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Global geographical variations in ST-segment elevation myocardial infarction management and post-discharge mortality☆,☆☆

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ABSTRACT

Background: There is a shortage of information on regional variations in ST-segment elevation myocardial infarction (STEMI) management and prognosis at a global level. We aimed to compare patient profiles, in-hospital management and post-discharge mortality across several world regions.
Methods: In total, 11,559 patients with STEMI were enrolled in two prospective studies of acute coronary syndrome survivors: EPICOR (4943 patients from 555 hospitals in 20 countries in Europe and Latin America recruited between September 2010 and March 2011) and EPICOR Asia (6616 patients from 218 hospitals in eight Asian countries recruited between June 2011 and May 2012). Comparisons were performed by eight pre-defined regions: Northern Europe (NE), Southern Europe (SE), Eastern Europe (EE), Latin America (LA), China (CN), India (IN), Southeast Asia (SA), and South Korea/Hong Kong/Singapore (KS).
Results: Reperfusion therapy rates ranged between 53.9% (IN) and 81.2% (SE), primary percutaneous coronary intervention (PCI) between 24.8% (IN) and 65.6% (NE) and fibrinolysis between 8.1% (CN) and 34.2% (SA). Median time to primary PCI (h) ranged from 3.9 (NE) to 20.9 (IN) and to fibrinolysis from 2.4 (SE) to 6.3 (IN). Two-year mortality ranged between 2.5% in NE and 7.4% in LA. Regional variations in mortality persisted after adjustment for reperfusion therapy and known prognostic factors.
Conclusions: Among patients with STEMI, there is a wide regional variation in clinical profiles, hospital care and mortality. Substantial room for improvement remains at a global level for increasing reperfusion rates, reducing delays and post-discharge mortality in patients with STEMI.

1. Introduction

Acute myocardial infarction is one of the leading causes of morbidity and mortality worldwide [1]. A number of evidence-based interventions have been adopted in recent decades, leading to widespread improvement in prognosis [2]. However, the burden of cardiovascular risk factors and the incidence of acute myocardial infarction are increasing disproportionately in some geographical regions, and remain a major global health concern [3,4].

Despite standard, evidence-based therapy advocated by international guidelines, marked geographical disparities in clinical management and mortality have been reported. Randomized clinical trials (RCT) [5,6] and registries [7–10] have shown considerable variation in practice across countries, highlighting a large gap between guideline recommendations and received patient care.

Data from EPICOR (long-tErm follow uP of antithrombotic management patterns In acute CORonary syndrome patients) and EPICOR Asia cohorts have shown an unexplained variation in mortality [11] and identified geographical region as an independent predictor of 2-year

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mortality [12]. The aim of the present study is to describe regional variation in patient profile, hospital management, including evidence-based management, and 2-year mortality of patients with ST-segment elevation myocardial infarction (STEMI), using combined data from the EPICOR and EPICOR Asia studies.

2. Methods

EPICOR (NCT01171404) and EPICOR Asia (NCT01361386) are prospective, international, observational, real-world practice cohort studies comprising consecutive patients hospitalized for an acute coronary syndrome within 24 h (EPICOR) or 48 h (EPICOR Asia) of symptom onset, who survived to hospital discharge.

The protocol and case record form were almost identical for both studies, and their rationale and designs have been described elsewhere [13,14]. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The current study is a pre-defined secondary objective of both studies.

Results for STEMI patients were analyzed according to eight pre-specified regions: Southern Europe (France, Greece, Italy and Spain), Northern Europe (Belgium, Denmark, Finland, Germany, Luxembourg, the Netherlands, Norway and UK), Eastern Europe (Poland, Romania, Slovenia and Turkey), Latin America (Argentina, Brazil, Mexico and Venezuela) [12], China, India, Southeast Asia (Malaysia, Vietnam and Thailand) and South Korea/Hong Kong/Singapore. Supplementary Table S1 lists the participating regions and the number of patients enrolled per country.

2.1. Statistical analysis

Continuous parameters were mostly presented as mean (standard deviation) and regions were compared using one-way analysis of variance. Ordinal and highly skewed distributed variables were presented by median and inter-quartile range, and regions were compared using the non-parametric Kruskal–Wallis test. Categorical data were expressed as percentages and compared between regions using Chi-square tests. Overall survival curves were obtained using the Kaplan–Meier method and compared using the log-rank test. We used Poisson regression models to estimate 2-year mortality rates in each region, adjusted for 16 known predictors of 2-year mortality in the overall study population. These predictors were previously obtained from a risk scoring system developed using forward stepwise Cox regression to estimate 2-year mortality risk in acute coronary syndrome patients and with well reported goodness-of-fit, discriminatory power and internal validation [12]. Those predictors were (ranked by predictive strength) age, low ejection fraction, no coronary revascularization or thrombolysis, elevated serum creatinine, poor EQ-5D score, low hemoglobin, previous cardiac disease, previous chronic obstructive pulmonary disease, elevated blood glucose, on diuretics at discharge, male sex, lower education level, on aldosterone inhibitor at discharge, body mass index, in-hospital cardiac complications and Killip class [12]. All p-values were two-sided and values of <0.05 were considered statistically significant. All statistical analyses were performed using STATA software, version 13.1 (Stata Corp, College Station, TX, USA). Results are reported according to the research reporting guidelines for observational studies (STROBE guidelines) [15].

