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Differences in the Korea Acute Myocardial Infarction Registry Compared with Western Registries

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

ABSTRACT

The Korea Acute Myocardial Infarction Registry (KAMIR) is the first nationwide registry that reflects current therapeutic approaches and acute myocardial infarction (AMI) management in Korea. The results of the KAMIR demonstrated different risk factors and responses to medical and interventional treatments. The results indicated that the incidence of ST-elevation myocardial infarction (STEMI) was relatively high, and that the prevalence of dyslipidemia was relatively low with higher triglyceride and lower high-density lipoprotein cholesterol levels. Percutaneous coronary intervention (PCI) rates were high for both STEMI and non-ST-elevation myocardial infarction (NSTEMI) with higher use of drug-eluting stents (DESs). DES were effective and safe without increased risk of stent thrombosis in Korean AMI patients. Triple antiplatelet therapy, consisting of aspirin, clopidogrel, and cilostazol, was effective in preventing adverse clinical outcomes after PCI. Statin therapy was effective in Korean AMI patients, including those with very low levels of low-density lipoprotein cholesterol and those with cardiogenic shock. The KAMIR score had a greater predictive value than Thrombolysis in Myocardial Infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) scores for long-term mortality in AMI patients. Based on these results, the KAMIR will be instrumental for establishing new therapeutic strategies and effective methods for secondary prevention of AMI and guidelines for Asian patients.

Keywords: Myocardial infarction; Risk factors; Hydroxymethylglutaryl-CoA reductase inhibitors; Percutaneous coronary intervention

INTRODUCTION

Acute myocardial infarction (AMI) is a leading cause of mortality worldwide. The Korea Acute Myocardial Infarction Registry (KAMIR) is the first nationwide, multicenter data collection registry, including 55 community and teaching hospitals in Korea, with patients in all stages of AMI. Since the KAMIR was started in 2005, more than 62,000 patients have been registered, and a total of 178 papers have been published.

Author Contributions

Conceptualization: Jeong MH; Data curation: Sim DS; Formal analysis: Sim DS; Investigation: Sim DS; Methodology: Sim DS; Project administration: Jeong MH; Resources: Sim DS; Supervision: Jeong MH; Validation: Jeong MH; Writing - original draft: Sim DS; Writing - review & editing: Jeong MH.

KAMIR STUDY OUTCOMES

The KAMIR study showed that Korean AMI patients had different characteristics compared with Western AMI registries with respect to etiologies, risk factors, drug responses, and treatment strategies.[1-6] These findings have provided important information to predict prognosis as well as better diagnostic and treatment tools to improve the quality of care, tailored for Korean AMI patients. The KAMIR study was limited, however, because it provided data of up to 1-year follow-up, although this has been improved by increased quality and database registry utility.

TEMPORAL TRENDS IN AMI INCIDENCE AND OUTCOMES

The incidence of ST-elevation myocardial infarction (STEMI) decreased from 60.5% in 2006 to 48.1% in 2013, while the incidence of non-ST-elevation myocardial infarction (NSTEMI) increased from 39.5% in 2006 to 51.9% in 2013. The ratio of STEMI/NSTEMI in Korea changed in 2012 when a higher incidence of NSTEMI than STEMI was reported (**Figure 1A**). In-hospital mortality in patients with STEMI remained relatively constant, but in-hospital

