

Implementation of a Regional Network for ST-Segment–Elevation Myocardial Infarction (STEMI) Care and 30-Day Mortality in a Low- to Middle-Income City in Brazil: Findings From Salvador’s STEMI Registry (RESISST)

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Background—Few data exist on regional systems of care for the treatment of ST-segment–elevation myocardial infarction (STEMI) in developing countries. Our objective was to describe temporal trends in 30-day mortality and identify predictors of mortality among STEMI patients enrolled in a prospective registry in Brazil.

Methods and Results—From January 2011 to June 2013, 520 patients who received initial STEMI care at 23 nonspecialized public health units or hospitals, some of whom were transferred to a public cardiology referral center, were identified through a regional STEMI network supported by telemedicine and the local prehospital emergency medical service. We stratified patients into five 6-month periods based on presentation date. Mean age (\pm SD) of patients was 62.0 (\pm 12.2) years, and 55.6% were men. The mean Global Registry of Acute Coronary Events (GRACE) score was 145 (\pm 34). Overall mortality at 30 days was 15.0%. Use of dual antiplatelet therapy and statins increased significantly from baseline (January 2011) to period 5 (June 2013): 61.8% to 93.6% ($P<0.001$) and 60.4% to 79.7% ($P<0.001$), respectively. Rates of primary reperfusion also increased (29.1%–53.8%; $P<0.001$), and more patients were transferred to the referral center (44.7%–76.3%; $P=0.001$). Thirty-day mortality rates decreased from 19.8% to 5.1% ($P<0.001$). In multivariable analysis, factors independently associated with 30-day mortality were higher GRACE score, history of previous stroke, lack of transfer to the referral center, and lack of use of optimized medical therapy.

Conclusions—Implementation of a regional STEMI system was associated with lower mortality and higher use of evidence-based therapies. (*J Am Heart Assoc.* 2018;7:e008624. DOI: 10.1161/JAHA.118.008624.)

Key Words: Brazil • mortality • regional care • registry • ST-segment–elevation myocardial infarction

Coronary heart disease, including the acute manifestation of acute myocardial infarction, is the leading cause of mortality and disability globally.^{1,2} In Brazil specifically, acute coronary syndromes are the third ranking cause of hospitalization, and mortality rates of 15% to 20% following ST-segment–elevation acute myocardial infarction (STEMI) have

been reported.^{3,4} Large gaps in STEMI care remain in Brazil. Compared with other countries, there is a striking time delay from onset of symptoms to presentation at the emergency department and delay to the first ECG.⁵ In addition, the populations of low- and middle-income countries such as Brazil are more exposed to cardiovascular risk factors and

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Clinical Perspective

What Is New?

- Few data exist on regional systems of care for the treatment of ST-segment–elevation myocardial infarction (STEMI) in developing countries.
- We investigated temporal trends in 30-day mortality and identified predictors of mortality among STEMI patients enrolled in a prospective registry in Brazil.

What Are the Clinical Implications?

- The implementation of an integrated regional network to establish rapid reperfusion and use of evidence-based therapies for STEMI patients in Salvador, Brazil is feasible and might improve survival.
- There are still opportunities to improve clinical care for STEMI patients in underdeveloped geographic regions of the world.
- This approach should be tested in other regions of the world to potentially improve the care of patients with STEMI.

have less access to health care, including emergency medical services. Globally, several factors contribute to the lack of optimization in the management of STEMI relative to the recommendations of the main national and international guidelines.^{6–8} In fact, approximately one third of the patients eligible for reperfusion therapy in the United States do not achieve recommended door-to-device time of <120 minutes.⁹

Worldwide, the implementation of integrated regional care networks for STEMI has improved quality of care with increased rates and speed of reperfusion.^{10,11} However, socioeconomic status and initial treatment at nonspecialized health units are both associated with poorer outcomes. These factors are particularly relevant to developing countries. The Registry of STEMI care of Salvador (RESISST) is a Brazilian registry that includes patients with STEMI who were first seen in small healthcare units or tertiary hospitals in the country's public Unified Health System. Populations of STEMI patients such as this have been poorly represented in existing registries.⁵ The primary objective of RESISST was to identify predictors of 30-day mortality among patients with STEMI from a low- to middle-income population. Secondly, we assessed how implementation of an integrated regional care network for STEMI patients was associated with the use of evidence-based medications and with clinical outcomes.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure as this was not

planned as part of our original institutional review board approval.