3. Results

In total, 11,559 patients with STEMI were enrolled between September 2010 and March 2011 from 555 hospitals in 20 countries across Europe and Latin America (EPICOR, $n = 4943$), and between June 2011 and May 2012 from 218 hospitals across eight countries and regions in Asia (EPICOR Asia, $n = 6616$). Fig. 1 shows the

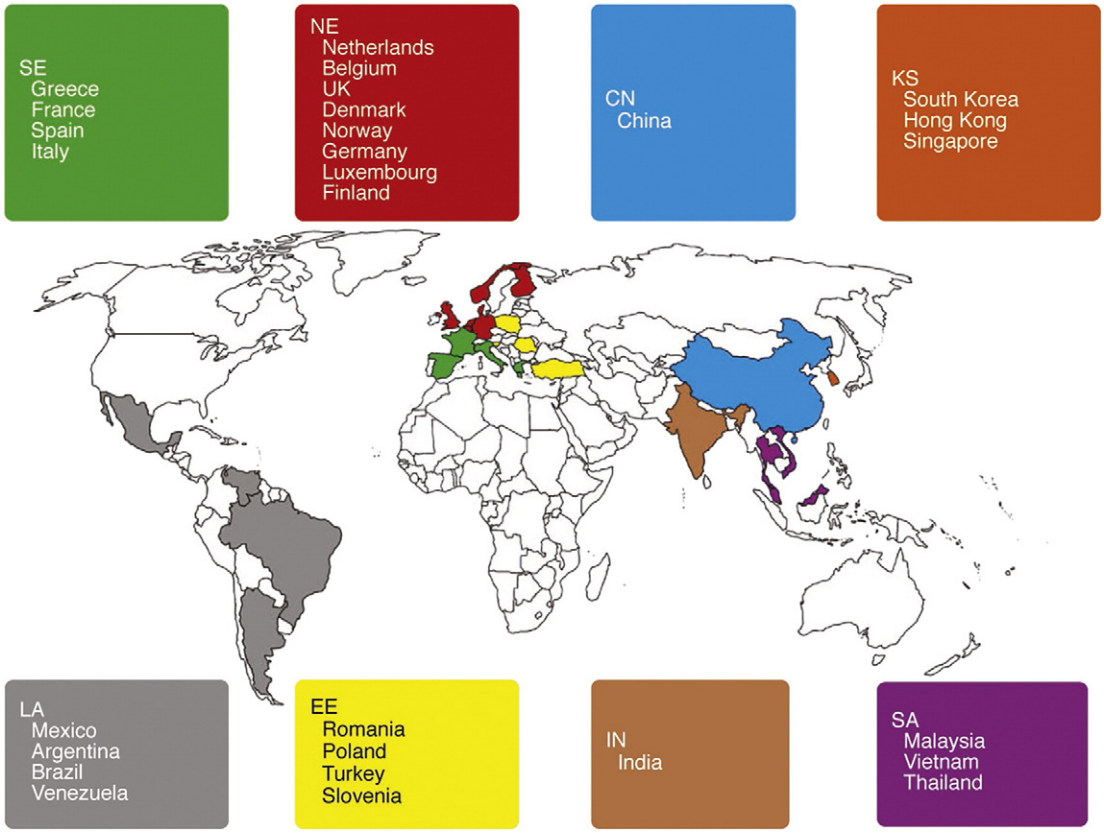

Fig. 1. Geographical distribution of EPICOR study. Patients were distributed across the following regions: Southern Europe ($n = 1124$), Northern Europe ($n = 1608$), Eastern Europe ($n = 1145$), Latin America ($n = 1066$), China ($n = 3961$), India ($n = 1482$), Southeast Asia ($n = 751$) and South Korea, Hong Kong and Singapore ($n = 422$). CN, China; EE, Eastern Europe; IN, India; KS, South Korea/Hong Kong/Singapore; LA, Latin America; NE, Northern Europe; SA, Southeast Asia; SE, Southern Europe.

Table 1
Patient and hospital characteristics.

