REVIEW

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Current status of acute myocardial infarction in Korea

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Coronary artery disease, especially acute myocardial infarction (AMI), is a leading cause of death in the Asia-Pacific region. The Korea Acute Myocardial Infarction Registry (KAMIR) is the first nationwide, prospective, multicenter registry of Korean patients with AMI. Since the KAMIR first began in November 2005, more than 70,000 patients have been enrolled, and 230 papers have been published (as of October 2018). Moreover, published data from the KAMIR have revealed different characteristics from those of Western AMI registries regarding risk factors, interventional strategies, and clinical outcomes. As a result, the KAMIR study has improved the outcomes of percutaneous coronary intervention and reduced mortality. We propose the use of the KAMIR score in the prediction of 1-year mortality. Using data from the KAMIR, we provide an overview of the current status of AMI in Korea, including trends in demographic characteristics, risk factors, medications, treatment strategies, and clinical outcomes.

Keywords: Myocardial infarction; Risk factors; Percutaneous coronary intervention; Mortality; Prognosis

INTRODUCTION

Although acute myocardial infarction (AMI) continues to be a major cause of mortality in the Asia-Pacific population, there is still a lack of data on the characteristics of patients with AMI in Asia [1]. The Korea Acute Myocardial Infarction Registry (KAMIR) is the first nationwide, prospective, multicenter registry of Korean patients with AMI. The KAMIR provides the public and physicians in the “real-world” clinical field access to the demographic characteristics, treatment strategies, and clinical outcomes of patients with AMI [2]. Since the KAMIR first began in November 2005, more than 70,000 patients have been enrolled, and a total of 230 papers have been published (as of October 2018). Moreover, published data from the KAMIR have revealed different characteristics than those from Western AMI registries [3,4]. Using data from the KAMIR, we provide an overview of the current status of AMI in Korea, including trends in demographic characteristics, risk factors, medications, treatment strategies, and clinical outcomes.

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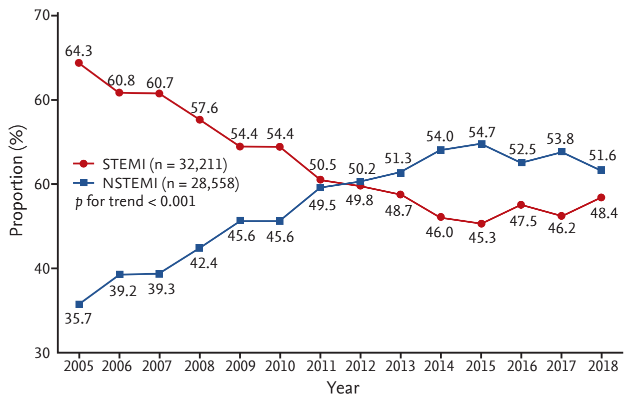

Figure 1. Annual incidence rates of ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) from 2005 to 2018.

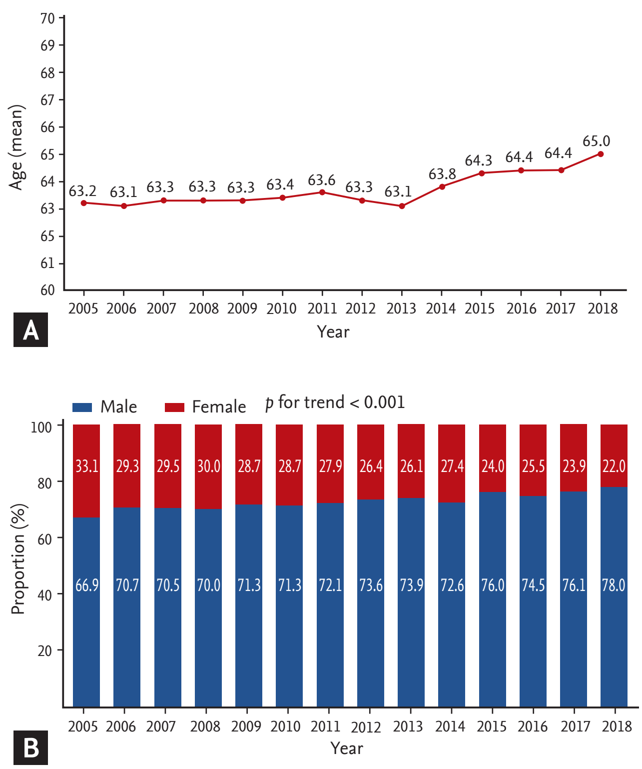

Figure 2. Temporal trends in the (A) mean age and (B) sex ratio among Korean patients with AMI.

