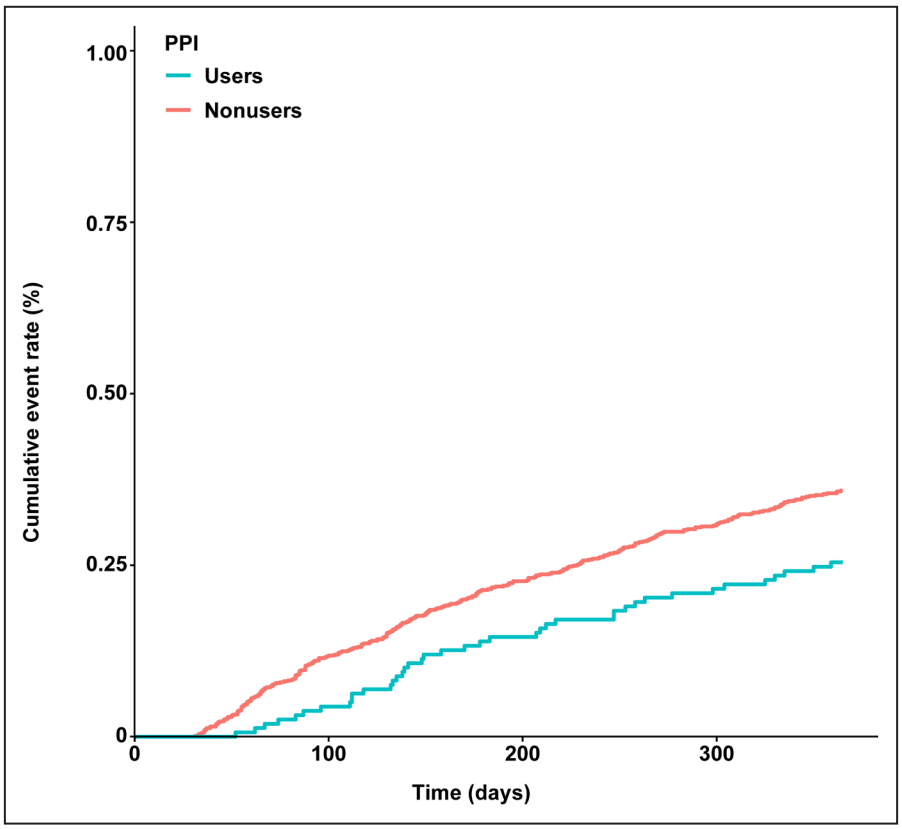

Figure 3. Cumulative incidence of significant UGIB according to the use of PPI.
PPI decreased the risk of significant UGIB in patients with IS on DAPT during 12 months of follow-up (log-rank test, *P*=0.040). DAPT indicates dual antiplatelet therapy; IS, ischemic stroke; PPI, proton pump inhibitor; and UGIB, upper gastrointestinal bleeding.

Studies on the use of PPIs to mitigate UGIB risks in patients with IS are limited, partly because of concerns regarding PPI-related side effects. These concerns include potential adverse effects from long-term PPI use, such as diminished DAPT efficacy, especially with the concomitant use of clopidogrel and omeprazole, and increased risk of renal disease, dementia, malignancy, and cardiovascular events.[22] Furthermore, several studies suggest an association between regular PPI use and a higher risk of first-time IS.[23–25] A meta-analysis also suggested the association of concomitant use of PPI and thienopyridines (a type of P2Y12 inhibitor, including clopidogrel, prasugrel, and ticlopidine) with increased risk of IS.[26] However, these concerns have not been definitively established in randomized controlled trials, and the possibility of residual bias owing to high-risk UGIB and ischemic event profiles in PPI-treated patients should be considered.[27,28] Previous electronic database based studies conducted in patients with myocardial infarction showed that PPI use decreased the risk of UGIB; however, the association was not statistically significant in high-risk patients.[29,30] In accordance with these studies,[29,30] our study found that PPI use was not associated with the risk of significant UGIB in high-risk groups, but it decreased the risk of significant UGIB in low-risk groups. This paradoxical association should be interpreted cautiously, considering the possible residual confounding effect. A previous observational study indicated that the increased risk of complications associated with PPI use is likely influenced by confounding factors linked to underlying conditions associated with PPIs, because after adjusting for PPI indications, regular PPI use was not associated with recurrent IS risk.[27] In a large randomized trial, 3 years of PPI use was associated only with a slight increase in the incidence of enteric infections, with no other vascular events.[31] In patients with coronary artery disease on DAPT, a randomized trial showed that PPIs effectively reduced UGIB incidence without significant cardiovascular interactions between clopidogrel and omeprazole.[10] Consequently, the American Gastroenterology Association recommends periodic review and discontinuation of PPIs in patients without clear indications.[32] They also advise against stopping PPI treatment solely due to potential adverse events.[32] This accumulating evidence may have changed clinicians' concept of PPI-associated adverse events, hence explaining an increasing trend in PPI use.

