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ORIGINAL RESEARCH

Incidence, Relevant Patient Factors, and Clinical Outcomes of the Misdiagnosis of ST-Segment–Elevation Myocardial Infarction: Results From the Korea Acute Myocardial Infarction Registry

Kyung Hoon Cho, MD, PhD; Min-Ho Shin, MD, PhD; Min Chul Kim, MD, PhD; Doo Sun Sim, MD, PhD; Young Joon Hong, MD, PhD; Ju Han Kim, MD, PhD; Youngkeun Ahn, MD, PhD; Hyo-Soo Kim, MD, PhD; Seung-Ho Hur, MD, PhD; Sang Rok Lee, MD, PhD; Jin-Yong Hwang, MD, PhD; Seok Kyu Oh, MD, PhD; Kwang Soo Cha, MD, PhD; Myung Ho Jeong, MD, PhD; on behalf of the Korea Acute Myocardial Infarction Registry (KAMIR) Investigators*

BACKGROUND: Data on the incidence, relevant patient factors, and clinical outcomes of the misdiagnosis of ST-segment–elevation myocardial infarction (STEMI) in the modern era of percutaneous coronary intervention are limited.

METHODS AND RESULTS: Data from KAMIR (Korea Acute Myocardial Infarction Registry) between November 2011 and June 2020 were analyzed. Out of 28 470 patients with acute myocardial infarction, 11 796 were eventually diagnosed with STEMI following a coronary angiogram. They were classified into 2 groups: patients with an initial working diagnosis of STEMI before starting the initial treatment and patients with an initial working diagnosis of non-STEMI (misdiagnosed group). Out of 11 796 patients with a final diagnosis of STEMI, 165 (1.4%) were misdiagnosed. The door-to-angiography time in the misdiagnosed group was 5 times longer than that in the timely diagnosed group (median 220 [interquartile range {IQR}, 66–1177] versus 43 [IQR, 31–58] minutes; $P<0.001$). In a multivariable adjustments model, patients with a history of heart failure, atypical chest pain, anemia, or symptom-to-door time ≥4 hours had significantly higher odds, whereas those with systolic blood pressure <100 mm Hg or anterior ST elevation or left bundle-branch block on ECG had lower odds of STEMI misdiagnosis. For patients with culprit lesions in the left anterior descending artery (n=5838), the adjusted 1-year mortality risk for STEMI misdiagnosis was 1.84 (95% CI, 1.01–3.38).

CONCLUSIONS: Misdiagnosis of STEMI is not rare and is associated with a significant delay in coronary angiography, resulting in increased 1-year mortality for patients with culprit lesions in the left anterior descending artery.

Key Words: coronary angiography ■ diagnostic errors ■ incidence ■ percutaneous coronary intervention ■ registries ■ ST-segment–elevation myocardial infarction

In spite of considerable advances in cardiovascular care, there still have been largely missed opportunities in the prevention and treatment of cardiovascular disease.[1] Rapid myocardial revascularization in patients with ST-segment–elevation myocardial infarction (STEMI) who present within 48 hours of symptom onset is critical

Correspondence to: Myung Ho Jeong, MD, PhD, Principal Investigator of Korea Acute Myocardial Infarction Registry, Department of Cardiology, Chonnam National University Medical School, Jebong-ro 42, Dong-gu, Gwangju, 61469, South Korea. Email: myungho@chollian.net

*A complete list of the Korea Acute Myocardial Infarction Registry (KAMIR) Investigators can be found in the Supplemental Material.

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CLINICAL PERSPECTIVE

What Is New?

- In a nationwide Korean registry of acute myocardial infarction, the misdiagnosis of ST-segment–elevation myocardial infarction occurred in 1.4% of the patients and was independently associated with multiple patient factors.
- Misdiagnosis of ST-segment–elevation myocardial infarction was associated with a 5-times increase in time to coronary angiography, resulting in increased 1-year mortality for patients with culprit lesions in the left anterior descending artery.

What Are the Clinical Implications?

- Additional efforts, including reinforcement of the initial working diagnosis process, are required for the timely diagnosis of ST-segment–elevation myocardial infarction in real-world practice, especially in patients with suspected acute left anterior descending artery occlusion.

Nonstandard Abbreviations and Acronyms

KAMIR	Korea Acute Myocardial Infarction Registry
TIMI	Thrombolysis In Myocardial Infarction

for increasing the chances and extent of myocardial salvage and better clinical outcomes.[2–5] The initial diagnosis of STEMI based on symptoms and signs, including an ECG, is critical to achieving timely myocardial revascularization.[6] However, it was reported that ≈10% to 20% of patients with STEMI have no chest pain or atypical symptoms like dyspnea at presentation.[7,8] Furthermore, there are variations in interpreting potential STEMI ECGs among physicians.[9] In addition, diverse health care professionals, including primary care physicians, residents, emergency medical physicians, and cardiologists, alone or collaboratively, make the initial working diagnosis in patients presenting with acute coronary syndromes. Failure to timely diagnose acute myocardial infarction (AMI), including STEMI (missed diagnosis), is not rare and leads to delay in the initiation of appropriate treatment or failure of reperfusion therapy.[10–12] However, there have been few investigations on why STEMI is not diagnosed timely and the clinical consequences of delayed diagnosis in the contemporary percutaneous coronary intervention (PCI) era. Understanding these issues may be helpful in optimizing care delivery and improving the clinical outcomes of STEMI.

In the present study, we sought to investigate the incidence, relevant patient factors, and clinical outcomes of the misdiagnosis of STEMI as non–ST-segment–elevation myocardial infarction (NSTEMI) from a nationwide, prospective Korean registry of AMI.

METHODS

Data Sources and Participants

The anonymized data that support the results of this study can be made available upon reasonable request. The patients were recruited from KAMIR (Korea Acute Myocardial Infarction Registry). KAMIR is a nationwide prospective multicenter cohort registry that reflects the real-world practice and outcomes in Korean patients with AMI, with support from the Korean Circulation Society since November 2005.[13] We analyzed patients enrolled in KAMIR involving 31 teaching hospitals between November 2011 and June 2020. Participating institutions, investigators, and steering committees are listed in Data S1. In regard to the inclusion criterion, patients diagnosed with AMI aged ≥18 years based on the universal definition were included.[14] The exclusion criteria included (1) patients with in-hospital AMI related to other procedures or treatments (eg, surgery) and (2) those who refused to provide informed consent. Data including outcomes were collected by trained clinical research coordinators using a web-based case report form and a formal audit process. Of 28 470 patients diagnosed with AMI, 12 727 were finally diagnosed with STEMI after coronary angiography (Figure 1). The completeness of follow-up at 1 year was 93.8% (26 718/28 470). Patients who had received thrombolysis before presenting to the hospital or those who presented within ≥48 hours of symptom onset were excluded. Consequently, we analyzed 11 796 patients (median age, 62.0 years; interquartile range [IQR], 53.0–72.0; men, 79.9%) who were ultimately diagnosed with STEMI after a coronary angiogram. They were divided into 2 groups: 11 631 patients who were correctly diagnosed with STEMI before the initial treatment strategy was established (timely diagnosed group) and 165 patients who had an initial working diagnosis of NSTEMI (misdiagnosed group). The present study was conducted in accordance with the Declaration of Helsinki. The ethics committee of each participating center approved the study protocols (approval numbers: CNUH–2011–172 and CNUH–2016–075). Written informed consent was obtained from all participants.

