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Original Article

The Use Pattern and Clinical Impact of New Antiplatelet Agents Including Prasugrel and Ticagrelor on 30-day Outcomes after Acute Myocardial Infarction in Korea: Korean Health Insurance Review and Assessment Data

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Conflict of Interest
The authors have no financial conflicts of interest.

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ABSTRACT

Background and Objectives: Despite the favorable efficacy of new antiplatelet agents demonstrated in randomized controlled trials, their clinical implications in Korea are unclear. The purpose of this study was to investigate trends in antiplatelet agent use for acute myocardial infarction (AMI) and their impact on 30-day clinical outcomes.

Methods: AMI patients undergoing percutaneous coronary intervention between 2010 and 2015 were assessed using claim data from the Health Insurance Review and Assessment Service.

Results: The use of new antiplatelet agents has rapidly increased since 2013 and has been preferred over clopidogrel (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals) since 2015. Both prasugrel (Effient; Eli Lilly and Company) (odds ratio [OR], 0.45; 95% confidence interval [CI], 0.31–0.67; p<0.001) and ticagrelor (Brilinta; AstraZeneca Pharmaceuticals LP) (OR, 0.84; 95% CI, 0.71–0.98; p=0.032) had an independent effect on lowering 30-day mortality in a weighted multivariable logistic regression model. However, new antiplatelet agents had no significant effect on other clinical outcomes including myocardial infarction, stroke, bleeding, and readmission within 30 days.

Conclusion: The use of new antiplatelet agents is rapidly increasing, and they have been used more commonly than clopidogrel since 2015. We demonstrated that new antiplatelet agents have a favorable effect on reducing 30-day mortality in AMI patients in Korea.

Keywords: Myocardial infarction; Prasugrel; Ticagrelor; Clopidogrel; Percutaneous coronary intervention

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INTRODUCTION

Obtaining sufficient platelet inhibition using aspirin and P2Y12 receptor antagonist has been a mainstay of treatment for acute myocardial infarction (AMI). Clopidogrel, an irreversible P2Y12 inhibitor (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals, Bridgewater, NJ, USA), has been widely used for coronary artery disease including AMI. However, there have been concerns about its genetic susceptibility and delayed-onset antiplatelet effect.

New P2Y12 receptor antagonists including prasugrel (Effient; Eli Lilly and Company, Indianapolis, IN, USA) and ticagrelor (Brilinta; AstraZeneca Pharmaceuticals LP, Wilmington, DE, USA) have demonstrated better clinical efficacy as well as more potent platelet inhibition compared to clopidogrel in AMI.[1)2)] Contemporary clinical practice guidelines now preferentially recommend new antiplatelet agents over clopidogrel for patients with AMI.[3-5)] These drugs became available in January 2011 and have been covered by national health insurance since July 2012 in Korea.

However, there is not sufficient data available regarding the changes in and current status of new antiplatelet drug use and the clinical implications. We sought to investigate trends in antiplatelet agent use and their impact on clinical outcomes in AMI patients using the national health insurance database in Korea.

METHODS

Study population

Korea has a universal national health insurance system that covers approximately 98% of the Korean population.[6)] We used claim data from the Health Insurance Review and Assessment Service (HIRA) including age, sex, diagnosis, procedure, surgery, and prescribed medications for analyses in this study. HIRA independently conducted the identification and sampling of information from the database. All processed data was provided after blinding personally identifiable information.

We extracted all patients who were admitted to healthcare service providers for AMI and underwent percutaneous coronary intervention (PCI) between 2010 and 2015. The International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnostic codes I21, I22, and I23 defined patients with AMI. Subcategorical codes including I21.0, I21.1, I21.2, I21.3 indicated ST-segment elevation myocardial infarction (STEMI), and I21.4 represented non-ST-segment elevation myocardial infarction (NSTEMI). The rest of the codes represented an unspecified myocardial infarction (MI). The patients were categorized into 3 groups for clopidogrel, prasugrel, and ticagrelor according to the most prescribed P2Y12 inhibitor during admission. Because few AMI patients were treated with new antiplatelet agents until 2012 (**Figure 1A and 1B**), we used patients between 2013 and 2015 for comparative analyses of the 3 different antiplatelet agents. A total of 53,221 AMI patients were identified during this period (**Figure 1C**). As prasugrel was not recommended and was rarely prescribed for patients ≥75 years old, we included 40,706 patients after exclusion of elderly patients (**Figure 1C and 1D**).