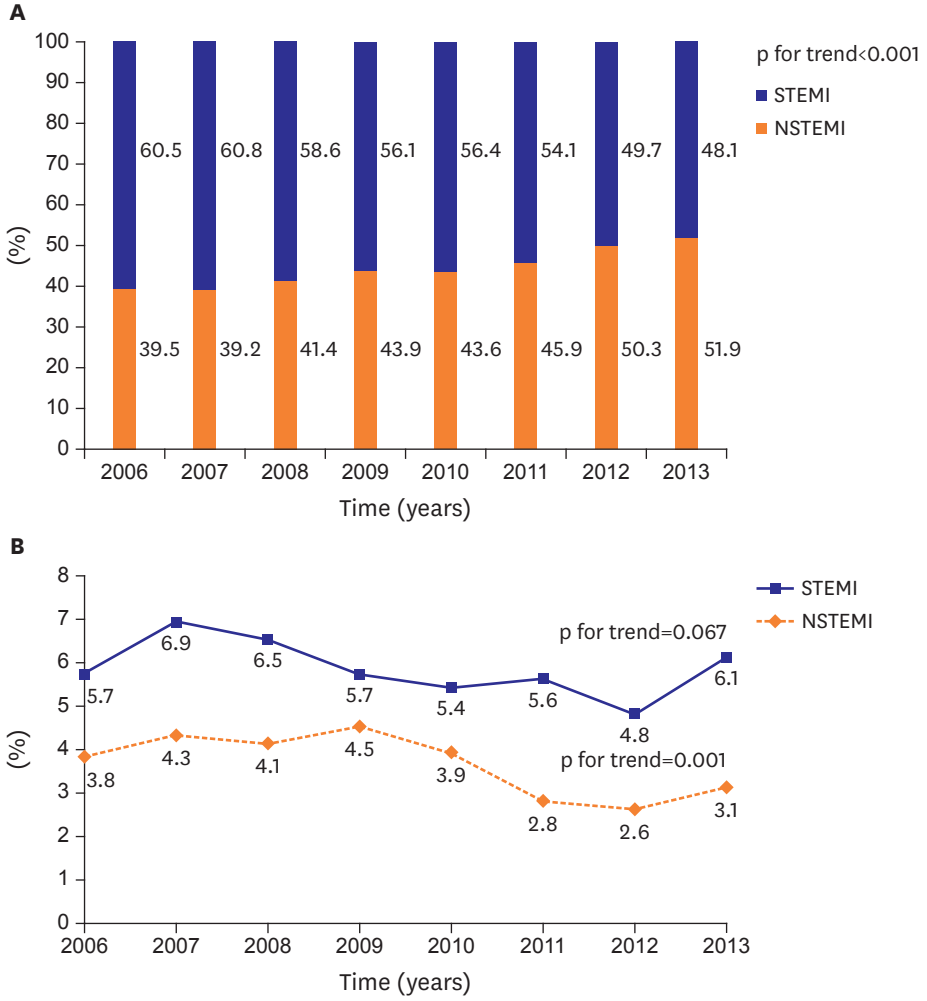

Figure 1. (A) Annual incidence rates of STEMI and NSTEMI from 2006 to 2013. (B) Annual in-hospital mortality rates of STEMI and NSTEMI from 2006 to 2013.
NSTEMI = non-ST-elevation myocardial infarction; STEMI = ST-elevation myocardial infarction.

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mortality in patients with NSTEMI decreased (**Figure 1B**).[1] Compared with Western registries, the proportion of STEMI was relatively high in the KAMIR (**Table 1**).

RISK FACTORS

Risk factors of Korean AMI patients are different from those of Western patients (**Table 1**). The prevalence of hypertension, diabetes mellitus, and dyslipidemia has increased, but the prevalence of smoking and obesity has decreased. Previously, smoking was the most common risk factor in Korean AMI patients. The prevalence of smoking decreased from 62.0% in 2006 to 44.6% in 2013 in STEMI patients and from 51.1% in 2006 to 34.5% in NSTEMI patients.[1] Smoking in female patients is a predictor of major adverse cardiac events (MACEs).[7]

The prevalence of dyslipidemia is relatively low and the pattern of dyslipidemia differs in Korean patients. Korean patients have a lower incidence of high low-density lipoprotein cholesterol (LDL-C) levels and higher incidence of high triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) levels. About half of the patients have low HDL-C, and one-quarter of the patients have high TG. Statin therapy was not effective for preventing clinical events, based on 2-year follow-up in this patient population, and a TG/HDL-C ratio >3.35 was associated with overall increased risk of MACE.[8] These findings suggest different benefits of statin therapy in Korean patients.[5] Low HDL-C after overnight fasting is associated with in-hospital mortality in STEMI patients, but not in NSTEMI patients.[9] MACE was associated with more than 50% reduction of LDL-C from baseline, but not with targeting an LDL-C <70 mg/dL in Korean patients.[10]

Table 1. Clinical characteristics of patients with AMI in Korea compared with other registries