DEMOGRAPHIC CHARACTERISTICS IN KOREAN PATIENTS WITH AMI

Temporal trends in the proportion of patients with AMI, including ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI), are shown in Fig. 1. STEMI decreased from 64.3% in 2005 to 48.4% in 2018, and thus the ratio of STEMI/NSTEMI decreased in 2012 (p for trend < 0.001) (Fig. 1). This trend is similar to that reported in previous Western studies [5,6]. The change in the STEMI/NSTEMI ratio can be explained by more sensitive cardiac-specific assays, such as the high-sensitive troponin assay [7-9]. With the wide use of these sensitive tests, the rate of NSTEMI has increased due to the early detection of myocardial necrosis in patients formerly considered to have unstable angina [10]. In only Japan registry, 77% of all patients with AMI were STEMI and the patients with STEMI increased between 2005 and 2014 [11].

Trends in the mean age and sex ratio of Korean patients with AMI are shown in Fig. 2. Between 2005 and 2018, the mean age of AMI patients gradually increased from 63.2 years in 2005 to 65.0 years in 2018 (Fig. 2A). In terms of the sex ratio, the proportion of males gradually increased from 66.9% in 2005 to 78.0% in 2018 (p for trend < 0.001). In the FAST-MI (French Registry of Acute ST-Elevation or non-ST-elevation Myocardial Infarction), the mean age decreased slightly from 64.0 years in 2005 to 63.5 years in 2015, and the proportion of males increased from 72.0% in 2005 to 75.0% in 2015 [12-14].

PREVALENCE OF CARDIOVASCULAR RISK FACTORS

Among the cardiovascular risk factors, KAMIR data from November 2005 to August 2018 revealed that hypertension is the most common comorbidity (57.2%), followed by current smoking (40.6%), diabetes mellitus (DM; 32.3%), and dyslipidemia (13.2%). In the analysis of risk factor trends, the rates of hypertension, DM, and dyslipidemia have gradually increased since 2005 (all p for trend < 0.001) (Fig. 3A). However, the proportion of current smokers among patients with AMI decreased from 43.7% in 2005 to 36.1% in 2018, and this tendency was the same in both STEMI and NSTEMI patients (all p for trend < 0.001) (Fig. 3B). The prevalences of hypertension, DM, and dyslipidemia increased to 75.4%, 41.8%, and 23.0% in 2018, respectively. We previously reported that a blood pressure less than 112.2/73.3 mmHg was associated with worse clinical outcomes because of the U curve phenomenon between blood pressure control and major adverse cardiac events (MACEs)

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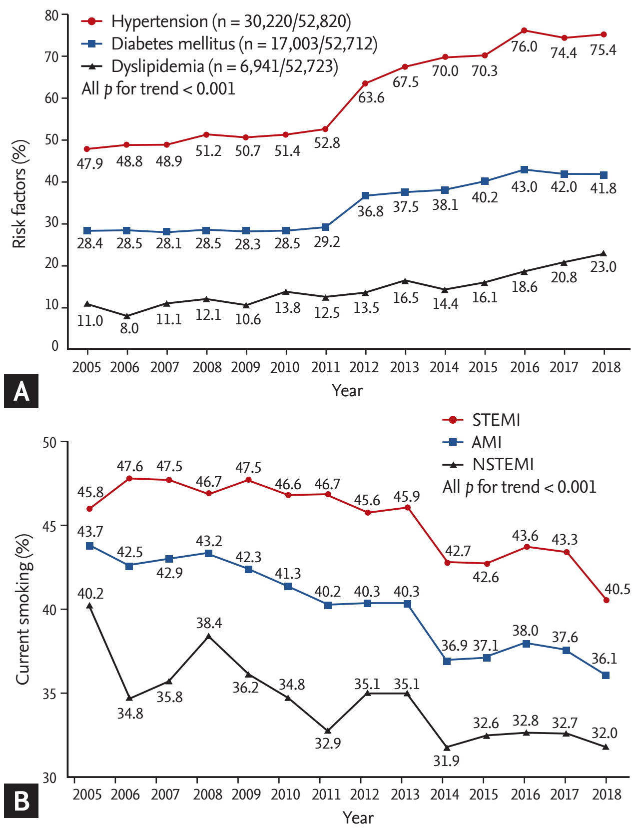

Figure 3. Temporal trends in cardiovascular risk factors among Korean acute myocardial infarction (AMI) patients from 2005 to 2018. Changes in (A) hypertension, diabetes mellitus, and dyslipidemia in patients with AMI and (B) current smoking in patients with AMI and both ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI).