Study Population

RESISST was a prospective observational registry that included patients who presented with STEMI and were treated in the public health system of Salvador, Brazil from January 2011 to June 2013. Participants were at least 18 years old; were evaluated for STEMI in a public health unit in Salvador, by the prehospital team of the Mobile Emergency Care Service of the metropolitan region of Salvador, or directly at general hospitals, with clinical and electrocardiographic characteristics suggestive of STEMI; had confirmation of diagnosis of myocardial infarction by cardiac necrosis markers, or had sudden cardiac death at presentation provided that presenting signs and symptoms were consistent with STEMI even without cardiac necrosis marker confirmation. STEMI was diagnosed according to the universal definition: symptoms suggestive of myocardial ischemia and ST-segment–elevation >2 mm in V2–V3 or >1 mm in other contiguous leads, or a new (or presumed-to-be-new) left bundle branch block.^{8,12} Patients with evidence of STEMI up to 48 hours after coronary artery bypass graft surgery, percutaneous coronary intervention (PCI), or any other surgical procedure were excluded.¹³

Human subject research regulations were observed in compliance with Resolution 466/12 of the National Health Council, through the National Committee for Ethics in Research. This study was approved by the Research Ethics Committee of Escola Bahiana de Medicina e Saúde Pública (no. 020/2011). All patients or, if unable, their guardians signed the informed consent form. No patients were excluded from the study because of lack of informed consent.

Regional Integrated Care Network for STEMI

In Salvador, all healthcare units, the Mobile Emergency Care Service, some participating hospitals, and the Telemedicine Center are interconnected through a Regional Integrated Care Network for STEMI. The complete description of the network has been previously published.⁵ In summary, once a patient with suspected STEMI arrives at the healthcare unit or at a participating hospital, and the first ECG is performed, the tracing is forwarded to the STEMI network physicians via the Telemedicine Center, which is responsible for identifying ECG findings of STEMI. The telemedicine system is implemented in 85% of the public healthcare units of Salvador, including all mobile prehospital ambulances, 16 nonspecialized prehospital fixed emergency units (emergency care units), and 7 general hospitals. Patients who first present at a nonspecialized prehospital or hospital may be transferred to 1 of 2 cardiology reference centers (CRCs) with ability to perform primary PCI.

Data Collection

Demographic characteristics and presence of comorbidities/risk factors such as smoking (current or previous), hypertension, dyslipidemia, diabetes mellitus, family history of coronary artery disease, physical inactivity, and body mass index were collected. Information on race was self-reported. The following characteristics of the STEMI event were recorded: clinical symptoms at presentation, Global Registry of Acute Coronary Events (GRACE) risk scores, Killip class at presentation, and cardiac markers (creatinine kinase-MB fraction, troponin) peak values. Typical symptoms of acute coronary syndrome were defined as chest pain or discomfort (burning or oppressive) located in the precordial region, with or without radiation to the shoulder and/or left arm, right arm, neck, or jaw, often accompanied by diaphoresis, nausea, vomiting, or dyspnea. Atypical symptoms were defined as malaise, indigestion, weakness or sweating, without chest pain, or pain localized in the neck, back, jaw, or head, followed by other symptoms such as weakness, sweating, nausea, dyspnea, or cough. Additionally, echocardiography and coronary angiography data were collected when available. Times were documented for the time of symptoms onset, presentation at a nonspecialized prehospital or hospital, first ECG performed, and primary reperfusion (needle time or balloon time). Presentation was deemed to have occurred in nonregular hours when it occurred between 8 PM and 8 AM Monday through Thursday or between 8 PM on Friday and 8 AM on Monday. To calculate door-to-needle times and door-to-balloon times, the time of the first presentation was used as the reference time point. Data were collected on the drugs administered in the acute phase (first 24 hours), transfer to the CRC, primary reperfusion therapy (use and type of reperfusion), in-hospital complications, and discharge medications. Data on contraindication to therapies were not systematically collected, but current guidelines recommendations and contraindications to evidence-based therapies were used to guide physicians' decisions. Primary PCI was defined as when PCI was performed in the first 12 hours following STEMI as primary reperfusion therapy. We also examined the use of rescue and facilitated PCI procedures. Regarding the clinical management performed as an adjuvant to reperfusion, optimal medical therapy was defined as the concomitant use of all of the following: aspirin, P2Y12 antagonist, β -blocker, statin, and angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. Patients were treated according to physician discretion.