Registry Title	KAMIR	GRACE	SCAAR	NRMI	MINAP	SWEDEHEART/RIKS-HIA
Region	Korea	Europe, America	Sweden	US	UK	Sweden
Time period	Nov 2005–Oct 2010	2004–2007	Jan 2003–Dec 2004	1994–2006	Jan 2004–Dec 2010	Jan 2004–Dec 2010
Sample size	27,852	28,449	19,771	542,008	391,077	119,786
Follow-up rate (%)	NA	89.8	95.2	NA	NA	NA
Follow-up duration	231.6 days	2 years	3 years	NA	NA	NA
Demographics						
Mean or median age (years)	63.2	65.0	65.7	64.0	69.5	71.2
Male (%)	75.0	68.4	72.0	59.0	65.2	63.7
Comorbidities (%)						
Hypertension	45.9	64.7	44.5	52.3	47.3	45.2
DM	24.6	25.2	18.1	22.4	17.6	22.7
Dyslipidemia	9.5	53.0	NA	28.0	NA	NA
Smoking	62.8	59.8	20.4	31.3	29.5	23.3
Previous MI	11.1	30.3	37.4	NA	18.3	22.4
Family history of CAD	7.9	NA	NA	28.0	NA	NA
CVA	5.6	NA	6.0	NA	8.5	10.1
HF	1.1	8.8	7.4	NA	5.3	9.7
STEMI (%)	56.6	35.9	22.6	41.8	40.3	32.1
Multivessel disease (%)	52.7	NA	50.0	NA	NA	NA
DES (%)	91.1	NA	30.5	NA	NA	NA
PCI success rate (%)	99.0	NA	NA	NA	NA	NA

Rate of follow-up at 6 months. Data modified from Table 1 of Kim et al.[2]
AMI = acute myocardial infarction; CAD = coronary artery disease; DES = drug-eluting stent; DM = diabetes mellitus; HF = heart failure; KAMIR = Korea Acute Myocardial Infarction Registry; GRACE = Global Registry of Acute Coronary Events; SCAAR = Swedish Coronary Angiography and Angioplasty Registry; MI = myocardial infarction; MINAP = Myocardial Ischemia National Audit Project; NA = not available; NRMI = National Registry of Myocardial Infarction; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction; SWEDEHEART/RIKS-HIA = Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies/Register of Information and Knowledge about Swedish Heart Intensive Care Admissions.

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The prevalence of hypertension was similar in both populations, but the mean systolic blood pressure at admission was lower.[2] Korean AMI patients were more likely to exhibit a J-curve phenomenon: low blood pressure (<100/60 mmHg) and high blood pressure (>170/100 mmHg) were associated with MACE.[11]

The prevalence of diabetes is higher in Korean patients.[2] Hypoglycemia (<70 mg/dL) and hyperglycemia (≥260 mg/dL) at admission were associated with higher 1-month mortality rates in both diabetic and non-diabetic patients. Hypoglycemia in poorly controlled type 2 diabetic patients predicted 1-month mortality in AMI patients.[12] According to the Geriatric Nutritional Risk Index, undernutrition at admission was present in 18% of patients[13] and was associated with post-myocardial infarction (MI) complications and in-hospital mortality.

INTERVENTIONAL STRATEGIES

The KAMIR evaluated various interventional strategies and percutaneous coronary intervention (PCI) for complex coronary lesions in AMI setting. Primary PCI is the preferred reperfusion strategy in Korean STEMI patients. About 91% of patients with STEMI that presented <12 hours from symptom onset were treated by primary PCI, and the median door-to-balloon time in STEMI patients was 78 minutes.[14] Shorter door-to-balloon time was not significantly correlated with 1-month mortality, although total ischemic time <180 minutes was an independent predictor of 1-month survival.[15] Shortening symptom-to-door time might be more important than reducing door-to-balloon time in Korea, which indicates the importance of early pharmacologic therapy. For patients undergoing successful thrombolytic therapy, early elective PCI within 48 hours was associated with more favorable clinical outcomes than patients that later underwent PCI.[16] The comparison between pharmacoinvasive strategy (defined as thrombolytic therapy followed by PCI) and primary PCI showed that the pharmacoinvasive group had shorter time to reperfusion therapy, a higher rate of pre-PCI Thrombolysis in Myocardial Infarction (TIMI) grade 3, and similar 1-year survival rates. Equipoise between pharmacoinvasive strategy and primary PCI occurred when PCI-related delay was ≈100 minutes.[14] These findings were consistent with observations from Western studies.[17][18] The clinical benefit of reperfusion is controversial for stable patients with STEMI that present >24 hours after symptom onset.[19][20] In the KAMIR, stable early latecomers of STEMI that presented 12 to 72 hours after symptom onset had lower mortality and a lower incidence of death or MI at 12 months when they received PCI.[21]