Hospitals were categorized by the mean number of PCI cases per year for AMI as <50 cases, 50–150 cases, and >150 cases. Clinical outcomes of all-cause death, recurrent MI, stroke, bleeding, and readmission within 30 days after PCI were evaluated. All death and readmission

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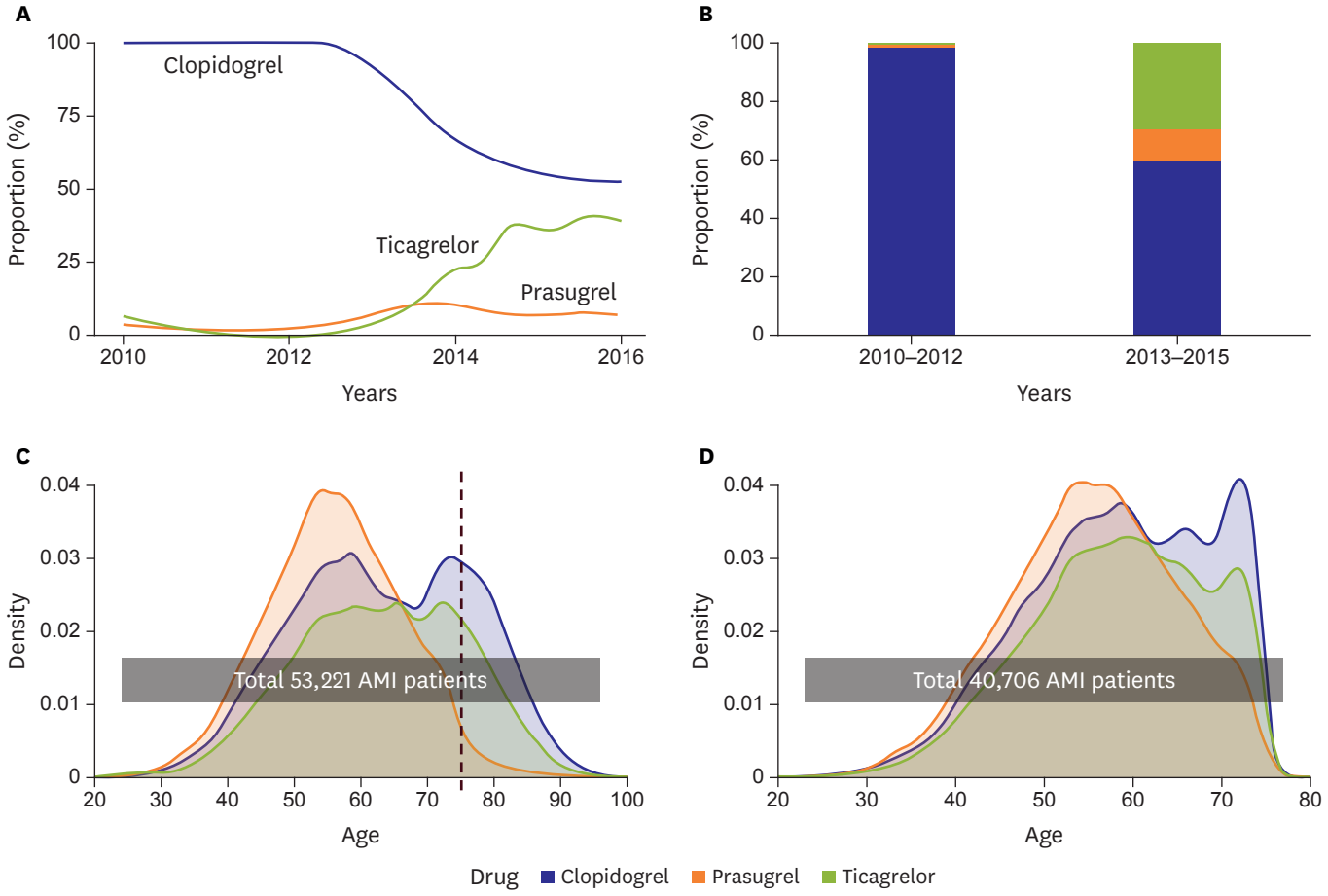