Follow-Up

Patient follow-up was performed by visiting the health unit or hospital where the patient was first seen. At 30 days after the event, the patient, guardian, or family member was contacted

by phone. At that time, information on mortality, morbidity, and echocardiogram results were collected. Mortality outcome was obtained through the Death Information System.¹⁴

Statistical Analysis

Categorical variables are expressed as frequencies and percentages, and compared using χ^2 test or Fisher exact test. Continuous variables with normal distribution are presented as mean and SD, and are compared using the Student *t* test for independent samples. Continuous variables with non-normal distribution are presented as median and quartiles (interquartile range), and are compared with a nonparametric Mann–Whitney test.

Multiple imputation was used for missing data. A total of 95.8% of eligible variables had at least 1 missing data, and 69.8% of patients had at least 1 missing variable. The percentage of missing data per variable ranged from 0.2% to 28.1%, with a missing completely at random pattern (test of Little, $P=0.369$). Six cases in which information about mortality was missing were used for the imputations, but not in the final analysis.

Multivariable analysis was performed to identify factors independently associated with 30-day mortality using multiple logistic regression, with results expressed in odds ratios (OR) and their respective 95% confidence intervals (CI). The model was adjusted for race (white versus nonwhite), diabetes mellitus, dyslipidemia, previous acute myocardial infarction, previous stroke, type of pain at presentation (typical versus atypical versus absent), dyspnea at presentation, STEMI wall (anterior versus nonanterior), admission to a CRC, GRACE score, primary reperfusion (regardless of the method, thrombolysis or primary angioplasty), and 6-month time period. GRACE score was included as a variable to adjust for the baseline risk of the patient. The potential confounding variables not included in the calculation of the GRACE score, identified in univariable analysis with *P* values up to 0.10, were included in the multivariable models. Collinearity was assessed by the examination of the model variables correlation coefficients and Tolerance/Variance Inflation Factor values. The assumption was met for the variables included. A landmark analysis was conducted to minimize survivor bias. The landmark method was used to evaluate the effect of very-early (24-hour) death as a time-dependent variable on a “delayed” outcome (30-day death).

For the analysis of treatment patterns over time, we used 6-month periods as unit of time. Thus, the study comprised the patients who first presented with STEMI at a nonspecialized prehospital or hospital unit until June 2013. The Kaplan–Meier method was used to estimate the survival functions; the curves were estimated by grouping patients according to the variables selected for the study using log-rank test (Mantel–Cox) for comparison. Hazard ratios were calculated with 95% CI, according to a Cox proportional hazards regression model.

The proportionality of the Cox model was checked by graphical methods and based on Schoenfeld residuals testing. Linearity of the continuous variables included in the final model was verified by graphic analysis of Martingale residuals, and calculations were based on a model that did not enter in the equation the variable under analysis.

All tests were 2-tailed, and $P < 0.05$ was considered statistically significant. Data were analyzed using Statistical Package for Social Sciences (version 17.0; SPSS, Chicago, IL).

Results

Baseline Characteristics

During the study period, 520 patients presenting with STEMI at participating public health units or hospitals in Salvador were included. Follow-up information was not available for 6.4% (N=33). Demographic and clinical characteristics of the study

population are shown in Table 1, both overall and stratified by 30-day mortality status. The mean age (\pm SD) of the population was 62.0 (\pm 12.2) years, 55.6% were male, and 83.9% were nonwhite. Overall, 76.1% had hypertension, and 36.5% had diabetes mellitus. The mean GRACE score was 145 (\pm 34). Patients who died in the first 30 days following STEMI (N=78) were older than those who survived (N=442). The patients who died within 30 days following STEMI had a higher prevalence of diabetes mellitus, previous acute myocardial infarction, or stroke. Patients who died within 30 days of STEMI also had a higher mean GRACE score (170.1 versus 140.7 points; $P < 0.001$) at presentation compared with 30-day survivors.