[15]. In terms of diabetic control, we demonstrated that intensive glycemic control prevented mortality in AMI patients with DM, whereas hypoglycemia should be avoided, as it was associated with increased mortality in AMI patients with DM, especially in the group with poor diabetic control [16]. The rate of dyslipidemia was relatively lower in the KAMIR data than in other Western registries [5,13,14]. This phenomenon could be explained by the different patterns of dyslipidemia in Korean patients with AMI. Approximately 60% of patients with AMI have low high-density lipoprotein (HDL) levels, and 25% of those have high triglyceride levels [17]. In addition, although statin therapy for AMI patients with a low-density lipoprotein level less than 70 mg/dL is proven to be beneficial, combination therapy with simvastatin and ezetimibe was only effective in Korean

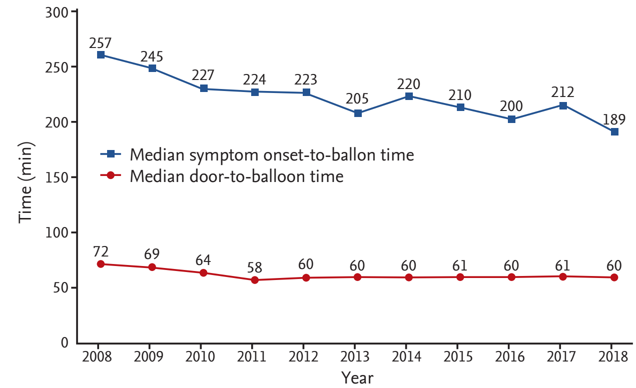

Figure 4. Annual symptom onset-to-balloon time and door-to-balloon time.

AMI patients with high-risk factors, such as old age, DM, and heart failure [18,19]. In terms of the current smoking trend in patients with AMI, it is similar to the trend in European registries but remains higher [14,20].

TIME TO PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN STEMI PATIENTS

The symptom onset-to-balloon (S2B) time and door-to-balloon (D2B) time in patients with STEMI are shown in Fig. 4. The S2B time has gradually decreased since 2005, although the D2B time has remained at approximately 60 minutes since 2012. We previously reported the relationship between the time to treatment and 30-day mortality rate among STEMI patients undergoing primary percutaneous coronary intervention (PCI) [21]. Reductions in S2B and D2B times did not lead to a parallel reduction in the 30-day mortality rate. In contrast, an S2B time of less than 180 minutes was identified as an independent predictor of the 30-day mortality rate. Based on KAMIR data of S2B time, educational programs on the manifestation of STEMI are needed to reduce the duration of out-of-hospital delays in Korea.

PROCEDURAL AND CORONARY ANGIOGRAPHIC CHARACTERISTICS

According to a previous KAMIR study, radial artery access has markedly increased in Korean patients with