For patients with non-ST-elevation acute coronary syndrome (ACS), immediate invasive approach has diagnostic benefits, facilitates treatment logistics, and can prevent further complications.[22] The KAMIR demonstrated that an immediate invasive approach was not associated with a statistically significant decrease of the 12-month rates of death, MI, death/MI, or MACE, but was associated with lower major bleeding risk and shorter hospital stay.[23] NSTEMI with chronic kidney disease (CKD) management indicated that a deferred invasive strategy was associated with higher 1-year death/MI-free survival than early invasive treatment.[24] In octogenarian patients with NSTEMI, MACE-free survival was similar between early and delayed interventions at 1-year.[25]

In AMI patients with unprotected left main coronary artery (LMCA) stenosis undergoing PCI from the KAMIR, culprit LMCA was associated with higher in-hospital mortality than non-culprit LMCA (16.0% vs. 8.9%; p=0.008), with similar clinical outcomes at 12-month follow-up.[26] Compared to coronary artery bypass graft surgery, PCI using drug-eluting stents

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(DESs) was more frequently performed for LMCA, with similar early and 12-month clinical outcomes. Multi-vessel PCI in NSTEMI patients with multi-vessel coronary artery disease (CAD) was associated with higher 1-year MACE-free survival and death/MI-free survival rates compared with culprit-only PCI.[27] Staged PCI in STEMI patients with multi-vessel disease compared to ad hoc or culprit-only PCI was associated with lower rates of cardiac death and MACE at 3 years, without an increase of repeat PCI.[28]

There are several unique characteristics of revascularization strategies for Korean AMI patients. First, PCI was performed in 96.7% and 82.7% of patients with STEMI and NSTEMI, respectively, and the procedural success rates were 99.4% and 99.5%, which is relatively higher than in Western countries.[2] Second, the DES penetration rate in AMI patients was >90% (97% currently) in Korea. Several observational studies that evaluated the efficacy and safety of DES in Korean AMI patients have been published and have indicated that the event rates were lower after DES implantation compared to bare metal stent (BMS), suggesting that DES could safely and effectively treat AMI patients without increasing the risks of mortality, MI, and stent thrombosis.[6] DES in large vessels (≥3.5 mm) in AMI was associated with lower repeat revascularization compared to BMS, without compromising the overall safety over the course of 1-year follow-up.[29] Zotarolimus- and everoliumus-eluting stents showed comparable clinical outcomes in STEMI patients with CKD undergoing primary PCI.[30] In octogenarian AMI patients, DES was associated with lower stent thrombosis rates compared to BMS, with similar target vessel failure-free survival at 1-year.[31] In patients with metabolic syndrome and AMI, Resolute® zotarolimus-eluting stents and everolimus-eluting stents (Medtronic, Santa Rosa, CA, USA) showed comparable outcomes in target lesion failure and MACE at 1-year.[32] In addition, intravascular ultrasound (IVUS)-guided PCI was performed in approximately 20% of AMI patients in Korea, but IVUS guidance was not an independent predictor of 12-month all-cause death in AMI patients that underwent PCI.[33]

Clinical benefits of manual thrombus aspiration (TA) during primary PCI remain controversial.[34-36] TA during primary PCI in STEMI patients in the KAMIR did not reduce MACE, but subgroup analysis indicated that administration of the glycoprotein IIb/IIIa inhibitor and culprit lesions in the left anterior descending artery were associated with lower MACE.[37] More recently, the benefit of manual TA during primary PCI in relation to total ischemic time was evaluated in 5,641 patients with STEMI (<12 hours) from the KAMIR who underwent primary PCI. After propensity matching (n=1,162 for each group), there were no differences in the 12-month outcomes between TA and PCI only. The effect of TA on 12-month outcome showed a U-shaped relationship, indicating that the impact of TA might become clinically relevant with longer total ischemic time.[38]

MEDICAL TREATMENT

Dual antiplatelet therapy with aspirin and a P2Y12 receptor blocker is recommended for all patients undergoing PCI with stenting. To prevent ischemic events after PCI, the safety and efficacy of triple antiplatelet therapy (cilostazol for at least 1-month, adding to aspirin and P2Y12 receptor blocker) was evaluated in patients with STEMI that were treated with primary PCI using DES.[39] At 8 months, the triple antiplatelet therapy group had significantly lower rates of cardiac death (2.0% vs. 3.2%; odds ratio [OR], 0.52; 95% confidence interval [CI], 0.32–0.84; p=0.007) and MACE (7.6% vs. 9.3%; OR, 0.74; 95% CI, 0.58–0.95; p=0.019), without an increased risk of major bleeding.[39]