Clinical Presentation

Overall, 18.2% of the patients had no pain or had atypical chest pain at presentation, and 52.5% were initially treated at a nonspecialized hospital, while 47.5% were initially treated at

Table 1. Baseline Characteristics of Patients in RESISST

	Overall (N=520)	30-D Mortality		P Value
		Yes (N=78)	No (N=442)	
Demographic characteristics				
Age (mean \pm SD), y	62.0 (\pm 12.2)	66.6 (\pm 12.0)	61.1 (\pm 12.0)	<0.001
Male sex	289/520 (55.6)	42/78 (53.8)	247/442 (55.9)	0.739
Nonwhite race*	350/417 (83.9)	32/44 (72.7)	318/373 (85.3)	0.032
Comorbidities/risk factors				
Hypertension*	389/511 (76.1)	63/76 (82.9)	326/435 (74.9)	0.134
Diabetes mellitus*	182/499 (36.5)	35/70 (50.0)	147/429 (34.3)	0.011
Dyslipidemia*	187/499 (43.9)	16/48 (33.3)	171/387 (44.1)	0.156
Previous stroke/TIA*	80/450 (17.8)	22/60 (36.7)	58/389 (14.9)	<0.001
Previous acute MI*	63/447 (14.1)	14/57 (24.6)	49/390 (12.6)	0.015
Previous myocardial revascularization (CABG or PCI)*	20/449 (4.5)	4/54 (7.4)	16/387 (4.1)	0.289
Smoking (current or previous)*	268/448 (59.8)	33/53 (62.3)	235/395 (59.5)	0.699
Physical inactivity*	283/415 (68.2)	30/43 (69.8)	253/372 (68.0)	0.894
Family history of CAD*	155/408 (38.0)	12/41 (29.3)	143/367 (39.0)	0.815
Clinical presentation				
Typical chest pain*	409/500 (81.8)	53/72 (73.6)	356/428 (83.2)	0.052
Killip class ≥ 2 *	149/439 (34.0)	33/60 (55.0)	116/378 (30.7)	<0.001
Mean systolic blood pressure (\pm SD), mm Hg	145.0 (\pm 34.9)	133.4 (\pm 34.7)	146.9 (\pm 34.5)	0.004
Mean GRACE score (\pm SD)	145.0 (\pm 34.0)	170.1 (\pm 37.9)	140.7 (\pm 31.3)	<0.001
Presented <12 h of symptoms*	317/375 (84.5)	43/48 (89.6)	274/327 (83.8)	0.300
ECG				
Left bundle branch block*	18/451 (4.9)	7/63 (11.1)	11/308 (3.6)	0.012
Anterior wall MI*	292/492 (59.3)	55/76 (72.4)	237/416 (57.0)	0.012

Frequencies are reported as n/total (%), unless otherwise specified. CABG indicates coronary artery bypass graft; CAD, coronary artery disease; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; PCI, percutaneous coronary intervention; RESISST, the Registry of STEMI Care of Salvador; SD, standard deviation; TIA, transient ischemic attack.

*Data are provided only for the group of patients for whom information was collected. Numerator/denominator=variable/total number excluding missing data.

prehospital units (Figure 1). More than half (60.2%) were transferred to a CRC, and intensive care unit hospitalization occurred for 51.4%. Presentation during nonregular hours occurred in 67.9% of the cases (Table 2).

The median time between the onset of chest pain and initial presentation was 180 minutes (interquartile range: 66–430). Overall, 15.5% of patients first presented >12 hours after the onset of chest pain. The median time interval between presentation and first ECG was 159 minutes (interquartile range: 70–379).

Management of STEMI

Optimal medical therapy was less frequently administered to patients who died within 30 days compared with those who survived (13.2% versus 32.3%, $P=0.001$) (Table 3). Overall,

40.7% (N=209) underwent primary reperfusion therapy (fibrinolysis in 80 patients and primary PCI in 129 cases). Among patients who underwent primary PCI, door-to-balloon median time was 419 minutes (interquartile range: 307.5–535), and the mortality rate was lower than for patients without reperfusion. Among those who underwent fibrinolysis, door-to-needle median time was 178.5 minutes (interquartile range: 120–332), and there was no difference in 30-day mortality compared with nonreperfusion patients. Rescue coronary angioplasty was performed in 18 patients and facilitated coronary angioplasty in 2 patients. Systolic and diastolic blood pressure were not statistically different between patients who received optimal medical therapy and those who did not (144.2 ± 35.6 mm Hg versus 146.6 ± 32.6 mm Hg; $P=0.56$; and 87.7 ± 20.0 versus 91.0 ± 22.6 ; $P=0.15$). No differences were observed in the