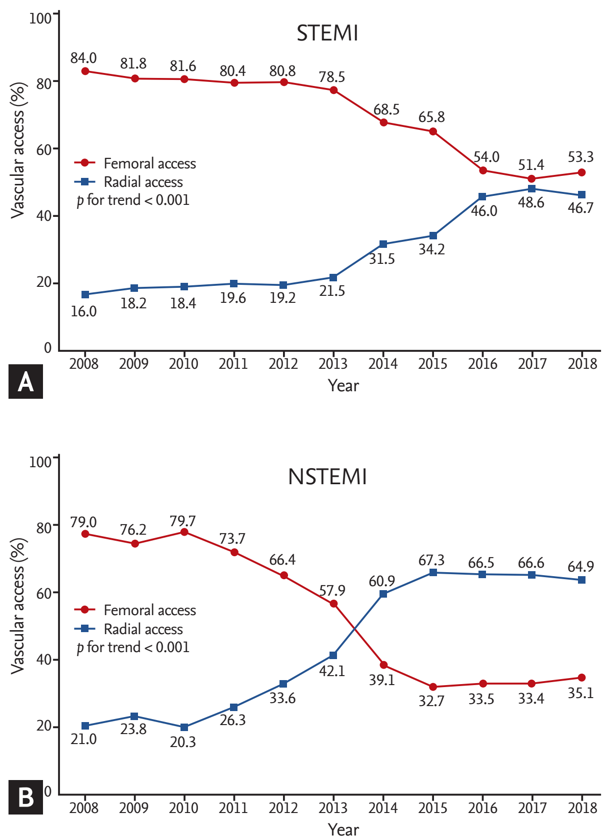

Figure 5. Changing trends in vascular access in patients with (A) ST-elevation myocardial infarction (STEMI) and (B) non-ST-elevation myocardial infarction (NSTEMI) in Korea.

STEMI but has not overtaken femoral access (2016) [4]. This tendency was also observed in extended KAMIR data, even though the rate of radial access has been greater than 50% in NSTEMI patients since 2014 (Fig. 5). The Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX (MATRIX), a large randomized multicenter trial, demonstrated that radial access is associated with better overall clinical outcomes compared with femoral access in patients with acute coronary syndrome [22,23]. Another KAMIR study also demonstrated that radial access is associated with a lower complication rate and better clinical outcomes in octogenarian patients with AMI [24]. According to the current guidelines, radial access is recommended over femoral access in patients with AMI by an experienced radial operator [25,26]. In Korea, although trend analyses have shown an increase in radial access in STEMI patients, the rate did not reach 50% in 2018. In NSTEMI patients, radial access

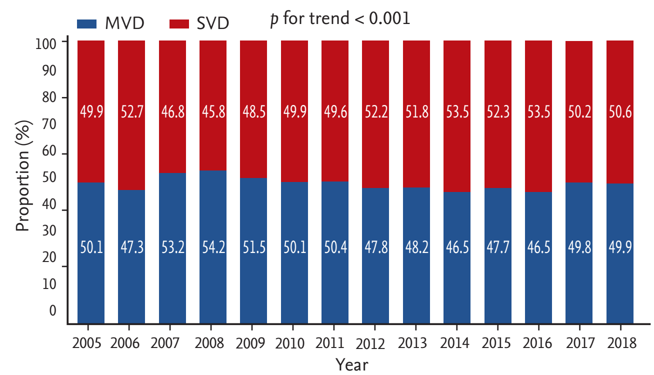

Figure 6. Rates of single-vessel disease (SVD) and multivessel disease (MVD) in patients with ST-elevation myocardial infarction from 2005 to 2018.

has also remained at approximately 60% since 2014. However, radial access is expected to increase in both STEMI and NSTEMI patients due to guideline recommendations.

Multivessel disease (MVD) was observed in half of all STEMI patients in Korea (Fig. 6). Regarding the clinical outcomes of STEMI with MVD, a previous KAMIR study demonstrated that MVD was associated with a significant increase in the 30-day mortality rate [27]. Regarding complete revascularization (CR), there are two types of revascularization [28-34]: one is simultaneous CR, which is defined as simultaneous CR for an infarct-related artery (IRA) and non-IRA during the primary PCI, and the other is staged CR, which is defined as CR with planned PCI for non-IRA within a few weeks after the index procedure, including during index hospitalization. Recent guidelines recommend that any type of CR, including simultaneous or staged CR, should be preferred in STEMI patients with MVD [25,26,34]. A 3-year follow-up single-center retrospective study in Korea demonstrated that staged CR in STEMI patients with MVD improved long-term clinical outcomes without an increase in the rate of repeated PCI [35]. Another study regarding the optimal timing of PCI for non-culprit vessels in patients with STEMI and MVD, the Convergent Registry of Catholic and Chonnam University for Acute Myocardial Infarction (COREA-AMI) registry, showed staged CR after 1 week index primary PCI was associated with the highest MACE, as compared to both simultaneous CR and early staged CR within 1 week [36]. Therefore, simultaneous or staged CR should be considered in Korean patients