	All patients	Southern Europe	Northern Europe	Eastern Europe	Latin America	China	SK/HK/Singapore	India	Southeast Asia
n, (%)	11,559 (100)	1124 (9.7)	1608 (13.9)	1145 (9.9)	1066 (9.2)	3961 (34.3)	422 (3.7)	1482 (12.8)	751 (6.5)
Patient characteristics at baseline									
Age, mean (SD)	58.9 (11.9)	**61.6 (12.7)**	59.6 (11.9)	57.7 (11.7)	58.7 (11.8)	59.4 (11.7)	59.1 (12.2)	*55.7 (11.2)*	59.2 (12.1)
Age ≥ 75, *n* (%)	1260 (10.9)	**221 (19.7)**	192 (11.9)	99 (8.7)	108 (10.1)	428 (10.8)	52 (12.3)	*74 (5.0)*	86 (11.5)
Male, *n* (%)	9370 (81.1)	917 (81.6)	*1238 (77.0)*	923 (80.6)	846 (79.4)	3231 (81.6)	358 (84.8)	**1259 (85.0)**	598 (79.6)
Hypertension, *n* (%)	5431 (47.5)	565 (50.8)	667 (42.2)	552 (48.9)	**625 (59.5)**	1950 (49.7)	207 (49.2)	*564 (38.6)*	301 (40.5)
Hypercholesterolemia, *n* (%)	2849 (25.8)	**521 (47.3)**	648 (41.9)	369 (34.0)	402 (41.4)	551 (14.5)	90 (21.6)	*84 (6.0)*	184 (25.0)
Diabetes mellitus, *n* (%)	2332 (20.5)	227 (20.5)	*192 (12.1)*	198 (17.7)	276 (26.4)	794 (20.3)	105 (24.9)	**421 (28.8)**	119 (16.1)
Smoking status, *n* (%)	3598 (33.3)	322 (30.2)	*410 (27.0)*	324 (29.8)	322 (32.0)	1214 (31.7)	135 (32.5)	**682 (59.1)**	189 (25.8)
Prior cardiovascular disease, *n* (%)	2194 (19.3)	213 (19.1)	325 (20.4)	**264 (23.2)**	240 (22.8)	820 (20.9)	63 (15.0)	*161 (11.5)*	108 (14.5)
Clinical status on admission									
Creatinine ≥1.2 mg/dL, *n* (%)	2469 (22.5)	*160 (15.2)*	298 (19.3)	176 (15.6)	195 (20.6)	944 (24.1)	124 (29.6)	341 (28.1)	**231 (30.8)**
Blood glucose >160 g/dL, *n* (%)	2730 (27.0)	269 (26.5)	*296 (22.3)*	290 (27.0)	264 (28.7)	956 (25.0)	**166 (45.5)**	334 (34.4)	155 (24.5)
Hemoglobin <13 g/dL, *n* (%)	2796 (25.6)	208 (19.8)	287 (18.8)	*201 (17.7)*	196 (21.3)	1048 (26.7)	78 (18.6)	482 (39.6)	**296 (39.7)**
Killip class									
I, *n* (%)	8714 (80.4)	923 (87.2)	**1159 (90.0)**	960 (85.6)	890 (86.7)	3027 (77.0)	296 (71.5)	*910 (70.8)*	549 (76.9)
II, *n* (%)	1386 (12.8)	96 (9.1)	*84 (6.5)*	123 (11.0)	94 (9.2)	638 (16.2)	61 (14.7)	**221 (17.2)**	69 (9.7)
III–IV, *n* (%)	738 (6.4)	39 (3.5)	*45 (2.8)*	39 (3.4)	43 (4.0)	264 (6.7)	**57 (13.5)**	155 (10.5)	96 (12.8)
Hospital characteristics[*]									
Coronary/intensive care unit, *n* (%)	11,371 (98.4)	1102 (98.0)	*1530 (95.2)*	1142 (99.7)	1039 (97.5)	3933 (99.3)	**422 (100)**	**1482 (100)**	721 (96.0)
Cath lab, *n* (%)	10,510 (90.9)	965 (85.9)	*1159 (72.1)*	1000 (87.3)	903 (84.7)	**3961 (100.0)**	417 (98.8)	**1482 (100)**	623 (83.0)
If yes, 24/7 PCI program, *n* (%)	9497 (82.2)	888 (79.0)	*828 (51.5)*	939 (82.0)	752 (70.5)	3756 (94.8)	395 (93.6)	**1441 (97.2)**	498 (66.3)
Cardiac surgery, *n* (%)	9100 (78.7)	508 (45.2)	*675 (42.0)*	740 (64.6)	922 (86.5)	3782 (95.5)	**417 (98.8)**	1449 (97.8)	607 (80.8)

p-Value was <0.001 in all comparisons between regions.
Bold text depicts the highest value of each row; italic text illustrates the lowest value.
Cath, catheterization; HK, Hong Kong; PCI, percutaneous coronary intervention; SD, standard deviation; SK, South Korea.
[*] Results are for number of patients, not number of hospitals (i.e., large hospitals contribute more patients).

distribution of patients across countries and regions: Southern Europe ($n = 1124$), Northern Europe ($n = 1608$), Eastern Europe ($n = 1145$), Latin America ($n = 1066$), China ($n = 3961$), India ($n = 1482$), Southeast Asia ($n = 751$) and South Korea/Hong Kong/Singapore ($n = 422$). Supplementary Table S1 illustrates each country contribution within regions.