Figure 1. The use of P2Y12 antagonists in patients with AMI. Trends over time of P2Y12 antagonist use (A) and proportion of these prescriptions during 2010–2012 and 2013–2015 (B). Density plot indicates the age distribution of the 3 antiplatelet agents clopidogrel, prasugrel, and ticagrelor before (C) and after (D) 75 years of age. Orange indicates clopidogrel, green indicates prasugrel, and red indicates ticagrelor.
AMI = acute myocardial infarction.

events were identifiable from the database. Other clinical events were determined by further admission with a new corresponding diagnostic code after discharge. Stroke, including both hemorrhagic and ischemic stroke, was determined by diagnostic codes I60 to I63. We obtained intracranial, gastrointestinal, and other bleeding events using the following codes: D62, D68.3, D69, I60.x, I61.x, I62.x, I85.01, I85.11, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.01, K29.21, K29.31, K29.41, K29.51, K29.61, K29.71, K29.81, K29.91, and R58 (**Supplementary Table 1** in the online-only).

Because the personally identifiable information of each individual was encrypted before patient-level analysis to protect privacy, the study was exempted from full review by the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine, and the requirement for obtaining informed consent was waived. The Institutional Review Board of Severance Hospital, Yonsei University College of Medicine approved this study.

Statistical analyses

Categorical data are expressed as number (%) and were analyzed with the χ^2 test. Age is expressed as median (interquartile range [IQR]) and was compared using the Mann-Whitney

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test because of the skewed distribution after truncation. Absolute standardized mean differences were calculated as the difference in mean rates of each variable between the treatment group and the total population divided by the standard deviation of the difference. The inverse probability of treatment-weighted estimation was applied to minimize imbalances of observed covariates.

We utilized generalized boosted models to estimate the propensity score weight of each treatment using methods developed for comparison of multiple treatments. The average treatment effect on the population weights was estimated using the mnps (multinomial propensity scores) function in the twang (Toolkit for Weighting and Analysis of Nonequivalent Groups) package in R Statistical Software (R Foundation for Statistical Computing, Vienna, Austria).[7] Using the optimal truncation from Crump et al.,[8] we used cases with a propensity score between 0.1 and 0.9 for weighted analyses. Logistic regression was used to assess the effect of each antiplatelet agent on 30-day clinical outcomes of death, MI, stroke, bleeding, and readmission. The baseline variables listed in **Table 1** were used as covariates in multivariable logistic regression models. For weighted logistic regression analysis, we implemented the svyglm function in survey package, which enabled analyses to weight the data on combined propensity score and survey weights.

All statistical analyses were performed with R Statistical Software (version 3.3.2; R Foundation for Statistical Computing). P values <0.050 were considered indicative of statistically significant differences.