Outcomes and Definition

The primary outcome was death from any cause at 1 year, whereas secondary outcomes included successful PCI, in-hospital mortality, cardiac death, noncardiac death, nonfatal myocardial infarction, repeat

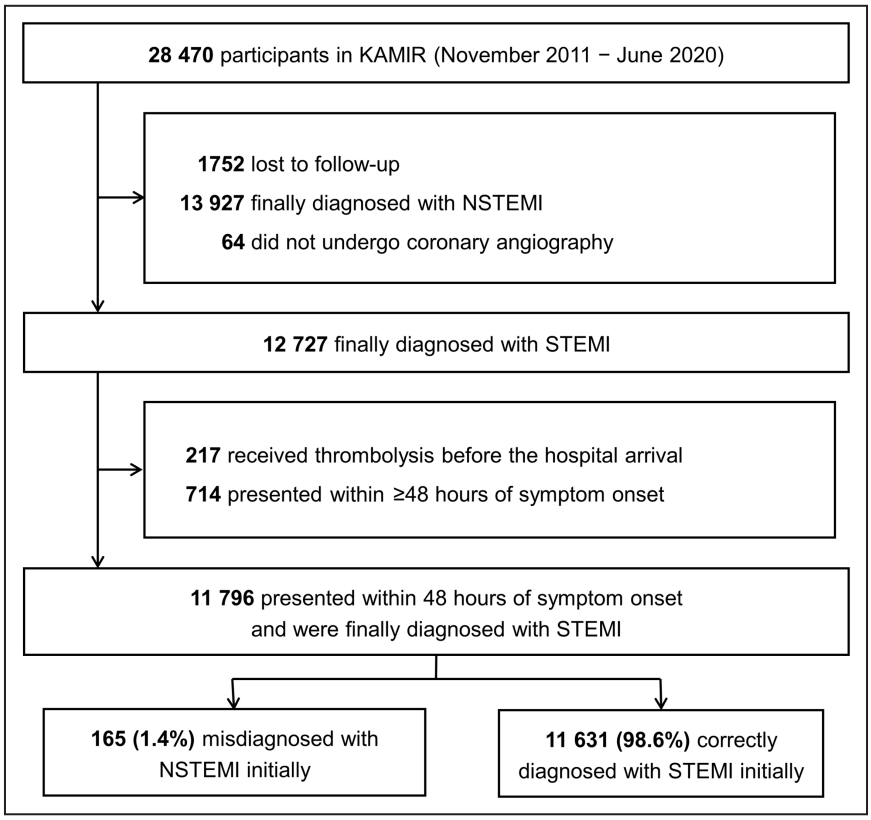

Figure 1. Study flow diagram.
The study population was from KAMIR. KAMIR indicates Korea Acute Myocardial Infarction Registry; NSTEMI, non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.

PCI, coronary artery bypass grafting, and nonfatal stroke at 1 year. KAMIR included variables of both the initial working diagnosis and the final diagnosis. The initial working diagnosis of STEMI was based on a new ST-segment elevation ≥0.1 mV in at least 2 contiguous leads (≥0.2 mV in V2–V3 leads) or a new left bundle-branch block on an ECG. The final diagnosis was made using the universal definition of myocardial infarction and electrocardiographic criteria of STEMI.[14] Misdiagnosis of STEMI was defined as an initial working diagnosis with NSTEMI before the initial treatment strategy was established, followed by a final diagnosis of STEMI after coronary angiography. The final adjudication of STEMI was done after coronary angiography and before discharge by investigators at participating centers. Atypical chest pain was defined as a patient complaining of chest pain that was inconsistent with AMI in terms of quality, location, and duration.[6] Anemia was defined according to the World Health Organization's definition as a hemoglobin level of <12 g/dL for women and <13 g/dL for men. Primary PCI strategy was considered when the procedure was expected to be performed as soon as possible after the diagnosis of STEMI. Door-to-angiography time was defined as the time from the patient's arrival at the index hospital to arrival at the catheterization laboratory. Successful PCI was defined as residual stenosis of <30% with postprocedural TIMI (Thrombolysis In Myocardial Infarction) flow grade ≥2.

Statistical Analysis

Baseline clinical characteristics, laboratory findings, and procedural details are described for patients with and without a misdiagnosis of STEMI. The variables were compared between the 2 groups using the χ^2, Fisher exact, and Kruskal-Wallis tests. To identify the correlates of the misdiagnosis of STEMI, we performed a multivariable logistic regression analysis. Potential confounders among baseline variables were considered when P was <0.1 in the univariate analysis between the 2 groups, specifically age, sex, anterior ST elevation or left bundle-branch block on ECG, symptom-to-door time, atypical chest pain, systolic blood pressure, diabetes, previous heart failure, current smoker, anemia, left circumflex artery as a culprit lesion, and multivessel disease. To assess the potential effect of unmeasured confounding, E values for independent factors of the misdiagnosis were calculated.[15] The E value is defined as the minimum strength of association, on the risk ratio scale, of an unmeasured confounder to overcome the observed

association of the measured variable with the misdiagnosis. The following variables with missing values were included in the multivariable analysis: anterior ST elevation or left bundle-branch block (n=113), systolic blood pressure (n=136), diabetes (n=2), previous heart failure (n=14), current smoker (n=200), anemia (n=27), and left circumflex artery as the culprit vessel (n=239), and for the misdiagnosed group, anterior ST elevation or left bundle-branch block (n=4), systolic blood pressure (n=6), current smoker (n=3), and left circumflex artery as the culprit vessel (n=11). The primary outcome between the 2 groups was compared using the Cox proportional hazards model in all populations and specific subgroups. Tests for heterogeneities between misdiagnosis of STEMI and subgroups were performed. To identify the correlates of primary outcomes, we used the Cox time-to-event multivariable model. We considered variables with $P<0.1$ in the univariable analysis and any other baseline variables judged to be of clinical relevance as potential confounders, specifically age, sex, anterior ST elevation or left bundle-branch block on ECG, atypical chest pain, symptom-to-door time, systolic blood pressure, heart rate, Killip class, body weight, hypertension, diabetes, previous myocardial infarction or revascularization, previous heart failure, previous cerebrovascular accident, current smoker status, family history of premature coronary artery disease, anemia, creatinine clearance, left ventricular ejection fraction, and the misdiagnosis of STEMI. The following variables with missing values were included in the multivariable analysis: anterior ST elevation or left bundle-branch block (n=113), systolic blood pressure (n=136), heart rate (n=101), Killip class (n=14), body weight (n=666), hypertension (n=1), diabetes (n=2), previous heart failure (n=14), previous cerebrovascular disease (n=13), current smoker (n=200), family history of premature coronary artery disease (n=230), anemia (n=27), creatinine clearance (n=56), and left ventricular ejection fraction (n=600). The maximum rate of missing value in the present study was small (666/11796, 5.6%), supporting the good quality of the data. Missing values were replaced using the multiple imputation method. The proportionality assumption was tested with log-minus-log plots. Eigensystem analysis was used to assess multicollinearity. Kaplan-Meier plots for death from any cause over 1 year were calculated in patients with culprit lesions in the left anterior descending artery (LAD). All the analyses were conducted using R software version 4.1.0 (R Foundation for Statistical Computing).

RESULTS

Baseline Clinical and Angiographic Findings

Baseline clinical and laboratory findings according to the misdiagnosis of STEMI are presented in Table 1. Overall, 165 (1.4%) out of 11 796 patients finally diagnosed with STEMI were initially misdiagnosed as NSTEMI. The patients in the misdiagnosed group were more often women; more likely to have atypical chest pain, longer symptom-to-door time, higher systolic blood pressure, higher heart rate, and lower hemoglobin level; they were less likely to have anterior ST elevation or left bundle-branch block on ECG compared with the timely diagnosed group. Additionally, they were more likely to have a history of diabetes and heart failure. Procedural profiles and medical treatments are described in Table 2. The patients in the misdiagnosed group did not receive the primary PCI for STEMI and were more likely to have longer door-to-angiography time (median, 220 [IQR, 66–1177] versus 43 [IQR, 31–58] minutes; $P<0.001$). Furthermore, there was an increased likelihood of left circumflex artery as a culprit lesion, multivessel coronary disease, and preprocedural TIMI flow grade 3, and less likelihood of preprocedural TIMI flow grade 0. They were less likely to be treated with PCI, including stenting, and to receive optimal medical therapy such as P2Y12 inhibitors, including clopidogrel, ticagrelor, or prasugrel, β-blockers, and renin-angiotensin-aldosterone system blockers.

Relevant Patient Factors

When assessing correlates of the misdiagnosis of STEMI using multivariable logistic regression analysis, the presence of previous heart failure (odds ratio [OR], 3.04 [95% CI, 1.06–8.71]), atypical chest pain (OR, 1.84 [95% CI, 1.23–2.74]), anemia (OR, 1.64 [95% CI, 1.13–2.39]), and symptom-to-door time ≥4 hours (OR, 1.55 [95% CI, 1.12–2.138]) were positively associated with the misdiagnosis of STEMI (Figure 2 and Table S1). On the other hand, the presence of systolic blood pressure <100 mm Hg (OR, 0.28 [95% CI, 0.14–0.55]), and anterior ST elevation or left bundle-branch block on electrocardiography (OR, 0.18 [95% CI, 0.11–0.28]) were negatively associated with misdiagnosis. The E values for ORs of independent factors were at least 2.47. The goodness-of-fit for the multivariable logistic regression model, as measured by the area under the curve, was determined to be 0.76. The Hosmer-Lemeshow test resulted in a P value of 0.55, indicating that the model's calibration is not significantly different from a perfectly calibrated model.