3.1. Patient profile

Significant differences were observed in patient profile across regions (Table 1). Mean age ranged between 55.7 years (India) and 61.6 years (Southern Europe), diabetes mellitus (DM) between 12.1% (Northern Europe) and 28.8% (India) and smoking between 25.8% (Southeast Asia) and 59.1% (India). The percentage of male patients was above 75% in all regions. India showed a marked difference in cardiovascular risk factors compared with other regions, with the lowest percentage of older patients, those with hypertension, hypercholesterolemia and prior cardiovascular disease but the highest percentage of male patients, DM and cigarette smoking.

Other patient characteristics at admission, including blood test results and Killip class, are also illustrated in Table 1. Of note, elevated serum creatinine and Killip class II to IV were more common in all Asian regions compared with other regions.

3.2. Hospital profile

There were major regional variations in the type of hospitals recruiting patients. While almost all hospitals had a coronary/intensive care unit, only 51.5% of patients in Northern Europe were attended in hospitals with 24/7 percutaneous coronary intervention (PCI) program, in contrast to 97.2% of patients in India. The percentage of patients

Table 2
Use of resources.

	All patients	Southern Europe	Northern Europe	Eastern Europe	Latin America	China	SK/HK/Singapore	India	Southeast Asia
Pre-hospital care									
Pre-hospital ECG, *n* (%)	4883 (42.4)	463 (41.2)	**945 (58.8)**	452 (39.5)	263 (24.7)	2059 (52.0)	*92 (21.8)*	355 (24.0)	254 (33.8)
Time from first-symptom to ECG (in h), median (IQR)	3.0 (1.3, 5.4)	*1.7 (0.9, 4.0)*	1.9 (1.0, 4.3)	2.5 (1.1, 6.0)	3.0 (1.5, 7.3)	4.0 (1.5, 11.4)	2.1 (1.1, 5.4)	**6.1 (2.7, 15.5)**	2.5 (1.2, 5.4)
In-hospital care									
Length of hospital stay, median in days (IQR)	6 (4,10)	6 (4, 8)	5 (3, 7)	5 (4, 8)	5 (4, 8)	**10 (7, 13)**	5 (4, 7)	*4 (3, 5)*	*4 (3, 6)*
LVEF recorded, *n* (%)	8615 (74.5)	**1023 (91.0)**	1174 (73.0)	978 (85.4)	706 (66.2)	3007 (75.9)	358 (84.8)	*777 (52.4)*	592 (78.8)
LVEF <40%, *n* (%)	1193 (10.3)	*105 (9.3)*	176 (11.0)	152 (13.3)	138 (13.0)	197 (5.0)	63 (14.9)	**254 (17.1)**	108 (14.4)

p-Value was <0.001 in all comparisons between regions.
Bold text depicts the highest value of each row; italic text illustrates the lowest value.
ECG, electrocardiogram; HK, Hong Kong; IQR, interquartile range; LVEF, left ventricular ejection fraction; SK, South Korea.

attending hospitals with on-site cardiac surgery was higher in Asia compared with Europe and Latin America.

3.3. Pre-hospital and in-hospital management

Pre-hospital electrocardiogram (ECG) was more frequently recorded in Northern Europe (58.8%) and China (52.0%) compared with other regions, in particular, South Korea/Hong Kong/Singapore (21.8%). Time to ECG was significantly longer in India compared with all other regions (Table 2). Mean length of stay ranged between 4 (India and Southeast Asia) and 10 days (China). During hospitalization, left-ventricular ejection fraction (LVEF) assessment also varied widely among countries, with marked differences in patients with significant left ventricular systolic dysfunction (Table 2).

The type of reperfusion and delays to primary percutaneous coronary intervention (PPCI) and fibrinolysis are illustrated in Fig. 2 and Supplementary Table S2. Reperfusion therapy rates ranged between 53.9% (India) and 81.2% (Southern Europe). Specifically, PPCI, according to the investigators' reports, ranged between 24.8% (India) and 65.6% (Northern Europe) and fibrinolysis between 8.1% (China) and 34.2% (Southeast Asia). The median time to PPCI (defined as time from symptom onset to PCI, in h) ranged from 3.9 h (Northern Europe) to 20.9 h (India) and to fibrinolysis from 2.4 h (Southern Europe) and 6.3 h (India). However, in those patients who underwent PPCI with recorded timings (62.3% of them), percentages of PCI within the first 12 h ranged from 86.6% (Eastern Europe) to 37.7% (India) (Supplementary Table S2).