Table 1. Baseline clinical characteristics

Variables	Clopidogrel (n=24,489)	Prasugrel (n=4,300)	Ticagrelor (n=11,917)	Total (n=40,706)	p value	Unweighted ASMD			Weighted ASMD		
						Clopidogrel	Prasugrel	Ticagrelor	Clopidogrel	Prasugrel	Ticagrelor
Age (years)	60 (52–68)	56 (49–62)	58 (51–65)	59 (51–67)	<0.001	0.100	−0.301	−0.098	0.002	0.002	0.003
Female	4,843 (20)	398 (9)	1,762 (15)	7,003 (17)	<0.001	0.162	−0.307	−0.096	0.005	−0.016	0.005
Hypertension	16,910 (69)	2,988 (69)	8,093 (68)	27,991 (69)	0.049	0.016	0.018	−0.026	0.001	0.006	−0.001
Diabetes mellitus	14,062 (57)	2,212 (51)	6,712 (56)	22,986 (56)	<0.001	0.048	−0.112	−0.004	0.001	0.006	−0.014
Heart failure	4,865 (20)	687 (16)	2,298 (19)	7,850 (19)	<0.001	0.037	−0.101	0.000	−0.003	−0.005	−0.001
Stroke	746 (3)	53 (1)	223 (2)	1,022 (3)	<0.001	0.078	−0.130	−0.067	0.000	0.000	0.002
Hemodialysis	634 (3)	35 (1)	101 (1)	770 (2)	<0.001	0.110	−0.134	−0.161	−0.007	−0.004	0.009
Clinical diagnosis					<0.001						
STEMI	7,588 (31)	1,979 (46)	4,853 (41)	14,420 (35)		−0.241	0.238	0.152	0.000	0.002	0.001
NSTEMI	6,495 (27)	873 (20)	3,106 (26)	10,474 (26)		0.045	−0.151	0.011	0.000	−0.002	0.012
Unspecified MI	10,406 (42)	1,448 (34)	3,958 (33)	15,812 (39)		0.185	−0.122	−0.169	0.000	0.000	−0.012
Hospital capability (cases/years)					<0.001						
<50	4,575 (19)	259 (6)	1,682 (14)	6,516 (16)		0.172	−0.469	−0.077	0.004	−0.014	0.004
50–150	10,918 (45)	2,056 (48)	5,993 (50)	18,967 (47)		−0.102	0.027	0.104	0.000	0.004	0.007
>150	8,996 (37)	1,985 (46)	4,242 (36)	15,223 (37)		−0.034	0.197	−0.053	−0.003	0.006	−0.010
Hospitalization (days)					<0.001						
<7	9,806 (40)	1,850 (43)	5,086 (43)	16,742 (41)		−0.056	0.043	0.044	0.000	0.004	−0.002
7–14	10,390 (42)	1,945 (45)	5,332 (45)	17,667 (43)		−0.049	0.041	0.038	−0.002	−0.002	0.005
>14	4,293 (18)	505 (12)	1,499 (13)	6,297 (15)		0.136	−0.129	−0.123	0.003	−0.003	−0.005
Years at admission					<0.001						
2013	10,177 (42)	1,613 (38)	1,525 (13)	13,315 (33)		0.451	0.111	−0.843	0.001	0.004	−0.006
2014	7,779 (32)	1,441 (34)	4,605 (39)	13,825 (34)		−0.118	−0.011	0.136	0.001	0.016	0.001
2015	6,533 (27)	1,246 (29)	5,787 (49)	13,566 (33)		−0.377	−0.107	0.431	−0.002	−0.020	0.005

Data are presented as number (%) or median (IQR). ASMD was calculated as the difference in the mean rate of each variable between the treatment group and total population divided by the SD of the difference.
ASMD = absolute standardized mean difference; IQR = interquartile range; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; SD = standard deviation; STEMI = ST-segment elevation myocardial infarction.

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RESULTS

Baseline clinical characteristics

Among a total of 40,706 AMI patients <75 years old who underwent PCI during admission between 2013 and 2015, the use of new antiplatelet agents, especially ticagrelor, has significantly increased since 2013 (**Figure 1A**). From 2010 to 2012, these agents were prescribed only for 1.2% patients with AMI during admission. The prescription rates of prasugrel and ticagrelor rapidly increased to 10.6% and 29.3% during 2013–2015, respectively (**Figure 1B**). **Table 1** demonstrates the baseline clinical characteristics. The prasugrel and ticagrelor groups were younger and contained fewer females compared to the clopidogrel group. These new antiplatelet agents were more commonly prescribed for patients with STEMI. Prasugrel was less frequently used in patients with diabetes mellitus or heart failure. However, it was more commonly used in hospitals with more than 150 cases per year. Clopidogrel was preferred over new antiplatelet agents for AMI patients with a longer stay (>14 days) in the hospital.

Thirty-day clinical outcomes

Table 2 indicates the crude incidence of 30-day clinical adverse events. Mortality and admission rates within 30 days were lowest in AMI patients treated with prasugrel (1.4% and 5.7%, respectively) and highest in those treated with clopidogrel (3.4% and 6.9%, respectively). They were also significantly lower in the ticagrelor group compared to the clopidogrel group. There was no significant difference in reoccurrence of MI or bleeding rate based on antiplatelet agent use. However, stroke incidence was highest in patients with clopidogrel.