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The safety and efficacy profile of some antiplatelet agents can differ depending on the patient's ethnicity. A small randomized study showed that aspirin plus prasugrel of both standard and low maintenance doses (10 mg and 5 mg) in STEMI patients was associated with lower levels of platelet reactivity units compared with triple anti-platelet therapy (aspirin, clopidogrel, and cilostazol), suggesting that, contrary to Western patients, low dose prasugrel might be effective in Korean AMI patients.[40] In addition, the KAMIR analysis showed that the usual dose of ticagrelor did not reduce the incidence of MACE, but increased TIMI major and minor bleeding risks, which indicates that a lower dose of ticagrelor might be necessary in Korean AMI patients.[3]

Oral beta-blockers are recommended for all patients without contraindications who have suffered STEMI.[41] The benefit of a long-term beta-blockade is not well established in patients with preserved left ventricular systolic function. The effect of beta-blocker therapy on clinical outcomes in STEMI patients that underwent primary PCI was investigated in 20,344 patients in the KAMIR. After propensity-score matching, beta-blocker use was associated with a lower rate of all-cause death (2.8% vs. 4.1%; hazard ratio [HR], 0.46; 95% CI, 0.27–0.78; p=0.004).[42]

Angiotensin receptor blockers (ARBs) could be used as an alternative to angiotensin-converting enzyme inhibitors (ACEIs) in STEMI patients with left ventricular systolic dysfunction.[43][44] However, the benefit of ARB is uncertain in patients with STEMI with preserved left ventricular systolic function. The effect of ARB therapy on clinical outcomes was evaluated in 6,698 patients with STEMI in the KAMIR who underwent primary PCI and had preserved left ventricular systolic function. After propensity score matching, patients receiving ARB had a lower rate of cardiac death or MI compared to the no renin-angiotensin system blocker group (1.7% vs. 3.1%; HR, 0.35; 95% CI, 0.14–0.90; p=0.030).[4] Treatment with insurmountable ARB such as valsartan, candersartan, irbesartan, telmisartan, and olmesartan was associated with lower MACE at 1-year compared to treatment with surmountable ARB such as losartan and eprosartan in Korean AMI patients.[45] Use of a renin-angiotensin system inhibitor in STEMI patients undergoing late PCI reduced the 1-year MACE, even in low-risk patients with relatively preserved left ventricular systolic function.[46]

Intensive statin therapy should be initiated as early as possible in all patients with ACS.[47][48] Statin therapy in AMI patients with LDL-C level <70 mg/dL (n=1,054) in the KAMIR significantly reduced the risks of cardiac death (HR, 0.47; 95% CI, 0.23–0.93; p=0.031) and MACE (HR, 0.56; 95% CI, 0.34–0.89; p=0.015).[49] Early statin therapy in statin-naïve AMI patients with cardiogenic shock who underwent revascularization was associated with lower in-hospital mortality and MACE at 1-year.[50] Statin therapy for spasm-induced AMI patients improved MACE-free survival at 1-year.[51] Statin plus ezetimibe did not significantly reduce MACE compared with high-intensity statin in Korea AMI patients.[52] On subgroup analysis, however, statin plus ezetimibe was effective in high-risk patients, such as those with diabetes mellitus, old age, and low left ventricular ejection fraction (LVEF).

RISK ASSESSMENT

Risk assessment scores that were specific for Korean AMI patient were developed from the KAMIR. The KAMIR score for NSTEMI consisted of the TIMI risk index, Killip class, and serum creatinine,[53] and the KAMIR hospital discharge score for AMI was composed of age, Killip class, PCI use, serum creatinine, LVEF <40% and admission hyperglycemia >180 mg/

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dL.[54] Both scores showed better predictive values than previous scoring systems established in Western countries, including TIMI or Global Registry of Acute Coronary Events (GRACE) scores (**Figure 2**). In addition, other risk scoring systems, including CHA2DS2-VASC score, high sensitive C-reactive protein, simple age, creatinine, and ejection fraction (ACEF) were validated in the KAMIR population.[55-57] About 50% of STEMI patients had one or more non-infarct-related artery (IRA) lesions, and the presence of IRA stenosis was associated with a significant increase in 30-day mortality in STEMI patients (3.6% vs. 2.5%; risk difference, 1.1%; 95% CI, 0.6%–1.7%; p<0.001).[58]