There were major variations across regions in regard to the key medications prescribed at discharge, as shown in Table 3. Dual

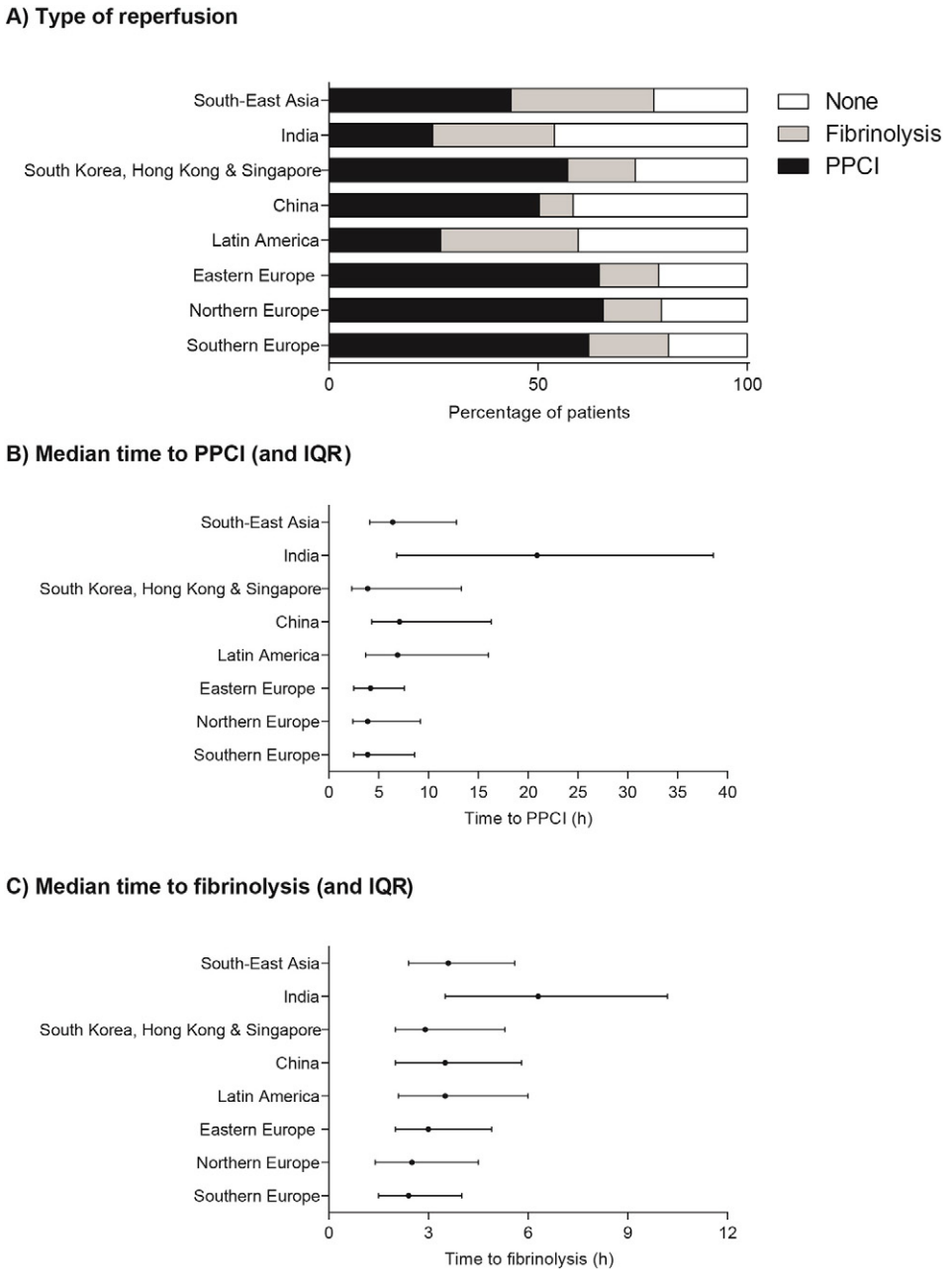

Fig. 2. Type of reperfusion therapy by region. Panel A depicts type of reperfusion; panel B shows median time (and its interquartile range) to PPCI; panel C illustrates median time (and its interquartile range) to fibrinolysis. IQR, interquartile range; PPCI, primary percutaneous coronary intervention.

Table 3
Medications used at discharge.

	All patients	Southern Europe	Northern Europe	Eastern Europe	Latin America	China	SK/HK/Singapore	India	Southeast Asia
Medication at discharge									
Antithrombotics									
DAPT, *n* (%)	10,574	1040	1489	1048	914	**3775**	396	*1206*	706
	(91.5)	(92.5)	(92.6)	(91.5)	(85.7)	**(95.3)**	(93.8)	*(81.4)*	(94.0)
Aspirin + clopidogrel	9771	891	1180	1014	866	**3773**	381	*961*	705
	(84.5)	(79.3)	(73.4)	(88.6)	(81.2)	**(95.3)**	(90.3)	*(64.8)*	(93.9)
Aspirin + prasugrel	766	146	**308**	11	48	*0*	15	238	*0*
	(6.6)	(13.0)	**(19.2)**	(1.0)	(4.5)	*(0.0)*	(3.6)	(16.1)	*(0.0)*
SAPT, *n* (%)	615	39	*46*	47	96	141	16	**205**	25
	(5.3)	(3.5)	*(2.9)*	(4.1)	(9.0)	(3.6)	(3.8)	**(13.8)**	(3.3)
Anticoagulant, *n* (%)	300	43	73	**50**	49	*14*	10	43	18
	(2.6)	(3.8)	(4.5)	**(4.4)**	(4.6)	*(0.4)*	(2.4)	(2.9)	(2.4)
Statin, *n* (%)	10,513	1070	**1536**	1068	984	3694	355	*1129*	677
	(91.0)	(95.4)	**(95.6)**	(93.3)	(93.4)	(93.5)	(84.3)	*(77.4)*	(90.2)
Beta-blockers, *n* (%)	8894	995	**1489**	1052	847	2867	351	864	*429*
	(76.9)	(88.5)	**(92.6)**	(91.9)	(79.5)	(72.4)	(83.2)	(58.3)	*(57.1)*
ACEI/ARB, *n* (%)	8239	897	1261	**987**	844	2598	341	*822*	489
	(71.3)	(79.8)	(78.4)	**(86.2)**	(79.2)	(65.6)	(80.8)	*(55.5)*	(65.1)
MRA, *n* (%)	1184	99	105	165	**159**	473	*23*	104	56
	(10.2)	(8.8)	(6.5)	(14.4)	**(14.9)**	(11.9)	*(5.5)*	(7.0)	(7.5)