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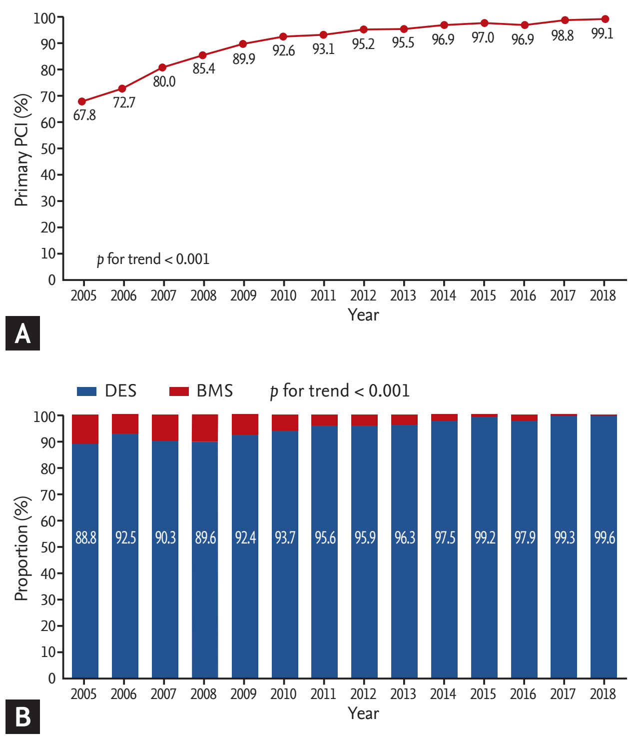

Figure 7. (A) Annual primary percutaneous coronary intervention (PCI) rate and (B) the proportion of drug-eluting stent (DES) and drug-eluting stent (BMS) implantations in patients with ST-elevation myocardial infarction from 2005 to 2018.

with STEMI and MVD, as per Western guidelines.

Another KAMIR study showed an increased rate of primary PCI and use of drug-eluting stents (DESs) in patients with STEMI between 2005 and 2016 [4]. An extended KAMIR data analysis in 2018 showed a 99.1% primary PCI rate (Fig. 7A) and 99.6% DES implantation rate (Fig. 7B) in STEMI patients. KAMIR data have also shown a notably high rate of primary PCI compared with those in Western registries [14,20].

Several KAMIR studies have reported the safety and efficacy of DESs in patients with AMI [37-40]. A recent KAMIR study demonstrated that the rate of 6-month definite-or-probable stent thrombosis was 0.3% (n = 4) among 1,486 patients with AMI who underwent implantation of a current second-generation DES [41]. Moreover, the rate of definite stent thrombosis at 1 year was 0.6% (n = 86) among 15,003 patients with STEMI who underwent stent implantation between 2005 and 2015 [4]. Therefore, KAMIR studies of DES implantation support the recommendation of implanting a second-generation DES over a bare-metal stent for primary PCI, as described in the current guidelines [25,26].

MEDICATION AT DISCHARGE

The medications prescribed to patients with AMI at discharge are shown in Table 1. Statins, renin-angiotensin system (RAS) blockers, and beta blockers are prescribed in approximately 80% of all AMI patients. RAS blockers, such as angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ARBs), are prescribed more for Korean patients with AMI (85.4%, 86.4%, and 89.6% of AMI, STEMI, and NSTEMI patients, respectively) compared with those in French and Swedish registries (64.0% and 57.0% of STEMI and NSTEMI patients, respectively, in the French registry and 56.2% of AMI patients in the Swedish registry) [20,42]. A previous KAMIR study demonstrated that insurmountable ARBs, including valsartan, candesartan, irbesartan, telmisartan, and olmesartan, had greater effects on 1-year clinical outcomes than did surmountable ARBs, such as losartan or eprosartan [43]. We also found that ARB therapy at discharge was associated with improved clinical outcomes in STEMI patients with a preserved left ventricular ejection fraction, and that the efficacy of ARBs was comparable with that of angiotensin-converting enzyme inhibitors in STEMI patients with a preserved left ventricular ejection fraction. Therefore, RAS inhibitors should be considered for Korean patients with AMI [44].