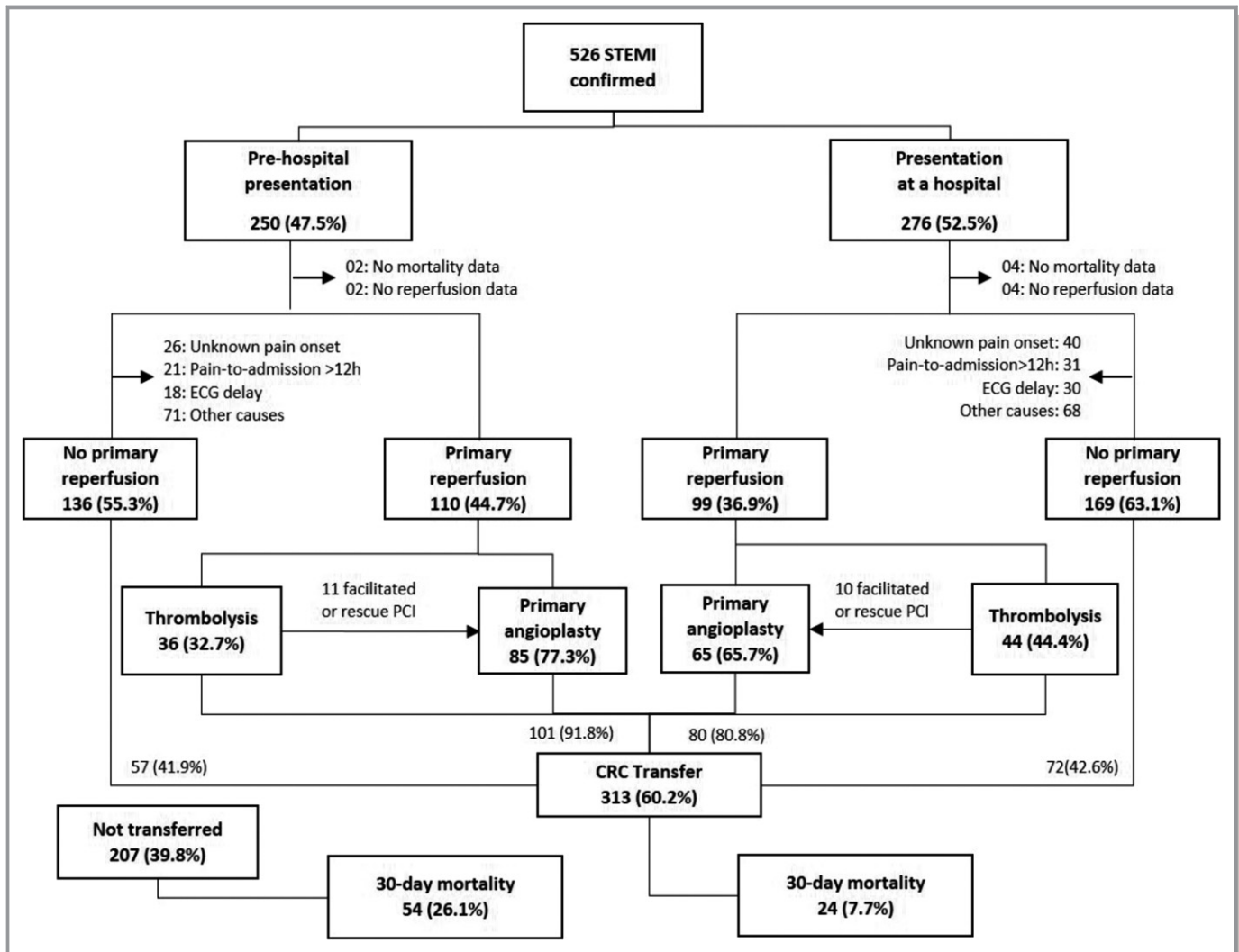


Figure 1. Flow chart for patients in RESISST (the Registry of STEMI care of Salvador), depicting the first medical contact health unit, reperfusion status, transfer to cardiology reference center (CRC), and outcomes. ECG indicates electrocardiogram; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction.