We conducted logistic regression models to analyze the impact of each new antiplatelet agent on clinical adverse events and applied a multivariable adjustment and/or propensity score weighting for each treatment (**Table 3**). Prasugrel was significantly correlated with lower incidence of 30-day mortality compared to clopidogrel. Using a crude model, the odds ratio (OR) for mortality was 0.41 (95% confidence interval [CI], 0.32–0.53; p<0.001). The OR was 0.46 (95% CI, 0.31–0.69; p<0.001) in the weighted multivariable model. Ticagrelor was correlated with a lower 30-day mortality rate compared to clopidogrel. The OR was 0.72 (95% CI, 0.63–0.82; p<0.001) with the crude model and 0.84 (95% CI, 0.71–0.98; p=0.032) with a weighted multivariable model. The 30-day readmission rate was significantly lower in patients treated with new antiplatelet agents compared with those treated with clopidogrel. However, the adjusted models demonstrated that there was no significant impact of each new antiplatelet drug. Weighted multivariable models showed that the ORs of prasugrel and ticagrelor were 0.93 (95% CI, 0.78–1.12; p=0.456) and 1.01 (95% CI, 0.91–1.13; p=0.822), respectively. Regarding MI and bleeding, logistic regression models demonstrated no significant impact of new antiplatelet agents. We found that ticagrelor was significantly correlated with lower incidence of stroke (OR, 0.51; 95% CI, 0.33–0.80; p=0.003) in the crude model. Though there was a trend toward reduction in 30-day stroke risk with ticagrelor

Table 2. Incidence of 30-day clinical adverse events

30-day outcomes	Clopidogrel (n=24,489)	Prasugrel (n=4,300)	Ticagrelor (n=11,917)	p value
Mortality	842 (3.4)	62 (1.4)	298 (2.5)	<0.001
MI	407 (1.7)	78 (1.8)	194 (1.6)	0.712
Stroke	96 (0.4)	10 (0.2)	24 (0.2)	0.006
Bleeding	30 (0.1)	5 (0.1)	14 (0.1)	0.988
Readmission	1,694 (6.9)	247 (5.7)	723 (6.1)	0.001

Data are presented as total number of events (%).
MI = myocardial infarction.

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Table 3. Adjusted ORs of ticagrelor and prasugrel for 30-day outcomes using logistic regression in the unweighted and IPTW models

30-day outcomes	Unweighted analysis						Weighted analysis*					
	Univariable model			Multivariable model†			Univariable model			Multivariable model†		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Prasugrel												
Mortality	0.41	0.32–0.53	<0.001	0.58	0.45–0.76	<0.001	0.30	0.21–0.44	<0.001	0.46	0.31–0.69	<0.001
MI	1.09	0.86–1.40	0.475	1.27	0.99–1.64	0.058	0.94	0.69–1.28	0.711	1.09	0.79–1.50	0.617
Stroke	0.59	0.31–1.14	0.115	0.79	0.41–1.54	0.492	0.81	0.39–1.69	0.573	1.07	0.50–2.30	0.863
Bleeding	0.95	0.37–2.45	0.914	1.13	0.43–2.97	0.812	1.11	0.38–3.24	0.853	1.34	0.45–3.94	0.597
Readmission	0.82	0.71–0.94	0.005	0.97	0.84–1.12	0.699	0.79	0.66–0.93	0.006	0.93	0.78–1.12	0.456
Ticagrelor												
Mortality	0.72	0.63–0.82	<0.001	0.86	0.75–0.99	0.040	0.84	0.73–0.98	0.028	0.84	0.71–0.98	0.032
MI	0.98	0.82–1.16	0.811	1.08	0.90–1.30	0.397	1.01	0.83–1.22	0.941	1.04	0.85–1.28	0.684
Stroke	0.51	0.33–0.80	0.003	0.63	0.39–1.01	0.054	0.73	0.43–1.24	0.247	0.77	0.44–1.36	0.370
Bleeding	0.96	0.51–1.81	0.897	1.05	0.54–2.05	0.892	0.76	0.39–1.51	0.438	0.72	0.37–1.41	0.335
Readmission	0.87	0.79–0.95	0.002	0.97	0.88–1.07	0.566	0.98	0.89–1.09	0.716	1.01	0.91–1.13	0.822

CI = confidential interval; IPTW = inverse probability of treatment weighting; MI = myocardial infarction; OR = odds ratio.
*Inverse probability of the treatment weighted estimation with propensity scores was computed using generalized boosted models as described in the Methods section, †Multivariable logistic regression model was used to adjust for the covariates shown in **Table 1**.

after multivariable adjustment (OR, 0.63; 95% CI, 0.39–1.01; p=0.054), weighted analyses displayed no significant impact of ticagrelor on stroke.