p-Value was <0.001 in all comparisons between regions.
Bold text depicts the highest value of each row; italic text illustrates the lowest value.
Anticoagulants were defined as taking warfarin or dabigatran regardless of other medication. DAPT was defined as aspirin plus another oral antiplatelet agent, such as clopidogrel, prasugrel or ticlopidine. SAPT was defined as taking aspirin alone or ≥1 other antiplatelet agent that did not include aspirin.
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DAPT, dual antiplatelet therapy; HK, Hong Kong; MRA, mineralocorticoid receptor antagonist; SAPT, single antiplatelet therapy; SK, South Korea.

antiplatelet therapy (DAPT) and statins showed relatively high prescription rates in most regions, above 90%. Cilostazol was used as an antiplatelet treatment only in 1.8% of patients in Asia, with relatively high rates of use in South Korea/Hong Kong/Singapore (12.1%).

Large variation in the use of beta-blockers and the use of either angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) was found, particularly between Eastern Europe (91.9% and 86.2%, respectively) and India (58.3% and 55.5%, respectively). The use of mineralocorticoid receptor antagonist (MRA) was particularly infrequent in South Korea/Hong Kong/Singapore (5.5%), despite having one of the highest percentages of patients with LVEF <40% (14.9%).

3.4. Post-discharge mortality

Two-year post-discharge mortality rates (cumulative incidence) ranged between 2.5% in Northern Europe and 7.4% in Latin America (Fig. 3A). Fig. 3B and Supplementary Table S3 illustrate that these regional variations in mortality persisted after adjustment for 16 established prognostic factors, with South Korea/Hong Kong/Singapore being the region with the lowest adjusted 2-year mortality rate (2.7%, 95% confidence interval [CI]: 1.1–4.4) and Latin America showing the highest (8.1%, 95% CI: 6.2–10), compared with other regions.

4. Discussion

Our descriptive analysis shows that, in spite of the dissemination of similar recommendations by practice guidelines worldwide, large regional variations in clinical practice patterns for patients with STEMI can still be found. We also observed significant differences across regions in post-discharge mortality risk. Overall, the results of our study suggest that there is substantial room for improvement in the management of STEMI and for improving patient outcomes following hospital discharge globally. However, different targets for intervention may be needed for different regions.

4.1. Major findings

Unsurprisingly, patient characteristics on admission differed between regions, reflecting regional differences in cardiovascular risk at a population level. While Southern Europe had the highest percentage of patients aged ≥75 years, the percentage in India was four-fold less, but with a markedly elevated proportion of patients with DM and currently smoking. EPICOR was designed to enrol a representative sample of hospitals at a national level [13]. However, hospitals in Asia were, overall, better equipped than those participating in European and Latin American regions. This might have had an influence on the rate of PCI procedures and potentially on patient outcomes [16].

Early reperfusion with PPCI or fibrinolytic therapy is a cornerstone in the treatment of STEMI [17,18]. However, up to a third of patients did not receive reperfusion therapy, with significant geographical differences between regions as well as in the preferred type of reperfusion therapy. Large inequalities in the use of reperfusion therapy for patients with STEMI have previously been reported in randomized trials and registries [6,7,10,19,20]. Large differences in the use of thrombolytic therapy (highest in India, Latin America and Southeast Asia) may be explained by differences in healthcare system organization. The low usage of reperfusion therapy and, in particular, long delays in India are of concern. Geography, weather, local resources and the organization of regional health system networking may all contribute [21]. Regardless of the long delays experienced in India, there is still substantial variation in the median times to PPCI across the other regions that need to be analyzed and corrected. These differences should not be interpreted from an economic perspective only, i.e., regional income level, but by other system features that may work as opportunities for improvement, such as the level of coordination within networks, availability and preparation for thrombolysis administration when needed, availability of adequately prepared transport systems for the local geography and weather, traffic issues and preferential pathways or health education at a population level. Without having a global and multidisciplinary approach tackling all factors involved in STEMI networks, it will be very difficult to reach evidence-based time frames needed for efficient PPCI programs at a global level [22]. Thus, this represents a sizeable health issue worldwide, with vast implications in both mortality and morbidity.