Table 2. Patient Pathway and ICU Admission

	Overall (N=520)	30-D Mortality		P Value
		Yes (N=78)	No (N=442)	
Initial prehospital or hospital unit				
Presentation	272/520 (52.3)	42/78 (53.8)	230/442 (52.0)	0.768
Presentation at nonregular hours*	318/468 (67.9)	46/66 (69.7)	272/402 (67.7)	0.743
Transfer to CRC	313/520 (60.2)	24/78 (30.8)	289/442 (65.4)	<0.001
ICU admission*	225/438 (51.4)	23/63 (36.5)	202/375 (53.9)	0.011
Median number of days (IQR)	2.0 (2.0–4.0)	2.5 (1.0–4.5)	2.0 (2.0–4.0)	0.398

Frequencies are reported as n/total (%), unless otherwise specified. CRC indicates cardiology reference center; IQR, interquartile range; ICU, intensive care unit.

*Data are provided only for the group of patients for whom information was collected. Numerator/denominator=variable/total number excluding missing data.

proportion of patients with Killip class \geq II at admission between patients who received optimal medical therapy and those who did not (33.6% versus 34.1%; $P=0.91$).

Coronary angiography was performed in 294 (56.5%) patients presenting with STEMI. Coronary stenosis \geq 70% was identified in the right coronary artery territory in 151 (51.4%), the left anterior descending artery territory in 168 (57.1%), and in the left circumflex system in 108 (36.8%).

The number of patients with left main coronary artery stenosis $>$ 50% or stenosis of the proximal anterior descending artery $>$ 70% was 12 (4.1%) and 62 (21.1%), respectively.

Our temporal analysis (January 2011–June 2013) showed no differences over time in age, sex distribution, comorbidities, symptoms at presentation, or average GRACE score. Regarding medical treatment in the acute stage, there was an

Table 3. Management of STEMI in RESISST Prehospital and Hospital Units

	Overall (N=520)	30-D Mortality		P Value
		Yes (N=78)	No (N=442)	
Treatment of the acute phase (<24 h)				
Morphine*	273/501 (54.5)	33/73 (45.2)	240/428 (56.1)	0.085
Supplemental oxygen*	433/515 (84.1)	58/78 (74.4)	375/437 (85.8)	0.011
Nitrate*	402/513 (78.4)	52/78 (66.7)	350/435 (80.5)	0.006
Aspirin*	486/512 (94.9)	70/77 (90.9)	416/435 (95.6)	0.092
β -Blocker*	346/516 (67.4)	48/77 (62.3)	298/436 (68.3)	0.299
P2Y12 inhibitor*	419/513 (81.7)	56/77 (72.7)	363/436 (83.3)	0.028
Anticoagulation*	364/514 (70.8)	57/77 (74.0)	307/437 (70.3)	0.502
ACEi or ARB*	280/513 (54.6)	33/78 (42.3)	247/435 (56.8)	0.018
Statin*	348/512 (68.0)	42/76 (55.3)	306/436 (70.2)	0.010
Optimal medical therapy*	151/512 (29.5)	10/76 (13.2)	141/436 (32.3)	0.001
Reperfusion				
Primary reperfusion (fibrinolysis or primary PCI)	209/514 (40.7)	20/77 (26.0)	189/437 (43.2)	0.004
Fibrinolysis [†]	80/387 (20.7)	11/68 (16.2)	69/319 (21.6)	0.308
Median door-to-needle time (IQR), min	178.5 (120–332)	265 (30.5–372.5)	177 (120–333.5)	0.817
Primary PCI [‡]	129/434 (29.7)	9/66 (13.6)	120/368 (32.5)	0.002
Median door-to-balloon time (IQR), minutes	419 (307.5–535)	462.5 (345–580)	419 (302–530)	0.817

Frequencies are reported as n/total (%), unless otherwise specified. ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; IQR, interquartile range; PCI, percutaneous coronary intervention; RESISST, the Registry of STEMI care of Salvador; STEMI, ST-segment–elevation myocardial infarction.

*Data are provided only for the group of patients for whom information was collected. Numerator/denominator=variable/total number excluding missing data.

[†]Fibrinolysis vs no primary reperfusion (excluding primary PCIs).