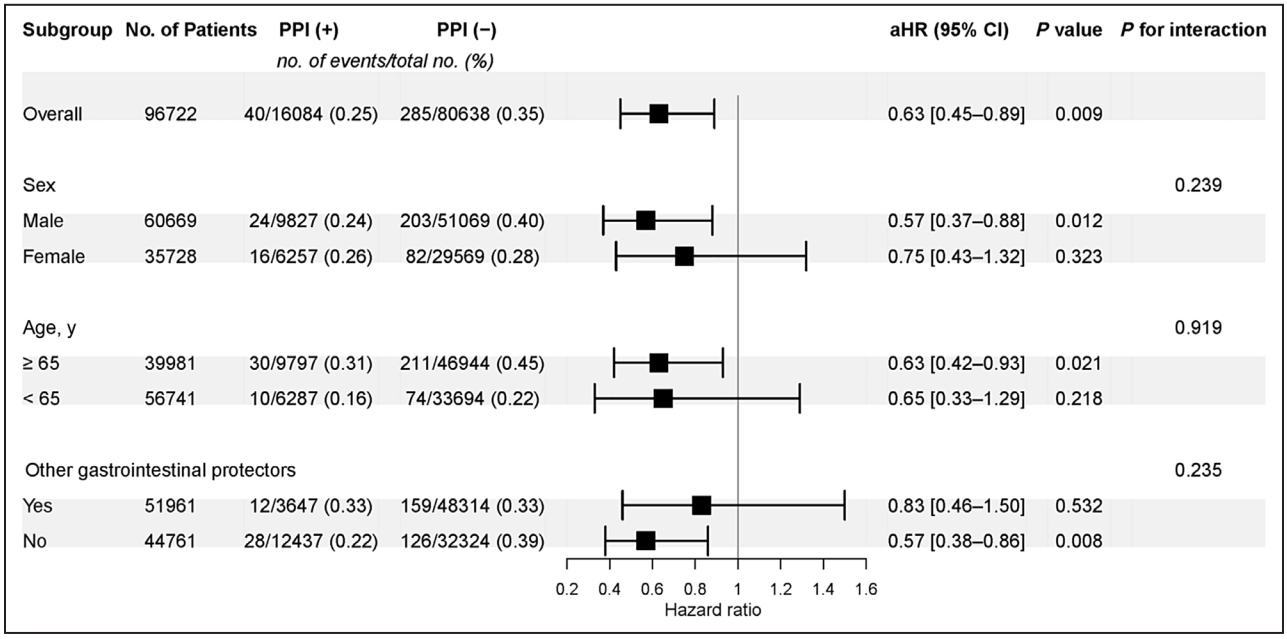

Figure 4. Subgroup analysis of the effect of PPIs on significant UGIB.
aHR indicates adjusted hazard ratio; and PPI, proton pump inhibitor.

This study had some limitations. First, we lacked data on the indications for or appropriateness of DAPT use. The use of a health claims database makes it challenging to confirm whether DAPT was prescribed based on guideline recommendations.[4] However, our study likely reflects real-world clinical practice because in such settings, adherence to guidelines for DAPT prescription can vary.[33] Second, outcomes were assessed 30 days post hospitalization; acute and subacute outcomes were not taken into account despite the common occurrence of bleeding events soon after starting DAPT.[6] Third, certain gastrointestinal bleeding risk factors, such as *H pylori* infection, the presence of reflux disorders, and a history of alcoholism, could not be accounted for in our analysis. This limitation restricted the optimal classification of high-risk patients. Nevertheless, our findings demonstrated that high-risk patients had a higher risk of significant UGIB compared with low-risk patients. Fourth, because this is a retrospective cohort study, possible biases and confounders may still exist, which might explain why no association was observed between the use of PPIs and the risk of significant UGIB. A future randomized trial is warranted to confirm the results. Finally, because this study used the Korean claims database, further studies are warranted to assess generalizability to other Asian and non-Asian populations.[34] Despite these limitations, this study had several strengths. It sheds light on the disparities between stroke guidelines and real clinical practice,[4] seeking solutions by applying methods already established in coronary guidelines.[12–15] Specifically, this study aimed to examine the real-world application of PPIs in patients with IS on DAPT who were considered at low risk for UGIB. We also evaluated the effectiveness of PPIs in preventing significant UGIB in this population, which encompassed a substantial number of patients from a nationwide health claims database. An important advantage of this study is its broad scope, which significantly reduces bias for selection.

CONCLUSIONS

Conclusively, PPI use was linked with a 12-month reduced risk of significant UGIB among Korean patients with IS on DAPT who were at low risk of UGIB. Despite the observed rise in PPI use, its usage remains suboptimal, with only 16.6% of patients receiving PPI treatment. PPI use may be considered an effective preventive strategy against significant UGIB until further randomized trials are conducted and the guidelines are updated. This underscores the need for an improved risk stratification system to accurately identify high-risk groups.

ARTICLE INFORMATION

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Disclosures

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Supplemental Material

Data S1
Data S2
Tables S1–S6
Figures S1–S2

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