In terms of P2Y12 inhibitors, the use of ticagrelor increased markedly from 10.5% in 2013 to 46.4% in 2018 in patients with AMI compared with prasugrel (Fig. 8A). This tendency was also observed in both the STEMI and NSTEMI groups (Fig. 8B and 8C). In the NSTEMI group, the use of ticagrelor increased from 9.0% in 2013 to 37.1% in 2018, but did not reached above 50.0%. In contrast, in the STEMI group, the use of ticagrelor increased from 12.1% in 2013 to 55.9% in 2018, and ticagrelor use overtook that of clopidogrel in 2016. According to current KAMIR data, the analysis of the trend in P2Y12 inhibitor use showed that clopidogrel is still prescribed more than P2Y12 inhibitors despite current guidelines that recommend newer P2Y12 inhibitors, including ticagrelor and prasugrel, in patients

Table 1. Medications prescribed to patients with AMI at discharge between 2005 and 2016

Variable	AMI (n = 54,402)		STEMI (n = 29,222)		NSTEMI (n = 25,180)		*p* value[a]
	Total no.	No. (%)	Total no.	No. (%)	Total no.	No. (%)	
Aspirin	49,541	48,166 (97.2)	26,440	25,863 (97.8)	23,101	22,303 (96.5)	< 0.001
P2Y12 inhibitor	49,249	46,039 (93.5)	26,353	25,270 (95.9)	22,896	20,769 (90.7)	< 0.001
Clopidogrel	46,039	40,986 (89.0)	25,270	22,487 (89.0)	20,769	18,499 (89.1)	0.780
Ticagrelor	46,039	3,622 (7.9)	25,270	1,955 (7.7)	20,769	1,667 (8.0)	0.250
Prasugrel	46,039	1,431 (3.1)	25,270	828 (3.3)	20,769	603 (2.9)	0.022
Statin	49,328	40,469(82.0)	26,321	21,807 (82.9)	23,007	18,662 (81.1)	< 0.001
RAS blocker	45,685	39,012 (85.4)	24,479	21,161 (86.4)	22,985	20,603 (89.6)	< 0.001
ACE inhibitor	48,951	26,775 (54.7)	26,162	15,430 (59.0)	22,789	11,345 (49.8)	< 0.001
ARB	48,628	12,647 (26.0)	25,911	5,949 (23.0)	22,717	6,698 (29.5)	< 0.001
Beta-blocker	49,273	38,535 (78.2)	26,316	20,988 (79.8)	22,957	17,547 (76.4)	< 0.001
Cilostazol	48,613	10,246 (21.1)	25,932	6,013 (23.2)	22,681	4,233 (18.7)	< 0.001
Calcium channel blocker	48,368	4,950 (10.2)	25,755	1,694 (6·6)	22,613	3,256 (14·4)	< 0.001
Nitrate	31,805	14,036 (44.1)	18,018	7,740 (43·0)	13,787	6,296 (45·7)	< 0.001
Nicorandil	31,658	6,805 (21.5)	17,956	3,981 (22.2)	13,702	2,824 (20.6)	0.001
Spirolactone	31,285	2,469 (7.9)	17,749	1,427 (8.0)	13,536	1,042 (7.7)	0.266
Diuretics	31,662	6,764 (21.4)	17,952	3,640 (20.3)	13,710	3,124 (22.8)	< 0.001

AMI, acute myocardial infarction; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; RAS, renin-angiotensin system; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.
[a]STEMI vs. NSTEMI.

with AMI who undergo PCI [25,26,45]. A higher rate of clopidogrel use can be explained by previous KAMIR studies regarding the comparison between clopidogrel and the newer P2Y12 inhibitors. Three KAMIR studies demonstrated that ticagrelor and prasugrel are associated with significantly higher rates of bleeding complications without reducing ischemic events compared with clopidogrel in patients with AMI [46-48]. Regarding the comparison of ticagrelor and prasugrel, another KAMIR study showed that both of these P2Y12 inhibitors showed similar efficacy and safety in patients with STEMI [49]. Therefore, a high bleeding tendency should be considered when prescribing antiplatelet therapy in Korean AMI patients.