In patients with STEMI, clinical guidelines recommend a variety of medications at discharge that are considered quality indicators: antithrombotics, statins, beta-blockers, ACE inhibitors or ARBs, and MRAs [23]. The gap between evidence-based guideline recommendations

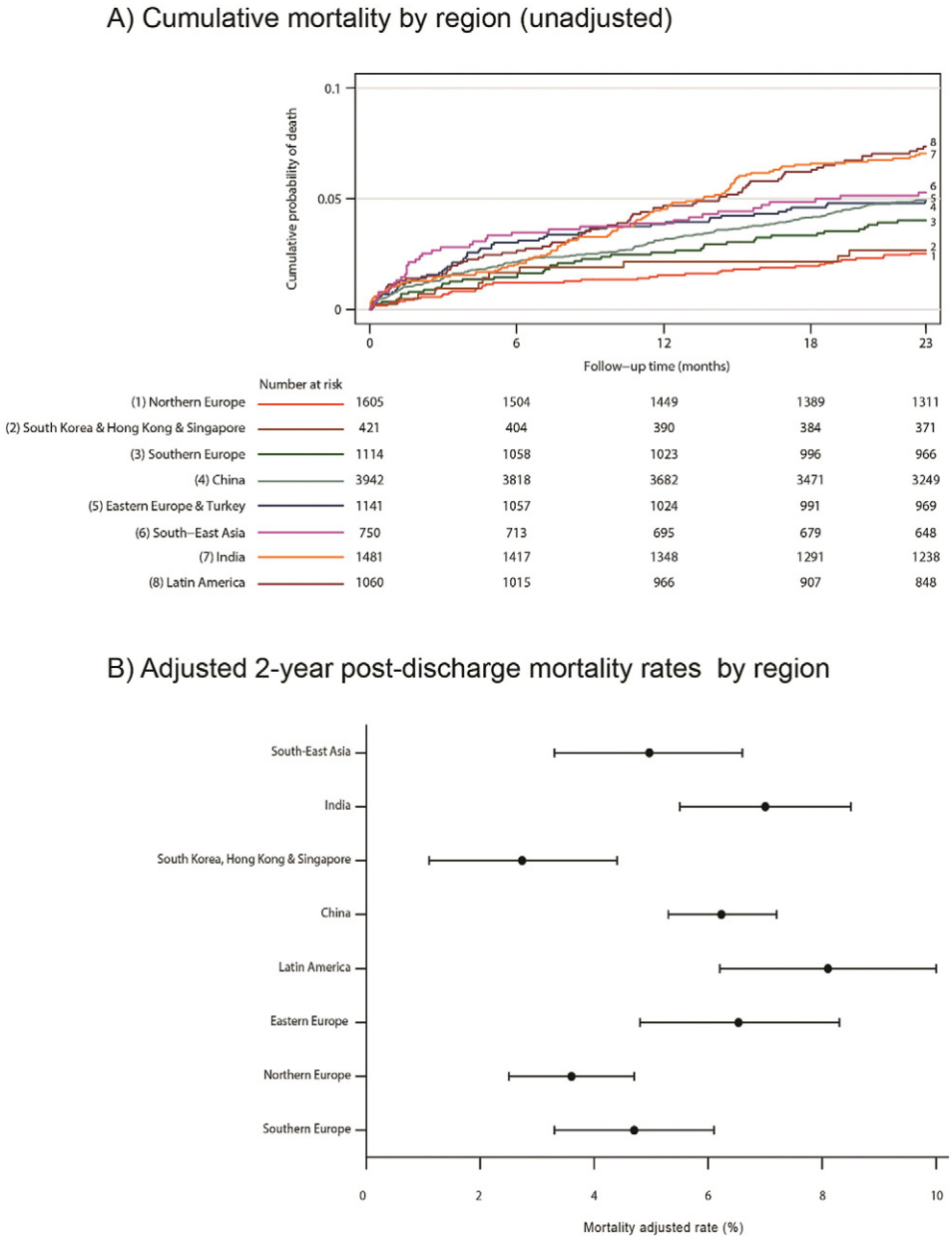

Fig. 3. Mortality by region. Panel A depicts unadjusted mortality; panel B illustrates adjusted mortality for 16 key factors.

and current practice is evident in our study, although we found a reasonable proportion of patients were discharged on DAPT and statins, above 90% in most regions. In the Global Registry of Acute Coronary Events (GRACE), the use of aspirin, statins and ACE inhibitors varied only modestly by geographical region compared with other treatments [16]. Reasons for underuse need to be clarified, although the Prospective Urban Rural Epidemiology (PURE) study has implicated availability and affordability of medications, patients' attitudes and knowledge towards preventative medicine, access to healthcare providers and prescribing patterns [24].