Clinical Outcomes

Clinical outcomes were investigated for up to 1 year (median 365 days [IQR, 358–365]). The primary outcome occurred in 9.7% (16/165) of the patients in the misdiagnosed group and 7.7% (891/11631) of the patients in the timely diagnosed group (hazard ratio [HR], 1.27 [95% CI, 0.78–2.09]; log-rank $P=0.340$). There

Table 1. Baseline Clinical and Laboratory Findings.*

Variables	Overall (n=11 796)	Timely diagnosed patients (n=11 631)	Misdiagnosed patients (n=165)	*P* value†
Demographics				
Age, y	62.0 (53.0–72.0)	62.0 (53.0–72.0)	64.0 (56.0–74.0)	0.072
Male sex	9422 (79.9)	9301 (80.0)	121 (73.3)	0.044
Initial presentation				
Atypical chest pain	1217 (10.3)	1185 (10.2)	32 (19.4)	<0.001
Means of arrival				
Direct visit	3235 (27.4)	3190 (27.4)	45 (27.3)	1.00
Emergency medical service	2845 (24.1)	2811 (24.2)	34 (20.6)	0.332
Transferred from another hospital	5716 (48.5)	5630 (48.4)	86 (52.1)	0.384
Body weight, kg	67.0 (60.0–75.0)	67.0 (60.0–75.0)	66.0 (58.0–74.0)	0.303
Symptom-to-door time, min	121.0 (60.0–276.0)	120.0 (60.0–274.0)	181.0 (64.0–552.0)	<0.001
Systolic blood pressure, mm Hg	128.0 (110.0–145.0)	128.0 (110.0–145.0)	130.0 (120.0–149.0)	0.006
Heart rate, bpm	76.0 (64.0–88.0)	76.0 (64.0–88.0)	78.5 (67.0–90.0)	0.013
Killip class on admission				
I	9151 (77.7)	9018 (77.6)	133 (80.6)	0.413
II	984 (8.4)	973 (8.4)	11 (6.7)	0.518
III	591 (5.0)	580 (5.0)	11 (6.7)	0.425
IV	1056 (9.0)	1046 (9.0)	10 (6.1)	0.239
Anterior ST elevation or LBBB on electrocardiography	5611 (48.0)	5588 (48.5)	23 (14.3)	<0.001
Left ventricular ejection fraction, %	51.0 (44.1–58.0)	51.0 (44.2–58.0)	51.0 (44.0–59.0)	0.944
Medical history				
Hypertension	5409 (45.9)	5325 (45.8)	84 (50.9)	0.218
Diabetes	2846 (24.1)	2791 (24.0)	55 (33.3)	0.007
Previous myocardial infarction or revascularization	507 (4.3)	499 (4.3)	8 (4.8)	0.875
Dyslipidemia	1420 (12.0)	1394 (12.0)	26 (15.8)	0.174
Heart failure	88 (0.7)	84 (0.7)	4 (2.4)	0.039
Cerebrovascular disease	610 (5.2)	597 (5.1)	13 (7.9)	0.161
Current smoker	5233 (45.1)	5172 (45.2)	61 (37.7)	0.065
Family history of premature coronary artery disease	880 (7.6)	867 (7.6)	13 (8.1)	0.940
Laboratory findings				
Hemoglobin, g/dL	14.5 (13.1–15.6)	14.5 (13.1–15.6)	13.8 (12.2–15.1)	<0.001
eGFR (MDRD), mL/min per 1.73 m^2	84.5 (67.3–103.4)	84.5 (67.4–103.4)	85.9 (65.0–105.5)	0.912
Total cholesterol, mmol/L	4.6 (3.9–5.4)	4.6 (3.9–5.4)	4.7 (3.9–5.6)	0.635
Triglyceride, mmol/L	1.3 (0.9–2.0)	1.3 (0.9–2.0)	1.2 (0.9–2.0)	0.660
HDL cholesterol, mmol/L	1.1 (0.9–1.3)	1.1 (0.9–1.3)	1.1 (0.9–1.3)	0.338
LDL cholesterol, mmol/L	2.9 (2.2–3.6)	2.9 (2.2–3.6)	2·0.8 (2.3–3.7)	0.986

Data are n (%) or median (interquartile range). eGFR indicates estimated glomerular filtration rate; HDL, high-density lipoprotein; LBBB, left bundle-branch block; LDL, low-density lipoprotein; and MDRD, Modification of Diet in Renal Disease.

*Values for body weight are missing in 666 cases, systolic blood pressure in 136, heart rate in 101, Killip class in 14, anterior ST elevation or LBBB on ECG in 113, left ventricular ejection fraction in 600, hypertension in 1, diabetes in 2, heart failure in 14, cerebrovascular disease in 13, current smoker in 200, family history of premature coronary artery disease in 230, hemoglobin in 27, eGFR in 56, total cholesterol in 1009, triglycerides in 1333, HDL cholesterol in 1268, and LDL cholesterol in 1656, and they are excluded from calculations.

†The *P* values are derived from the χ^2 test or Fisher exact test for categorical variables, when appropriate, and from the Kruskal-Wallis test for continuous variables for between-group comparisons.

Table 2. Procedural Profiles and Medical Treatments.*

Variables	Overall (n=11 796)	Timely diagnosed patients (n=11 631)	Misdiagnosed patients (n=165)	*P* value†
Primary PCI strategy for STEMI	11 543 (97.9)	11 543 (99.2)	0	<0.001
Door-to-angiography time, min	43 (31–59)	43 (31–58)	220 (66–1177)	<0.001
Procedural profiles				
Transradial approach	4010 (34.7)	3925 (34.4)	85 (55.6)	<0.001
Culprit lesion				
Left main artery	210 (1.8)	206 (1.8)	4 (2.6)	0.670
Left anterior descending artery	5838 (50.5)	5766 (50.6)	72 (46.8)	0.390
Left circumflex artery	1122 (9.7)	1093 (9.6)	29 (18.8)	<0.001
Right coronary artery	4387 (38.0)	4338 (38.0)	49 (31.8)	0.134
ACC/AHA lesion type B2/C	9911 (88.5)	9787 (88.6)	124 (84.9)	0.214
Multivessel disease	5595 (47.4)	5497 (47.3)	98 (59.4)	0.003
Preprocedural TIMI flow grade				
0	7459 (65.0)	7395 (65.3)	64 (42.7)	<0.001
1	1188 (10.4)	1170 (10.3)	18 (12.0)	0.596
2	1264 (11.0)	1241 (11.0)	23 (15.3)	0.117
3	1562 (13.6)	1517 (13.4)	45 (30.0)	<0.001
PCI	11 557 (98.0)	11 404 (98.0)	153 (92.7)	<0.001
Door-to-balloon time, min	61 (48–78)	60 (48–77)	264 (88–1233)	<0.001
Stenting	10 926 (94.5)	10 787 (94.6)	139 (90.3)	0.030
Drug-eluting stents	10 652 (94.8)	10 516 (94.8)	136 (94.4)	1.00
Postprocedural TIMI flow grade				
0	109 (0.9)	105 (0.9)	4 (2.6)	0.086
1	80 (0.7)	79 (0.7)	1 (0.6)	1.00
2	444 (3.8)	438 (3.8)	6 (3.9)	1.00
3	10 921 (94.5)	10 778 (94.5)	143 (92.9)	0.462
Medications at discharge				
Aspirin	11 688 (99.1)	11 527 (99.1)	161 (97.6)	0.102
P2Y12 inhibitor	11 494 (97.4)	11 341 (97.5)	153 (92.7)	<0.001
β-Blocker	9496 (80.5)	9377 (80.6)	119 (72.1)	0.008
ACEi or ARB	8992 (76.3)	8879 (76.4)	113 (68.5)	0.023
Statin	10 823 (91.8)	10 674 (91.8)	149 (90.3)	0.590
Oral anticoagulant	471 (4.0)	468 (4.0)	3 (1.8)	0.216

Data are n (%) or median (interquartile range). ACC/AHA indicates American College of Cardiology/American Heart Association; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and TIMI, Thrombolysis In Myocardial Infarction.

*Values for door-to-angiography time are missing in 358 cases, transradial approach in 240, culprit lesion in 239, ACC/AHA lesion type B2/C in 601, preprocedural TIMI flow grade in 323, door-to-balloon time in 375, stenting in 239, drug-eluting stents in 554, postprocedural TIMI flow grade in 242, ACEi or ARB in 4, and anticoagulant in 2, and they are excluded from calculations.