[‡]Primary PCI vs no primary reperfusion (excluding fibrinolysis, as well as rescue and facilitated PCIs).

increase in the prescription of dual antiplatelet therapy (aspirin and clopidogrel), from 61.8% in the first half of 2011 to 93.6% in the same period of 2013 ($P<0.001$), as well as in statin use, from 60.4% to 79.7% ($P=0.001$) (Figure 2). Additionally, the use of optimal medical therapy increased from 21.7% to 30.8% ($P=0.078$). There was no increase in the use of β -blockers and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in the acute phase of STEMI throughout the study period. Increased use of primary reperfusion (29.1%–53.8%; $P<0.001$) was also observed between the first half of 2011 and the same period of 2013, with a greater increase in primary PCI than in fibrinolysis during this period. There was also an increase in transfer to a CRC (44.7%–76.3%; $P=0.001$). These increases were linear and consistent over time.

Mortality at 30 Days

In total, 78 (15.0%) patients died of any cause within 30 days following STEMI, of whom 73 died in the hospital. The 30-day

mortality rate was lower among the patients transferred to a CRC compared with those who were not (4.5% versus 28.4%; $P<0.001$). A landmark analysis was conducted and similar results were seen when only patients who survived the first 24 hours after STEMI were included (a total of 7 patients died in the first 24 hours). In multivariable analysis, factors independently associated with 30-day mortality were the following: GRACE score (OR 1.195, per 10 units increase), previous stroke (OR 2.626), transfer to a CRC (OR 0.320), and use of optimal medical therapy (OR 0.406) (Table 4). The full model results are presented in Table 5. Primary reperfusion was not significantly associated with 30-day mortality, even when fibrinolysis and primary PCI were analyzed separately. Figure 3 shows 30-day mortality rates according to being transferred to a CRC and being treated with optimal medical therapy, adjusted for GRACE score and previous stroke. The 30-day mortality rate was higher among patients not transferred to a CRC and not treated with optimal medical therapy (28.4%), followed by patients not transferred to a CRC but treated with optimal medical therapy (10.5%), patients