DISCUSSION

Using a nation-wide population from the HIRA Korean database, we demonstrated a contemporary pattern of P2Y12 antagonist use and its favorable impact on 30-day mortality in AMI patients undergoing PCI. The results of our study revealed major changes in the use of P2Y12 antagonists for patients with AMI in Korea between 2010 and 2015. New antiplatelet agent use grew rapidly, with a preference for ticagrelor over prasugrel. Until 2012, when new antiplatelet agents started to be covered by national health insurance, both prasugrel and ticagrelor were rarely prescribed for AMI patients. Between 2013 and 2015, approximately 40% of AMI patients were treated with new antiplatelet agents. The prescription rate of new antiplatelet agents has been higher than that of clopidogrel since 2015.

Randomized trials demonstrated that both prasugrel[1] and ticagrelor[2] reduced major thromboembolic events, but had an elevated risk of bleeding compared to clopidogrel in patients with acute coronary syndrome. After 2012, American College of Cardiology/American Heart Association (ACC/AHA) guidelines for NSTEMI[9] and STEMI[10] were revised with a recommendation for the use of these drugs. However, the guidelines did not endorse prasugrel or ticagrelor over clopidogrel. There is a growing body of evidence to support new antiplatelet agents due to their rapid-onset, more potent platelet inhibition, and reduction in composite efficacy endpoints. In particular, the favorable impact on mortality of ticagrelor was proven by its landmark trial,[2] unlike prasugrel.[1] In addition, the strong preference of ticagrelor over prasugrel is attributable to prasugrell's contraindications (age >75 years, body weight <60 kg, and history of stroke) and lack of supporting evidence for clopidogrel's administration prior to diagnostic angiography (e.g., at the emergency room) and/or without revascularization.[11] Contemporary practice guidelines[3][5][12] recommend the use of new antiplatelet agents for patients with NSTEMI and STEMI. Despite similar recommendations for prasugrel and ticagrelor, the prescription rate of prasugrel has been gradually decreasing in Korea since 2013. A Swedish nationwide cohort study conducted between 2009 and 2013 also demonstrated a similar pattern of P2Y12 antagonist use among 104,012 patients with acute coronary syndrome.

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Ticagrelor became the predominant P2Y12 antagonist in patients undergoing angiography since 2013, whereas clopidogrel was preferred in patients with noninvasive treatment in Sweden.[13]

In this study, patients with longer hospital stay were less frequently prescribed prasugrel or ticagrelor. The reasons for lower utilization of new antiplatelet agents among such patients is unclear; however, these patients might have had more comorbidities or acute complications related to higher bleeding risk, which might make physicians hesitate to use clopidogrel instead of more potent drugs. The result of subgroup analyses from the Platelet Inhibition and Patient Outcomes (PLATO) trial demonstrated that the favorable effect of ticagrelor was consistent regardless of invasive treatment or Thrombolysis in Myocardial Infarction (TIMI) risk score at randomization.[2][14][15] However, the Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS) trial concluded that prasugrel did not improve clinical outcomes in patients without revascularization.[11] These results might support the use of ticagrelor among AMI patients regardless of successful revascularization, even in patients with higher bleeding risk at admission. However, further studies are required to determine the efficacy and safety of these drugs in patients with complications or deterioration during hospitalization.

In this study, 30-day mortality was significantly lower in patients receiving prasugrel (1.4%) or ticagrelor (2.5%) compared to those receiving clopidogrel (3.4%). The mortality rate of the clopidogrel group in the study was close to that of contemporary randomized trials and ranged from 2.4% to 3.2%.[1][16-18] The mortality rates of the prasugrel and ticagrelor groups were also similar to the results of substudies of randomized trials, which showed 1.6% in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction 38 (TRITON-TIMI 38)[19] and 2.6% in PLATO[17] in STEMI patients. Prasugrel and ticagrelor were independently correlated with lower 30-day mortality after multivariable and weighted analysis in our study. As mentioned above, the favorable impact of ticagrelor on mortality was consistently demonstrated in various subgroup analyses of the PLATO trial, including in patients with invasive treatment,[14] STEMI,[17] diabetes,[20] and renal dysfunction.[21] Another registry in Sweden[22] compared ticagrelor and clopidogrel and showed an association between ticagrelor and a lower risk of death, which was consistent with previous randomized trials and our study.