†The *P* values are derived from the χ^2 test or Fisher exact test for categorical variables, when appropriate, and from the Kruskal-Wallis test for continuous variables for between-group comparisons.

were no statistically significant differences in secondary outcomes between the 2 groups (Table S2). Furthermore, in a Cox time-to-event multivariable model, the adjusted risk for the STEMI misdiagnosis on the primary outcome was not significant (HR, 1.12 [95% CI, 0.68–1.85]; *P*=0.650; Table S3). A comparison of primary outcomes between the 2 groups in a specific population was assessed using a Cox time-to-event univariable model (Figure 3). The misdiagnosed group had a significantly higher all-cause mortality at 1 year as compared with the timely diagnosed group in 3 subgroups, showing significant misdiagnosis-by-subgroup heterogeneities: patients aged <65 years (n=6697; HR, 2.90 [95% CI, 1.43–5.88]; *P* for heterogeneity=0.008), male patients (n=9422; HR, 1.77 [95% CI, 1.02–3.06]; *P*=0.025), and patients with culprit lesions in the LAD (n=5838; HR, 2.09 [95% CI, 1.15–3.81]; *P*=0.040). In a Cox time-to-event multivariable model, the adjusted 1-year mortality risk in the misdiagnosed group was 1.58 (95% CI, 0.76–3.30; *P*=0.220) for

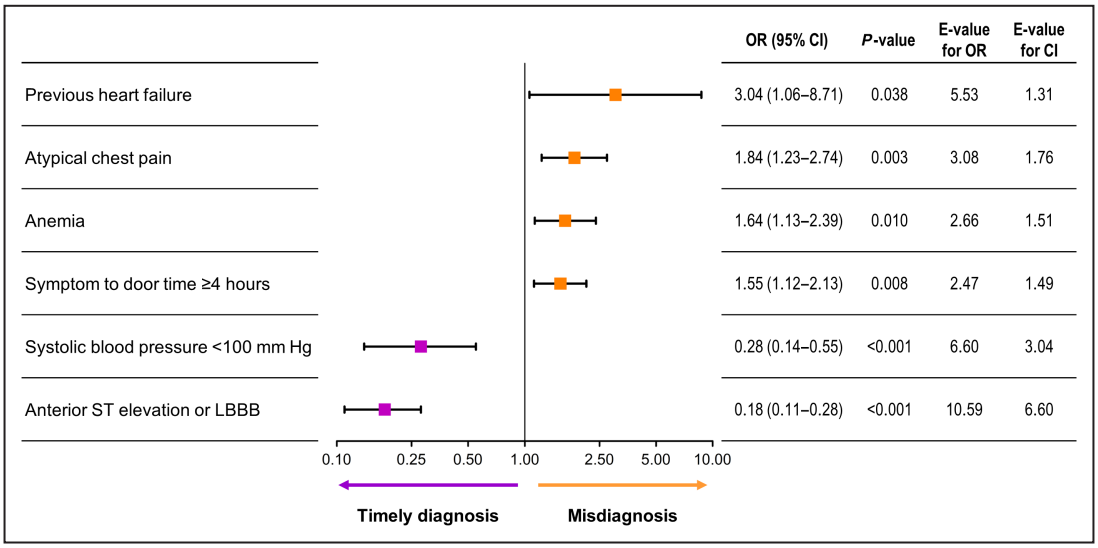

Figure 2. Independent factors for the misdiagnosis of ST-segment–elevation myocardial infarction.
Logistic regression analysis was performed. LBBB indicates left bundle-branch block; and OR, odds ratio.

patients aged <65 years, 1.36 (95% CI, 0.78–2.37; *P*=0.284) for male patients, and 1.84 (95% CI, 1.01–3.38; *P*=0.048) for patients with culprit lesions in the LAD (Table S4 through S6). The Kaplan-Meier curves revealed that there was a significant difference in 1-year mortality between the 2 groups in patients with culprit lesions in the LAD (Figure 4).

DISCUSSION

This nationwide, prospective Korean cohort study revealed that of 11 796 patients ultimately diagnosed with STEMI after a coronary angiogram, 165 (1.4%) had an initial working diagnosis of NSTEMI. In a multivariable adjustments model, patients with previous

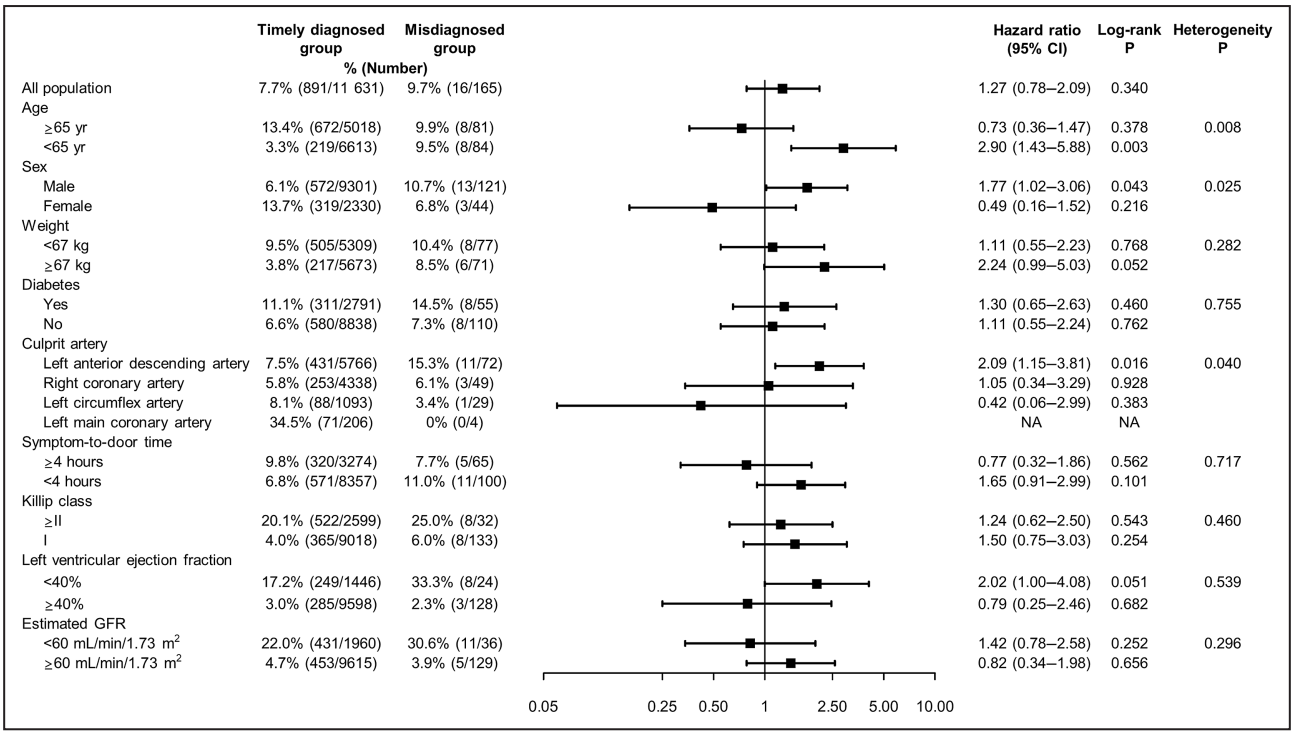

Figure 3. All-cause mortality rate at 12 months in the specific subgroups.
The Cox proportional hazards model was used. GFR indicates glomerular filtration rate; and NA, not applicable.

heart failure, atypical chest pain, anemia, or symptom-to-door time ≥4 hours had significantly higher odds of misdiagnosis, whereas those with systolic blood pressure <100 mm Hg or anterior ST elevation or left bundle-branch block on ECG had lower odds of the misdiagnosis of STEMI. The misdiagnosed group lost the opportunity to receive primary PCI and had 5 times longer door-to-angiography time than that observed in the timely diagnosed group. For the patients with culprit lesions in the LAD (half of the patients), the adjusted 1-year mortality risk for the misdiagnosis of STEMI was 1.84 (95% CI, 1.01–3.38) after adjustments for baseline variables. To the best of our knowledge, this is the first prospective, nationwide cohort study to investigate the real-world features of the misdiagnosis of STEMI in the contemporary PCI era, including coronary angiographic details.