The large variation in regional mortality is a matter of concern. Whether these differences reflect differences in patient characteristics, quality of care or, to some extent, patient selection is not clear. It is known that STEMI outcomes vary considerably worldwide, with differences in prognosis both within [8] and between countries [25]. Consistent with our results, Latin America has already been described as a region with a higher adjusted mortality risk compared with other regions such as Western Europe, Eastern Europe and North America [5]. In RCTs, discrepancies in treatment effect across regions [26] can partially be explained by differences in patient cohorts or management strategies. However, our data reveal an unexplained difference even after adjustment by confounding factors. This disparity may be partly explained by differences in the following four factors. Firstly, we recorded differences in patients' cardiovascular risk factors, which may be explained by different ethnic and regional backgrounds, encompassing both genetic and cultural contexts [3]. Secondly, differences in individual and regional socioeconomic status, either within [27] or between countries [28], are linked to mortality following STEMI. Thirdly, performance of national or regional healthcare systems (e.g., pre-hospital care access, STEMI networks, and access to medications) as well as hospital characteristics (e.g., catheterization facilities, 24/7 PCI programs, and number of beds) may also lead to health disparities [29]. Finally, there may be differences in local standard clinical practice in terms of the dosage and duration of post-discharge medication, approach to up-titration and changes in medication during the follow-up period, and patient adherence to drug regimens.

India deserves special attention in both the assessment of patient management and outcomes. Despite having the most PPCI-capable centres, it has the lowest rate of PPCI and the longest delays. Likewise, its adjusted post-discharge mortality was lower than in Latin America despite having a lower compliance to evidence-based treatment, as represented by both reperfusion and post-discharge medication. Several reasons may explain these characteristics or special features.

First, the long distances and the local healthcare system may explain the time delays in reperfusion [30]. Second, Indian patients were younger and showed a much higher prevalence of current smoking than in any other region. Third, a potential cohort survival effect given the nature of our inclusion criteria – the sickest patients may have died in-hospital and thus not had been eligible for our cohort. Of note, as important as assessing the causes of India's singularity is seeking for potential ground for outcome improvement. We highly encourage those initiatives aimed to narrow the disparities in patient management and outcomes between regions, such as the one recently published demonstrating that a hub-and-spoke model in South India improved STEMI care through greater use of PCI [31].

4.2. Strengths and limitations

Several considerations are important in interpreting our findings. Despite being adjusted by 16 known predictors of 2-year mortality, this study has limitations inherent to an analysis of observational data: differences on mortality across regions due to a potential patient selection bias cannot be completely ruled out. While both studies were designed to recruit representative patients from representative centres in each country, we cannot rule out bias in regard to the type of hospitals participating, which may not necessarily represent clinical practice in that geographical area. Hence, caution must be expressed in extrapolating our results to non-EPICOR recruiting centres. Moreover, regional grouping is needed for simplicity but is a somewhat artificial construct. Since there are many different approaches to forming geographical groupings, we considered countries' similarities in practice patterns in addition to geographical neighbourhood, but this cannot capture potential within-country and within-region variability. Finally, our study lacks an assessment of other regions such as Africa, the Middle East and North America.

A major strength of our study is that we assessed a comprehensive set of patient and hospital characteristics, practice patterns and adjusted 2-year mortality across an extended range of regions. The main evidence-based therapies for patients with STEMI, advocated by clinical guidelines, were compared across territories in our real-world clinical practice registry. Other strengths include a large sample size and a broad worldwide representativeness of our findings.

4.3. Future implications

EPICOR has provided a unique opportunity to investigate regional variations. This study should be interpreted as a preliminary step in mapping those gaps and needs that should be addressed worldwide. There is a global lack of continuous national quality of care and outcome registries for acute myocardial infarction, such as those present in the UK (NICOR/MINAP) and Sweden (SWEDEHEART/RIKS-HIA) [8]. National efforts are needed to improve the care and outcomes for patients with STEMI using national registries, including those in China [4], the USA [32], and other countries.

Our findings have several important research, policy and clinical implications. Firstly, they may help in the interpretation of geographical variations in outcomes and treatment effect observed in RCTs. Secondly, they can help focus quality improvement initiatives in individual countries and regions by targeting specific proven therapies that are underused. Lastly, although we lacked data on timing from symptom onset to PCI in 37.8% of STEMI patients, our available data suggest that delays to reperfusion are still too frequent. Reducing time to reperfusion is one of the goals to further improve outcomes, with room for additional enhancements in healthcare provision that should translate into clinical benefits.

4.4. Conclusions

Substantial geographical variation exists worldwide with regard to patient profile, practice patterns and post-discharge prognosis in patients with STEMI. Therapies with a proven benefit for STEMI are underused despite strong evidence and guideline recommendations. Our results may help to guide clinicians, researchers and policymakers in the commitment to reduce these disparities as well as to close the gap between evidence-based guideline recommendations for STEMI and current regional practice patterns.

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Conflicts of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2017.07.039.

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