Even though TRITON-TIMI 38[1] demonstrated no beneficial impact of prasugrel on mortality in all participants, the substudy[19] revealed a favorable effect of prasugrel on 30-day mortality in patients undergoing PCI for STEMI. Moreover, the favorable effect of prasugrel on mortality was also demonstrated by the TRITON-TIMI 38 sub-study with patients undergoing coronary artery bypass surgery.[23] Furthermore, a meta-analysis including 10 randomized controlled trials and one large retrospective study drew the conclusion that prasugrel, but not ticagrelor, offered a significant reduction in 30-day mortality in PCI-treated STEMI patients.[24] These results justify the utilization of prasugrel for patients who underwent revascularization.

There was no clinical impact of each new antiplatelet agent on 30-day MI mortality in the present study. Regarding composite efficacy endpoints including death, MI, and stroke, the superiority of prasugrel and ticagrelor has been demonstrated in previous studies. Better clinical efficacy of prasugrel was predominantly driven by a reduction in nonfatal MIs, rather than by reduction of death or stroke.[1] Prasugrel had a consistent benefit on efficacy endpoints including MI, stent thrombosis, and revascularization during the first 3 days and for the duration of the study.[25] It is remarkable that the incidence of MI within the first 3 days of that study was 4.3%

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(prasugrel) and 5.2% (clopidogrel), which was significantly higher than our result, which ranged from 1.6% to 1.8%. We showed a similar incidence of bleeding in our study (0.1%), which is lower than seen in contemporary trials. Because of the limitations of our study, many events such as acute bleeding immediately following the procedure could have been excluded. Studies with a prospective design or a longer duration of follow-up might be warranted.

This study has some limitations. This study reflects the nation-wide and real-world practice of antiplatelet therapy for AMI patients and its clinical impact. However, there are some unavoidable limitations because of the study design.

First, we could not evaluate the severity of disease at the index hospitalization. Severity indices such as clinical presentation, left ventricular ejection fraction, cardiac biomarkers, blood pressure, and concomitant use of mechanical circulation support were not available. Furthermore, angiographic and procedural information, such as the extent of diseased vessels; type of intravascular procedure; and implanted number, length, or type of stent, were not accessible. We tried to adjust and balance such confounding factors affecting clinical outcomes. However, there might still be limitations even with the statistical analyses.

We conducted the analyses based on diagnostic code due to the limitations of this study design. There was a possibility that some mis-entry or omission of diagnostic codes occurred at the index hospitalization and during follow-up, which might lead to analytic inaccuracy. Regarding bleeding complications, we identified the events based on particular diagnostic codes without any additional information to determine clinical relevance; however, this did not allow for analysis of the severity of bleeding events. Because we could determine the adverse events during admission to healthcare centers after discharge from the index hospitalization, the adverse events that occurred during the index hospitalization or out of the hospital might have be missed. However, mortality data were independently recorded, and all readmission events were found in the database. The implications of antiplatelet agents on the outcomes, therefore, might be more credible than those of other clinical events.

Lack of information about other medications was one of the limitations of our study. This information can be relevant for optimal medical treatment. Instead, we tried to determine the adequacy of treatment for patients by adjusting for hospital capability for PCI cases and admission year. However, there are some limitations when comparing the implementation procedures and medications to assess the appropriateness of treatment.

In conclusion, we demonstrated the trend toward increasing use of new antiplatelet agents in AMI patients undergoing PCI in Korea. As a result, the new antiplatelet agents were shown to superior to clopidogrel for AMI in Korea since 2015. There was a favorable effect of both prasugrel and ticagrelor on 30-day mortality. However, each agent had no significant impact on the other 30-day clinical outcomes of MI, stroke, bleeding, and readmission in our study.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

ICD-10-CM codes for bleeding events

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