In clinical practice, misdiagnosis may occur sometimes, and it is essential to mitigate its consequences for optimizing patient care. However, to date, there has been no consistent definition of the misdiagnosis of STEMI. AMI is classified into various types, based on pathological, clinical, and prognostic features.[14] Furthermore, it is commonly classified into STEMI and NSTEMI to distinguish patients with acute coronary occlusion who will benefit from rapid reperfusion therapy.[16] The initial working diagnosis of STEMI is based on symptoms consistent with myocardial ischemia and signs, including an ECG, in the acute phase of first medical contact.[6] However, the timely diagnosis of STEMI is occasionally challenging. Diverse health care professionals, including primary care physicians, residents, emergency medical physicians, and cardiologists, alone or collaboratively, make the initial working diagnosis in patients presenting with acute coronary syndromes. Physiologically, symptoms and signs of STEMI may vary by the stuttering course with intermittent occlusion and recanalization, coronary vasospasm, and collateral circulation.[17–19] A significant number of patients with STEMI do not have typical chest pain. In a large study involving >170 000 patients with STEMI from the National Registry of Myocardial Infarction of the United States, about 19% of the patients with STEMI did not present with chest pain and were at increased risk of delays in seeking medical attention, less intensive treatments, and consequent in-hospital mortality.[7] In the present study, 10.3% of patients did not present with typical chest pain. Previous studies on patients with STEMI demonstrated that, during coronary angiography, the infarct-related artery was not completely occluded in up to more than one-third of patients.[20–22] In the present study, 35% of patients did not have preprocedural TIMI flow grade 0 on the diagnostic coronary angiogram. Furthermore, a cross-sectional survey involving 124 physicians and 4392 ECGs demonstrated that there was significant disagreement among physicians in interpreting potential STEMI ECGs.[9]

In previous studies, there have been limited data about the misdiagnosis (missed diagnosis) of AMI, especially STEMI, which has no consistent definition (Table S7).[10–12,23–25] Pope et al[10] analyzed 10 689 patients with symptoms suggestive of acute myocardial ischemia in 1993 from the clinical trial and defined missed diagnoses as those instances when patients were mistakenly discharged from the emergency department and were later confirmed as AMI. Of 894 patients with AMI, 2.1% (19/894) were misdiagnosed. Multivariate analysis showed that non-White people, who is a person of any race than Caucasian (OR, 4.5 [95% CI, 1.8–11.8]) or nondiagnostic ECG (OR, 7.7 [95% CI, 2.9–20.2]) were independently associated with a missed diagnosis. Definitions of the misdiagnosis of AMI in other studies included the following: patients who were discharged without suspicion of AMI and were diagnosed with AMI within 30 days, patients diagnosed with AMI who had a previous visit within 7 days of index admission that matched a list of cardiac symptoms and illnesses suggestive of AMI, and patients who presented with STEMI and failed to receive reperfusion therapy within 4 hours. Most previous studies might also be vulnerable to missing patients who succumbed before receiving the correct diagnosis because of the definition of the misdiagnosis and retrospective nature of the study. Relevant factors of the misdiagnosis of AMI in other studies included the following: low-volume emergency department, younger age, and Black race had higher odds of the misdiagnosis, whereas higher chest pain acuity, high level of medical certification, larger hospital volume, higher academic status of the hospital, high emergency department admission rates, availability of cardiac catheterization, high in-patient occupancy rates, and urban location had lower odds of misdiagnosis. However, no study has been conducted to investigate the misdiagnosis of STEMI, in which patients did not have an initial working diagnosis of STEMI before commencing treatment and were then diagnosed with STEMI following a coronary angiogram. Furthermore, unlike previous studies, the present study included detailed information on angiographic and procedural findings, allowing for advanced analysis to identify relevant patient factors and clinical consequences of misdiagnosis of STEMI.

Theoretically, the misdiagnosed group may have poorer clinical outcomes due to delays or failure to receive appropriate reperfusion therapy. However, contemporary data showing the significant impact of the misdiagnosis of STEMI on major cardiovascular outcomes are scarce. Pope et al[10] demonstrated that the risk-adjusted mortality ratio of the missed diagnosis of AMI was 1.9, but it was not statistically significant (95%

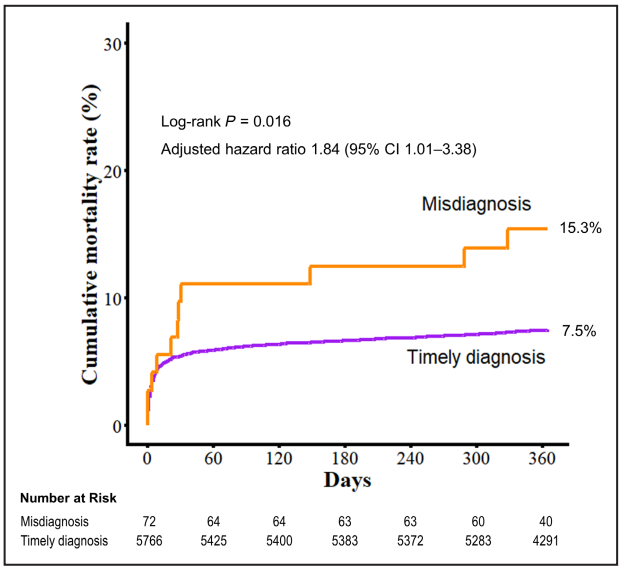

Figure 4. Time-to-event curves for death from any cause in patients with culprit lesions in the left anterior descending artery (n=5838).
Kaplan-Meier analysis over 1 year was performed using a log-rank test.

CI, 0.7–5.2). There could be several explanations for why there has been no convincing evidence that misdiagnosing AMI, including STEMI, is independently associated with increased mortality. First, misdiagnosed patients who succumbed before receiving the correct diagnosis were excluded from the analysis. This could have falsely attenuated the impact of the misdiagnosis on clinical outcomes. Second, the patients in the misdiagnosed group in this study were more likely to have higher systolic blood pressure and higher heart rate and were less likely to have anterior ST elevation or left bundle-branch block on ECG as compared with the timely diagnosed group. Furthermore, the proportion of total occlusion was 42.7% and 65.3% in the misdiagnosed group and the timely diagnosed group, respectively. It can be hypothesized, therefore, that patients with milder forms of STEMI may receive less attention from health care providers due to milder symptoms and signs, resulting in a delayed diagnosis. Of note, in the present study, there was significant misdiagnosis-by-subgroup heterogeneity for 1-year mortality according to the culprit artery (*P* for heterogeneity=0.040; HR, 2.09 [95% CI, 1.15–3.81] for LAD; HR, 1.05 [95% CI, 0.34–3.29] for right coronary artery; HR, 0.42 [95% CI, 0.06–2.99] for left circumflex artery). After adjustments for baseline variables, the adjusted 1-year mortality risk for the misdiagnosis of STEMI was significantly high, as compared with the timely diagnosis, particularly in patients with culprit lesions in the LAD. These findings indicate that the clinical impact of misdiagnosis of STEMI as NSTEMI may vary depending on the culprit artery.

The findings of our study should be considered with the following limitations. First, the participating centers in KAMIR tended to be teaching hospitals with a large number of patients, thus limiting the generalizability of the present findings to community hospitals, including primary health care centers. As previously stated, due to factors such as hospital bed volume, hospital teaching status, and geographical location, community hospitals may have higher rates of misdiagnosis than teaching university hospitals.[24,25] Second, details on ECGs associated with misdiagnosis, except for anterior ST elevation or left bundle-branch block, were not included in the analysis. Patients with STEMI may have dynamic changes in electrographic waveform, and serial ECG acquisition can provide critical information, especially if the ECG is nondiagnostic at the time of presentation.[14] The concept of the present study was first proposed in October 2021, which was outside of the completion of the 1-year clinical follow-up, indicating free from bias by the investigators due to their awareness of the study. Third, we focused on patient variables but not on system-related variables. As discussed earlier, several system-related factors may affect the rate of STEMI misdiagnosis. However, this study identifies relevant patient factors of STEMI misdiagnosis using detailed baseline characteristics and coronary angiographic profiles, providing valuable insights in making an initial working diagnosis for patients presenting with chest pain by health care providers. Finally, given the difference in time of coronary angiography between the 2 groups, attention should be paid to interpreting the angiographic findings.

CONCLUSIONS

Data from a nationwide, prospective Korean registry revealed that the misdiagnosis of STEMI occurred in 1.4% of the patients. In a multivariable analysis, previous heart failure, atypical chest pain, anemia, and late presentation were found to have significantly higher odds of misdiagnosis, whereas low blood pressure and anterior ST elevation or left bundle-branch block on ECG had lower odds. The door-to-angiography time in the misdiagnosed group was 5 times longer than that in the timely diagnosed group. For patients with culprit lesions in the LAD, misdiagnosis of STEMI was associated with increased 1-year mortality. Additional efforts, including reinforcement of the initial working diagnosis process, are required for the timely diagnosis of STEMI in real-world practice, especially in patients with suspected acute LAD occlusion.