TRENDS IN CLINICAL OUTCOMES

The in-hospital mortality rates are shown in Fig. 9. Between November 2005 and August 2018, the in-hospital mortality rate in patients with AMI decreased gradually from 4.8% in 2005 to 3.8% in 2018. Although this tendency was observed in both the STEMI and NSTEMI groups, it was higher in the former. Furthermore, the rate of in-hospital mortality in STEMI patients was greater than 4.0% throughout the study period. The 1-year clinical outcomes were analyzed between 2005 and 2015 (Fig. 10). The 1-year rate of MACEs, including all-cause mortality, MI, and any revascularization, decreased from 20.4%, 20.5%, and 20.1% in 2005 to 12.3%, 13.4%, and 11.4% in 2015, respectively (Fig. 10A). The 1-year mortality rate also decreased from 2005 to 2015 in both STEMI and NSTEMI patients with AMI (Fig. 10B). The 1-year clinical outcomes improved and were relatively lower than those in Western registries [4]. Mortality is influenced by many factors in AMI patients, including age, comorbidities, and invasive treatment strategies. Higher rates of PCI and primary PCI were observed in KAMIR data relative to Western registries [4]. A high rate of invasive treatment strategies may have led to differences between the KAMIR and Western registries. Moreover, differences in long-term outcomes

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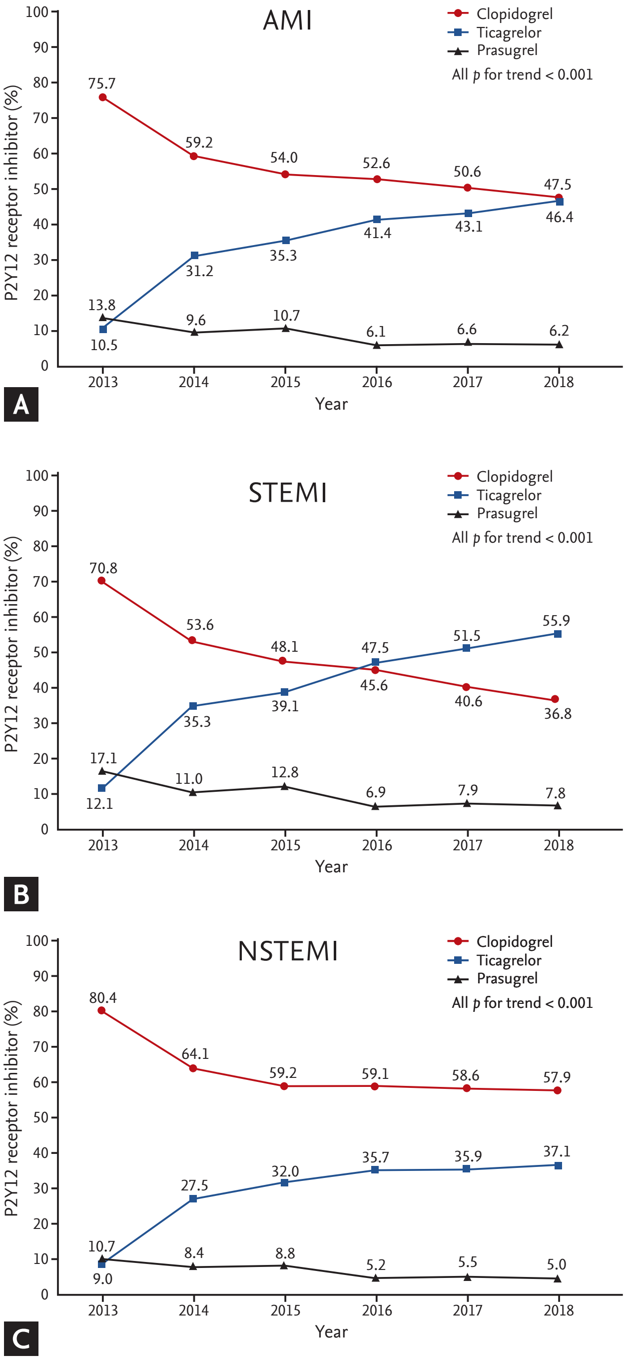


Figure 8. Changing trends in P2Y12 inhibitors prescribed to patients with (A) acute myocardial infarction (AMI), (B) ST-elevation myocardial infarction (STEMI), and (C) non-ST-elevation myocardial infarction (NSTEMI).

from Western registries led to a new risk score, the KAMIR score, which is more suitable for predicting 1-year mortality in Korean patients with AMI than the Thrombolysis in Myocardial Infarction (TIMI) and Global Reg-