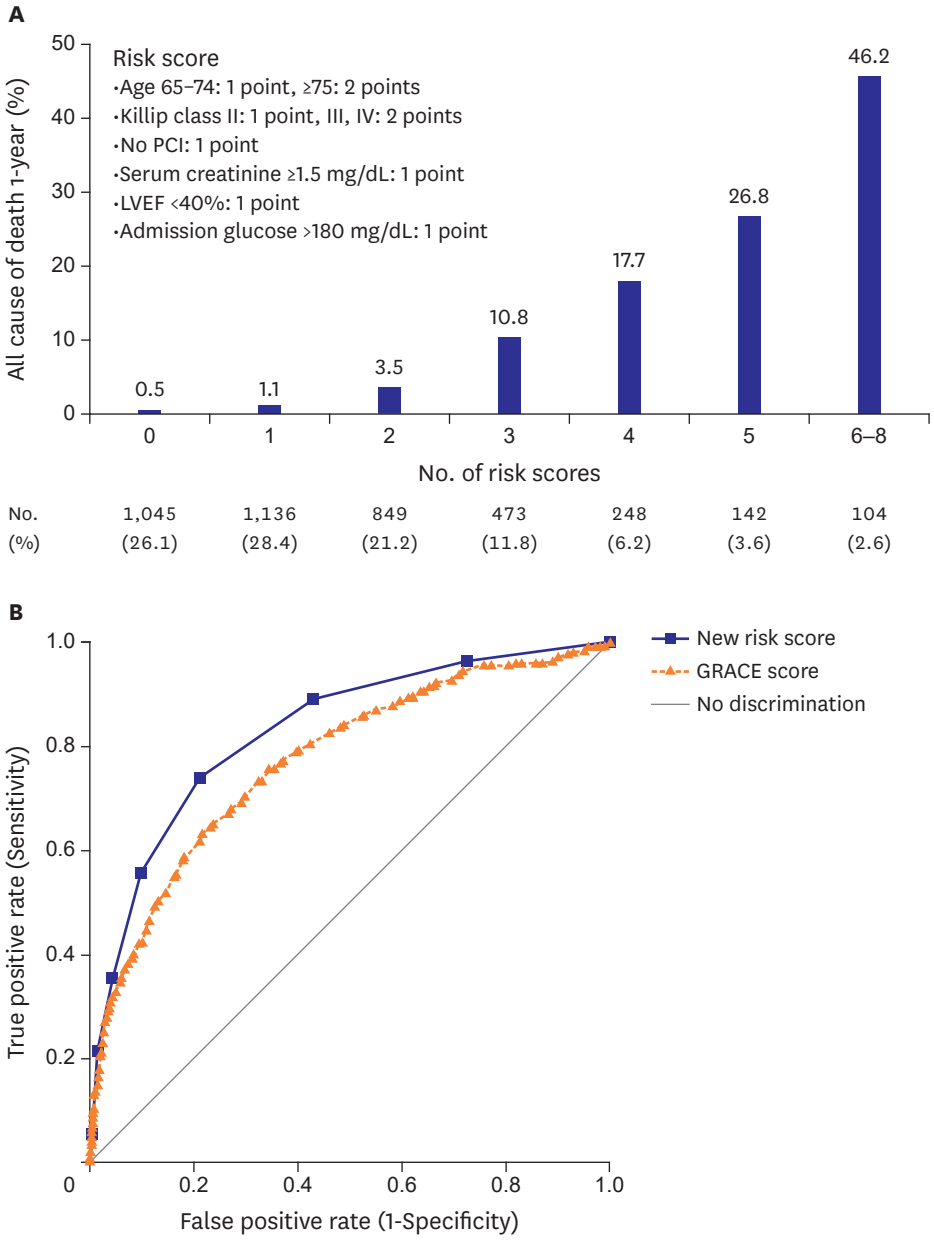

Figure 2. (A) A new risk score for predicting 1-year death from AMI. (B) Receiver operator characteristic curves for 1-year mortality in patients with AMI.
AMI = acute myocardial infarction; GRACE = Global Registry of Acute Coronary Events; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.

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CONCLUSION

AMI is a major challenge for health care systems. The KAMIR has allowed prospective follow-up to assess the incidence and characteristics of AMI and to perform comprehensive analyses of AMI in the Korean population. The feedback from this registry will help with continuous tracking, outcome measurement, and adherence to evidence-based care processes for AMI. The KAMIR has provided and will provide vital contributions to the assessment and improvement of treatment outcomes in patients with AMI. Ultimately, the KAMIR study will be instrumental for establishing Asian AMI guidelines.

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