ARTICLE INFORMATION

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Affiliations

Department of Cardiology, Chonnam National University Hospital and Medical School, Gwangju, South Korea (K.H.C., M.C.K., D.S.S., Y.J.H., J.H.K., Y.A., M.H.J.); Department of Preventive Medicine, Chonnam National University Medical School, Gwangju, Hwasun-gun, South Korea (M-H.S.); Department of Cardiology, Seoul National University Medical School, Seoul, South Korea (H-S.K.); Department of Cardiology, Keimyung University Dongsan Medical Center, Daegu, South Korea (S-H.H.); Department of Cardiology, Chonbuk National University Medical School, Jeonju, South Korea (S.R.L.); Department of Cardiology, Gyeongsang National University Medical School, Jinju, South Korea (J-Y.H.); Department of Cardiology, Wonkwang University Hospital, Iksan, South Korea (S.K.O.); and Department of Cardiology, Pusan National University Medical School, Busan, South Korea (K.S.C.), Pusan National University Medical School, Busan, South Korea.

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Disclosures

None.

Supplemental Material

Data S1.
Tables S1–S7

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Supplemental Material

Data S1.

KAMIR participating institutions and investigators:

1. Bucheon St. Mary's Hospital, Gyeonggi-do, Korea; Hee-Yeol Kim
2. Cheongju St. Mary's Hospital, Cheongju, Korea; Ju Yeol Baek
3. Chonbuk National University Hospital, Jeonju, Korea; Jei Keon Chae
4. Chonnam National University Hospital, Gwangju, Korea; Myung Ho Jeong
5. Chungbuk National University Hospital, Cheongju, Korea; Kyung-Kook Hwang
6. Chungnam National University Hospital, Daejeon, Korea; In-Whan Seong
7. Dongguk University Gyeongju Hospital, Gyeongju, Korea; Deuk-Young Nah
8. Eulji University Hospital, Daejeon, Korea; Kyung Tae Jeong
9. Gangdong Kyunghee University Hospital, Seoul, Korea; Jong Jin Kim
10. Gangneung Asan Hospital, Gangwon-do, Korea; Sang-Yong Yoo
11. Gachon University Gil Medical Center, Incheon, Korea; Seng Hwan Han
12. Gyeongsang National University Hospital, Jinju, Korea; Jin Yong Hwang
13. Inje University Haeundae Paik Hospital, Busan, Korea; Dong-Kie Kim
14. Jeju National University Hospital, Jeju, Korea; Seung-Jae Joo
15. Jeonju Jesus Hospital, Jeonju, Korea; Jay Young Rhew
16. Korea University Guro Hospital, Seoul, Korea; Seung-Woon Rha
17. Keimyung University Dongsan Medical Center, Daegu, Korea; Seung-Ho Hur
18. Kyungpook National University Hospital, Daegu, Korea; Shung Chull Chae
19. Kyung Hee University Hospital at Gangdong, Seoul, Korea; Chong Jin Kim
20. Pusan National University Hospital, Busan, Korea; Kwang Soo Cha
21. Samsung Changwon Hospital, Changwon, Korea; Yong Hwan Park

22. Seoul Boramae Hospital, Seoul, Korea; Sang-Hyun Kim

23. Seoul National University Hospital, Seoul, Korea; Hyo-Soo Kim

24. Seoul National University Bundang Hospital, Seongnam, Korea; Chang-Hwan Yoon

25. Seoul Samsung Medical Center, Seoul, Korea; Hyeon-Cheol Gwon

26. Seoul St. Mary's Hospital, Seoul, Korea; Kiyuk Chang

27. St. Vincent Hospital, Gyeonggi-do, Korea; Gi Dong Yoo

28. Suncheon St. Garolo Hospital, Suncheon, Korea; Jang Hyun Cho

29. Wonju Severance Christian Hospital, Wonju, Korea; Jung Han Yoon

30. Wonkwang University Hospital, Iksan, Korea; Seok Kyu Oh

31. Yeungnam University Hospital, Daegu, Korea; Jong Seon Park

KAMIR steering committee

Myung Ho Jeong, PhD, Chonnam National University Hospital, Gwangju, Korea (Chair); Ju Han Kim, PhD, Chonnam National University Hospital, Gwangju, Korea; Kyung Hoon Cho, PhD, Chonnam National University Hospital, Gwangju, Korea; Sang Rok Lee, PhD, Chonbuk National University Hospital, Jeonju, Korea; Kyung-Kook Hwang, PhD, Chungbuk National University Hospital, Cheongju, Korea; Jin Yong Hwang, PhD, Gyeongsang National University Hospital, Jinju, Korea; Seung-Jae Joo, PhD, Jeju National University Hospital, Jeju, Korea; Jang Hoon Lee, PhD, Kyungpook National University Hospital, Daegu, Korea; Jay Young Rhew, PhD, Jeonju Jesus Hospital, Jeonju, Korea; Seung-Woon Rha, PhD, Korea University Guro Hospital, Seoul, Korea; Seung-Ho Hur, PhD, Keimyung University Dongsan Medical Center, Daegu, Korea; Kwang Soo Cha, PhD, Pusan National University Hospital, Busan, Korea; Yong Hwan Park, PhD, Samsung Changwon Hospital, Changwon, Korea; Joo-Yong Hahn, PhD, Seoul Samsung Medical Center, Seoul, Korea; Jang Hyun Cho, PhD, Suncheon St. Garolo Hospital, Suncheon, Korea; Seok Kyu Oh, PhD, Wonkwang University Hospital, Iksan, Korea; Deuk-Young Nah, PhD, Dongguk University Gyeongju Hospital, Gyeongju, Korea

Table S1. Results of logistic regression analysis to assess correlates of the misdiagnosis of STEMI.

	Odds ratio (95% confidence interval)			
	No adjustment	***P* value**	**Adjustment**	***P* value**[a]
Previous heart failure	3.42 (1.24–9.42)	0.018	3.04 (1.06–8.71)	0.038
Atypical chest pain	2.12 (1.44–3.13)	<0.001	1.84 (1.23–2.74)	0.003
Anemia	1.92 (1.37–2.69)	<0.001	1.64 (1.13–2.39)	0.010
Symptom-to-door time ≥4 hours	1.66 (1.21–2.27)	0.002	1.55 (1.12–2.13)	0.008
Left circumflex artery as a culprit lesion	2.27 (1.54–3.36)	<0.001	1.39 (0.93–2.07)	0.110
Multivessel disease	1.63 (1.19–2.23)	0.002	1.37 (1.00–1.88)	0.054
Diabetes mellitus	1.58 (1.14–2.20)	0.006	1.33 (0.95–1.86)	0.098
Age >65 years	1.27 (0.93–1.73)	0.127	0.88 (0.61–1.26)	0.494
Current smoker	0.73 (0.53–1.00)	0.053	0.88 (0.61–1.26)	0.471
Male sex	0.69 (0.49–0.98)	0.036	0.83 (0.56–1.22)	0.339
Systolic blood pressure <100 mmHg	0.40 (0.20–0.78)	0.008	0.28 (0.14–0.55)	<0.001
Anterior ST elevation or LBBB on electrocardiography	0.17 (0.11–0.27)	<0.001	0.18 (0.11–0.28)	<0.001

LBBB, left bundle branch block; STEMI, ST elevation myocardial infarction.

[a]Adjusted for age, sex, atypical chest pain, systolic blood pressure, anemia, anterior ST-elevation or LBBB, symptom-to-door time, diabetes mellitus, current smoker status, previous heart failure, multivessel disease, and left circumflex artery as a culprit lesion. Binary logistic regression analysis was performed.

Table S2. Clinical outcomes of up to 12 months in the total population.

	Overall (N=11,796)	Timely diagnosed patients (N=11,631)	Misdiagnosed patients (N=165)	*P* value[a]
Successful percutaneous coronary intervention[b]	11,389 (98.7%)	11,239 (98.7%)	150 (98.0%)	0.745
In-hospital mortality	586 (5.0%)	575 (4.9%)	11 (6.7%)	0.406
12-month outcomes				
Death from any cause	907 (7.7%)	891 (7.7%)	16 (9.7%)	0.408
Cardiac death	722 (6.1%)	709 (6.1%)	13 (7.9%)	0.432
Non-cardiac death	185 (1.6%)	182 (1.6%)	3 (1.8%)	1.000
Non-fatal myocardial infarction	134 (1.1%)	132 (1.1%)	2 (1.2%)	1.000
Percutaneous coronary intervention	385 (3.3%)	383 (3.3%)	2 (1.2%)	0.203
Coronary artery bypass grafting	19 (0.2%)	19 (0.2%)	0	1.000
Non-fatal stroke	122 (1.0%)	119 (1.0%)	3 (1.8%)	0.539

[a]The p values are derived from the Chi-square test or Fisher's exact test, when appropriate, for between-group comparisons.

[b]Values for successful percutaneous coronary intervention are missing in 253 cases, and they are excluded from percentage calculations.