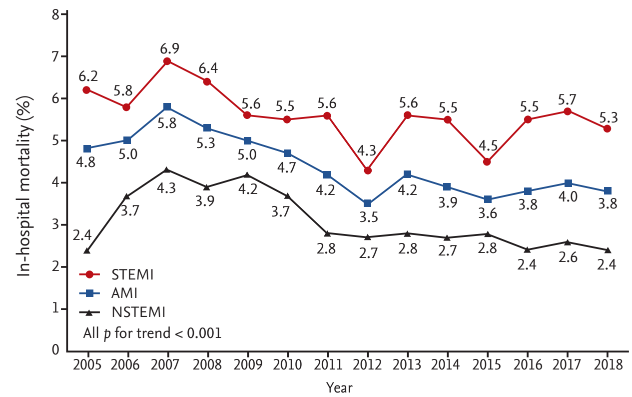
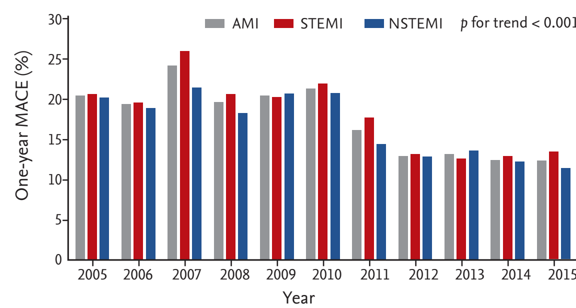
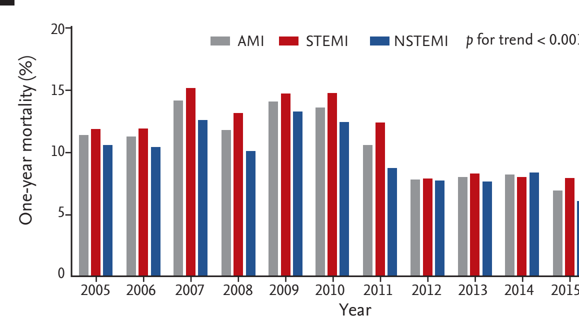


Figure 9. Temporal trends in the in-hospital mortality rate between 2005 and 2018. STEMI, ST-elevation myocardial infarction; AMI, acute myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction.



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
AMI, %	20.4	19.3	24.1	19.6	20.4	21.3	16.1	12.9	13.1	12.4	12.3
STEMI, %	20.5	19.5	25.9	20.5	20.3	21.8	17.7	13.1	12.6	12.8	13.4
NSTEMI, %	20.1	18.9	21.4	18.2	20.6	20.7	14.4	12.8	13.5	12.1	11.4

A



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
AMI, %	11.4	11.3	14.2	11.8	14.1	13.6	10.6	7.8	8.0	8.8	6.9
STEMI, %	11.9	11.9	15.2	13.2	14.7	14.8	12.4	7.9	8.3	8.8	7.9
NSTEMI, %	10.6	10.4	12.6	10.1	13.3	12.4	8.7	7.7	7.6	8.4	6.1

B

Figure 10. Temporal trends in (A) 1-year major adverse cardiac event (MACE) and (B) mortality rates from 2005 to 2015. AMI, acute myocardial infarction; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction.

istry of Acute Coronary Events (GRACE) scores [50,51].

CONCLUSIONS

Using KAMIR data, we observed several trends in Korean patients with AMI. The rate of STEMI decreased, consistent with Western registries. The mean age and proportion of males also gradually increased in Korean patients with AMI. The prevalences of risk factors, including hypertension, DM, and dyslipidemia, increased, but that of dyslipidemia was lower compared with other Western registries. However, the different patterns of dyslipidemia, low HDL and high triglyceride levels, should be considered in Korean patients with AMI. The D2B time has remained at approximately 60 minutes, but the S2B time has gradually decreased. Although radial artery access has markedly increased in Korean patients with STEMI in recent years, it still remains below 50%. Regarding STEMI patients with MVD in Korea, simultaneous or staged CR should be considered, as in the current guidelines. In terms of interventional strategies, the rate of PCI has been over 90% since 2010, and the use of DES implantation in patients with STEMI is notably higher (over 90% since 2006). Clopidogrel has still high proportion in P2Y12 inhibitors in patients with AMI who undergo PCI, despite current guidelines recommend newer P2Y12 inhibitors. In-hospital mortality has decreased among both STEMI and NSTEMI patients with AMI but is still high in STEMI patients (over 4.0%). The 1-year rates of clinical outcomes, including MACEs and mortality, decreased between 2005 and 2015. KAMIR data can provide physicians with useful information regarding AMI in Korea.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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