Table S3. Results of the Cox proportional hazard models to assess correlates of death from any cause at12 months in the total population.

	Hazard ratio (95% confidence interval)					
	No adjustment	***P* value**	**Model 1[a]**	***P* value**	**Model 2[b]**	***P* value**
Age >75 years	6.16 (5.25−7.22)	<0.001	5.68 (4.79−6.73)	<0.001	2.41 (1.98−2.94)	<0.001
Age 65−74 years	2.51 (2.08−3.01)	<0.001	2.41 (2.00−2.90)	<0.001	1.50 (1.23−1.83)	<0.001
Killip class >I	5.49 (4.81−6.26)	<0.001			2.35 (2.03−2.73)	<0.001
Left ventricular ejection fraction <40%	4.89 (4.29−5.58)	<0.001			2.34 (2.02−2.71)	<0.001
Systolic blood pressure <100 mmHg	3.86 (3.36−4.43)	<0.001			1.99 (1.71−2.31)	<0.001
eGFR (MDRD) <60 mL/min/1.73 m^2	5.20 (4.57−5.92)	<0.001			1.90 (1.65−2.20)	<0.001
Anemia	4.82 (4.24−5.50)	<0.001			1.78 (1.54−2.07)	<0.001
Atypical chest pain	3.39 (2.93−3.93)	<0.001			1.75 (1.50−2.04)	<0.001
Heart rate >100 beats/minute	3.05 (2.63−3.55)	<0.001			1.67 (1.42−1.97)	<0.001
Anterior ST elevation or LBBB	1.34 (1.18−1.53)	<0.001			1.28 (1.11−1.47)	<0.001
Weight <67 kg	2.41 (2.09−2.77)	<0.001			1.13 (0.96−1.33)	0.129
Misdiagnosis of STEMI	1.27 (0.78−2.09)	0.340	1.15 (0.70−1.89)	0.574	1.12 (0.68−1.85)	0.650
Male sex	0.44 (0.38−0.50)	<0.001	0.81 (0.70−0.94)	0.006	0.89 (0.76−1.04)	0.142
Current smoker	0.44 (0.38−0.51)	<0.001			0.86 (0.73−1.02)	0.075
Symptom-to-door time ≥4 hours	1.43 (1.24−1.63)	<0.001			Eliminated	NA

Diabetes mellitus	1.74 (1.52–2.00)	<0.001	Eliminated	NA
Hypertension	1.83 (1.61–2.09)	<0.001	Eliminated	NA
Previous myocardial infarction or revascularization	1.69 (1.31–2.19)	<0.001	Eliminated	NA
Previous heart failure	4.33 (2.93–6.39)	<0.001	Eliminated	NA
Previous cerebrovascular accident	2.28 (1.85–2.81)	<0.001	Eliminated	NA
Family history of premature coronary artery disease	0.55 (0.40–0.75)	<0.001	Eliminated	NA

eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; NA, not applicable; STEMI, ST elevation myocardial infarction.

[a]Adjusted for age, sex, and misdiagnosis of STEMI.

[b]Adjusted for age, sex, body weight, atypical chest pain, anterior ST elevation or left bundle branch block, Killip class, heart rate, systolic blood pressure, left ventricular ejection fraction, creatinine clearance, anemia, symptom-to-door time, diabetes mellitus, hypertension, previous myocardial infarction or revascularization, family history of premature coronary artery disease, current smoker status, previous heart failure, previous cerebrovascular accident, and misdiagnosis of STEMI. Cox regression analysis using the enter method was performed with misdiagnosis of STEMI and remaining variables in the backward elimination selection.

Table S4. Results of the Cox proportional hazard models to assess correlates of death from any cause at12 months in patients aged <65 years (n = 6697).

	Hazard ratio (95% confidence interval)					
	No adjustment	***P* value**	**Model 1[a]**	***P* value**	**Model 2[b]**	***P* value**
Killip class >I	6.49 (4.99–8.44)	<0.001			2.96 (2.19–4.00)	<0.001
Left ventricular ejection fraction <40%	5.93 (4.54–7.74)	<0.001			2.62 (1.95–3.52)	<0.001
Anemia	5.57 (4.17–7.42)	<0.001			2.52 (1.85–3.45)	<0.001
Systolic blood pressure <100 mmHg	4.43 (3.36–5.84)	<0.001			2.28 (1.67–3.11)	<0.001
Heart rate >100 beats/minute	4.10 (3.09–5.43)	<0.001			2.08 (1.52–2.83)	<0.001
Atypical chest pain	3.79 (2.81–5.11)	<0.001			2.04 (1.49–2.79)	<0.001
Previous cerebrovascular accident	2.47 (1.44–4.25)	0.001			1.68 (0.98–2.90)	0.061
eGFR (MDRD) <60 mL/min/1.73 m^2	4.58 (3.44–6.10)	<0.001			1.63 (1.18–2.23)	0.003
Anterior ST elevation or LBBB	1.45 (1.11–1.88)	0.006			1.42 (1.08–1.88)	0.013
Misdiagnosis of STEMI	2.90 (1.43–5.88)	0.003	2.85 (1.40–5.76)	0.004	1.58 (0.76–3.30)	0.220
Current smoker	0.62 (0.48–0.80)	<0.001			0.73 (0.56–0.96)	0.023
Previous myocardial infarction or revascularization	1.86 (1.08–3.19)	0.025			Eliminated	NA
Hypertension	1.18 (0.90–1.54)	0.222			Eliminated	NA
Male sex	0.64 (0.43–0.95)	0.028	0.65 (0.44–0.96)	0.032	Eliminated	NA

Previous heart failure	6.01 (2.24–16.16)	<0.001	Eliminated	NA
Family history of premature coronary artery disease	0.76 (0.47–1.23)	0.258	Eliminated	NA
Symptom-to-door time ≥4 hours	1.19 (0.89–1.59)	0.252	Eliminated	NA
Weight <67 kg	1.54 (1.18–2.00)	0.001	Eliminated	NA
Diabetes mellitus	1.77 (1.34–2.35)	<0.001	Eliminated	NA

eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; NA, not applicable; STEMI, ST elevation myocardial infarction.

[a]Adjusted for sex and misdiagnosis of STEMI.

[b]Adjusted for sex, body weight, atypical chest pain, anterior ST elevation or left bundle branch block, Killip class, heart rate, systolic blood pressure, left ventricular ejection fraction, creatinine clearance, anemia, symptom-to-door time, diabetes mellitus, hypertension, previous myocardial infarction or revascularization, family history of premature coronary artery disease, current smoker status, previous heart failure, previous cerebrovascular accident, and misdiagnosis of STEMI. Cox regression analysis using the enter method was performed with misdiagnosis of STEMI and remaining variables in the backward elimination selection.

Table S5. Results of the Cox proportional hazard models to assess correlates of death from any cause at12 months in male patients (n = 9422).

	Hazard ratio (95% confidence interval)					
	No adjustment	***P* value**	**Model 1[a]**	***P* value**	**Model 2[b]**	***P* value**
Killip class >I	5.84 (4.95–6.88)	<0.001			2.45 (2.03–2.96)	<0.001
Left ventricular ejection fraction <40%	5.51 (4.68–6.49)	<0.001			2.42 (2.02–2.91)	<0.001
Age >75 years	5.92 (4.90–7.17)	<0.001	5.91 (4.88–7.15)	<0.001	2.20 (1.74–2.77)	<0.001
Age 65–74 years	2.51 (2.04–3.09)	<0.001	2.51 (2.04–3.09)	<0.001	1.44 (1.15–1.80)	0.001
Anemia	5.63 (4.78–6.62)	<0.001			1.98 (1.64–2.40)	<0.001
Atypical chest pain	3.81 (3.18–4.57)	<0.001			1.91 (1.58–2.31)	<0.001
Systolic blood pressure <100 mmHg	4.07 (3.43–4.83)	<0.001			1.90 (1.57–2.29)	<0.001
eGFR (MDRD) <60 mL/min/1.73 m^2	5.39 (4.58–6.34)	<0.001			1.85 (1.54–2.23)	<0.001
Heart rate >100 beats/minute	3.29 (2.74–3.96)	<0.001			1.62 (1.32–1.98)	<0.001
Anterior ST elevation or left bundle branch block	1.35 (1.15–1.59)	<0.001			1.31 (1.10–1.56)	0.003
Weight <67 kg	2.21 (1.88–2.61)	<0.001			1.22 (1.02–1.46)	0.029
Misdiagnosis of STEMI	1.77 (1.02–3.06)	0.042	1.63 (0.94–2.83)	0.082	1.36 (0.78–2.37)	0.284
Current smoker	0.52 (0.44–0.61)	<0.001			0.87 (0.73–1.04)	0.124
Previous myocardial infarction or revascularization	1.85 (1.36–2.52)	<0.001			Eliminated	NA

Hypertension	1.59 (1.35–1.87)	<0.001		Eliminated	NA
Symptom-to-door time ≥4 hours	1.41 (1.19–1.68)	<0.001		Eliminated	NA
Previous heart failure	4.53 (2.71–7.57)	<0.001		Eliminated	NA
Family history of premature coronary artery disease	0.58 (0.40–0.84)	0.004		Eliminated	NA
Diabetes mellitus	1.70 (1.43–2.02)	<0.001		Eliminated	NA
Previous cerebrovascular accident	2.41 (1.84–3.14)	<0.001		Eliminated	NA

eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; NA, not applicable; STEMI, ST elevation myocardial infarction.

[a]Adjusted for age and misdiagnosis of STEMI.

[b]Adjusted for age, body weight, atypical chest pain, anterior ST elevation or left bundle branch block, Killip class, heart rate, systolic blood pressure, left ventricular ejection fraction, creatinine clearance, anemia, symptom-to-door time, diabetes mellitus, hypertension, previous myocardial infarction or revascularization, family history of premature coronary artery disease, current smoker status, previous heart failure, previous cerebrovascular accident, and misdiagnosis of STEMI. Cox regression analysis using the backward elimination selection was performed.

Table S6. Results of the Cox proportional hazard models applied to assess correlates of death from any cause at12 months in patients with culprit lesions in the left anterior descending artery (n = 5838).

	Hazard ratio (95% confidence interval)					
	No adjustment	***P* value**	**Model 1[a]**	***P* value**	**Model 2[b]**	***P* value**
Age >75 years	7.25 (5.76–9.12)	<0.001	6.69 (5.23–8.56)	<0.001	3.01 (2.29–3.96)	<0.001
Age 65–74 years	2.71 (2.07–3.54)	<0.001	2.61 (2.00–3.43)	<0.001	1.76 (1.33–2.33)	<0.001
Systolic blood pressure <100 mmHg	5.00 (4.04–6.19)	<0.001			2.59 (2.06–3.25)	<0.001
Left ventricular ejection fraction <40%	4.63 (3.84–5.57)	<0.001			2.15 (1.76–2.62)	<0.001
Killip class >I	5.04 (4.18–6.07)	<0.001			2.11 (1.71–2.60)	<0.001
Misdiagnosis of STEMI	2.09 (1.15–3.81)	0.016	1.96 (1.08–3.57)	0.028	1.84 (1.01–3.38)	0.048
Anemia	5.31 (4.40–6.40)	<0.001			1.81 (1.46–2.24)	<0.001
eGFR (MDRD) <60 mL/min/1.73 m^2	5.27 (4.37–6.36)	<0.001			1.66 (1.34–2.06)	<0.001
Atypical chest pain	2.80 (2.23–3.51)	<0.001			1.53 (1.21–1.94)	<0.001
Heart rate >100 beats/minute	2.67 (2.17–3.29)	<0.001			1.53 (1.23–1.91)	<0.001
Weight <67 kg	2.60 (2.12–3.20)	<0.001			1.28 (1.02–1.61)	0.030
Previous myocardial infarction or revascularization	1.96 (1.38–2.80)	<0.001			1.32 (0.92–1.89)	0.134
Hypertension	2.07 (1.71–2.50)	<0.001			1.21 (0.99–1.48)	0.068
Male sex	0.41 (0.33–0.49)	<0.001	0.82 (0.70–1.02)	0.068	Eliminated	NA

Previous heart failure	5.01 (2.88–8.70)	<0.001	Eliminated	NA
Family history of premature coronary artery disease	0.57 (0.36–0.91)	0.018	Eliminated	NA
Symptom-to-door time ≥4 hours	1.62 (1.34–1.96)	<0.001	Eliminated	NA
Current smoker	0.48 (0.39–0.59)	<0.001	Eliminated	NA
Diabetes mellitus	1.81 (1.49–2.21)	<0.001	Eliminated	NA
Previous cerebrovascular accident	2.00 (1.44–2.77)	<0.001	Eliminated	NA

eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; NA, not applicable; STEMI, ST elevation myocardial infarction.

[a]Adjusted for age, sex, and misdiagnosis of STEMI.

[b]Adjusted for age, sex, body weight; atypical chest pain, Killip class, heart rate, systolic blood pressure, left ventricular ejection fraction, creatinine clearance, anemia, symptom-to-door time, diabetes mellitus, hypertension, previous myocardial infarction or revascularization, family history of premature coronary artery disease, current smoker status, previous heart failure, previous cerebrovascular accident, and misdiagnosis of STEMI. Cox regression analysis using the backward elimination selection was performed.

Table S7. Previous studies investigating the misdiagnosis of acute myocardial infarction.

Study	Design	Population	Definition of misdiagnosis	Findings regarding incidence and relevant factors
Pope JH, N Engl J Med 2000	A cohort study from the ACI-TIPI multicenter clinical trial; the US in 1993	894 patients diagnosed with AMI aged ≥30 years	Patients with symptoms suggestive of acute myocardial ischemia who were mistakenly discharged from the emergency department and were later confirmed as AMI.	The rate of misdiagnosis was 2.1% (19/894). Multivariable analysis showed that non-white people or nondiagnostic electrocardiogram were independently associated with a misdiagnosis.
Christenson J, CMAJ 2004	Prospective multicenter cohort study; Canada in 2000 and 2001	241 patients diagnosed with AMI aged ≥25 years	Patients who were discharged without suspicion of AMI and were diagnosed with AMI within 30 days.	The rate of misdiagnosis was 4.6% (11/241).
Schull MJ, Ann Emerg Med 2006	Retrospective multicenter cohort study; Canada in 2002 and 2003	19,663 patients admitted for AMI aged ≥20 years	Patients diagnosed with AMI who had previous visit within 7 days of index admission that matches a list of cardiac symptoms and illnesses suggestive of AMI.	The rate of misdiagnosis was 2.1% (419/19,663). After controlling for patient factors, the lower-volume emergency departments had up to 2-fold higher odds of missing AMI than those in the highest-volume emergency departments.
Wilson M, Acad Emerg Med 2014	Retrospective multicenter cohort study from health insurance data; the US in 2004 and 2005	371,638 patients diagnosed with AMI aged ≥65 years	Patients who were discharged home from their initial emergency department visits and were subsequently admitted to the hospital for AMI.	The median percentage of unadjusted hospital-level misdiagnosis was 0.52% (interquartile range 0–3.45%). Multivariable analysis showed that a higher chest pain acuity, American Board of Emergency Medicine certification, larger hospital bed size, and academic status were associated with lower odds of having missed diagnosis.

Moy E, Diagnosis (Berl) 2015	Retrospective multicenter cohort study; the US in 2007	111,973 patients diagnosed with AMI aged ≥18 years	Patients who had visited an emergency department with chest pain or cardiac conditions, were released and were subsequently admitted for AMI within 7 days.	The rate of misdiagnosis was 0.9% (993/111,973). Univariable analysis showed that younger age and black race were associated with higher odds of having missed diagnosis. In contrast, hospital teaching status, high emergency department admission rates, availability of cardiac catheterization, high inpatient occupancy rates, and urban location were associated with lower odds of a missed diagnosis.
Williams T, Int J Cardiol Heart Vasc 2019	Retrospective multicenter cohort study; Australia in 2011−2016	1392 patients presented with STEMI	Patients who presented with STEMI and failed to receive reperfusion therapy within four hours.	The rate of misdiagnosis was 7.2% (100/1392). Of the misdiagnosed patients who died, rural hospitals recorded the highest inpatient mortality. Misdiagnosed patients as compared to treated STEMI patients had higher 30-day readmission and longer length of stay.
Cho KH	Prospective multicenter cohort study; Korea in 2011-2020	11,796 patients diagnosed with AMI aged ≥18 years	Patients who had an initial working diagnosis of non-STEMI and were eventually diagnosed with STEMI after a coronary angiogram.	The rate of misdiagnosis was about 1.4% (165/11,796). Multivariable analysis showed that patients with previous heart failure, atypical chest pain, anemia, and symptom-to-door time ≥4 hours had significantly higher odds, whereas those with systolic blood pressure <100 mmHg and anterior ST-elevation or left bundle branch block on electrocardiogram had lower odds of STEMI misdiagnosis.
ACI-TIPI, Acute Cardiac Ischemia Time-Insensitive Predictive Instrument; AMI, Acute Myocardial Infarction; STEMI, ST elevation myocardial infarction.				