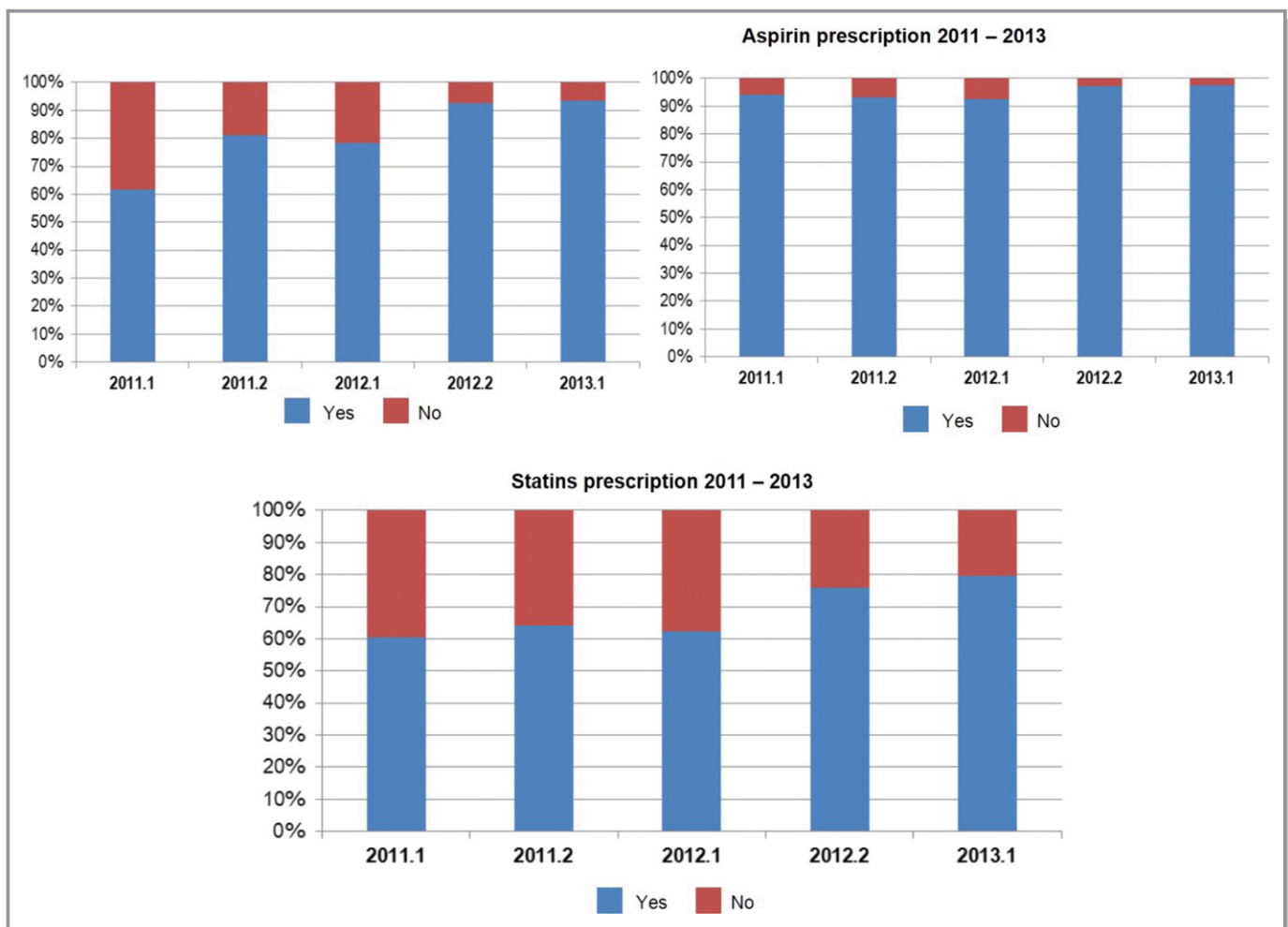


Figure 2. Use of aspirin, clopidogrel, and statins throughout the study period.

transferred to a CRC but not treated with optimal medical therapy (8.2%), and those transferred to a CRC and treated with optimal medical therapy (4.5%).

Figure 4 shows the analysis of 30-day mortality after adjusting for GRACE score, transfer to a CRC, primary reperfusion, optimal medical therapy, and previous stroke. The mortality rate was 19.8% in the first half of 2011 and 5.1% in the first half of 2013. The variable “period of time of patient presentation” was statistically associated with the risk of mortality at 30 days (hazard ratio 0.725, 95% CI, 0.602–0.873; $P=0.001$).

Discussion

RESISST is a Brazilian registry including patients with STEMI who first presented at healthcare units and general hospitals from the public health system, a population poorly represented in previous registries. Our study highlights major opportunities to improve clinical care for patients with STEMI in Brazil, and potentially in other low- and middle-income countries. We identified a long delay from symptom onset to presentation and from presentation to first ECG, and only half of the patients who presented within 12 hours of symptoms underwent primary reperfusion therapy. Additionally, patients who were transferred to a CRC had better prognosis than those not transferred, although survival bias may explain some of this difference. Finally, the implementation of an integrated regional network to establish rapid reperfusion for STEMI patients in Salvador was significantly associated with more use of evidence-based therapies and with better 30-day survival.

We observed a high 30-day mortality rate among patients with STEMI treated in a low- to middle-income city in Brazil. In international registries, mortality rates ranging from 4.2% to 13% have been reported.^{15,16} Because of the long symptom

Table 4. Factors Significantly Associated With 30-Day Mortality in Multivariable Analysis

Variable*	Beta±SE	OR	95% CI	P Value
GRACE score (per 10 units increase)	0.180±0.060	1.195	1.072–1.331	0.002
Transfer to CRC	−1.253±0.385	0.320	0.151–0.681	0.003
Optimal medical therapy	−0.803±0.413	0.406	0.181–0.913	0.029
Previous stroke	0.870±0.391	2.626	1.218–5.662	0.014

CI indicates confidence interval; CRC, cardiology reference center; GRACE, Global Registry of Acute Coronary Events; OR, odds ratio; SE, standard error.

*Adjusted for ethnicity (white vs nonwhite), diabetes mellitus, dyslipidemia, previous acute myocardial infarction, anterior wall myocardial infarction, type of pain at presentation (typical vs atypical or painless), dyspnea at presentation, primary reperfusion (regardless of the method, thrombolysis or primary angioplasty), 6-month time period, and the other variables of the table.

Table 5. Full Model of 30-Day Mortality

Variable	Beta±SE	OR	95% CI	P Value
GRACE score (per 10 units increase)	0.180±0.060	1.195	1.072–1.331	0.002
Transfer to CRC	−1.253±0.385	0.320	0.151–0.681	0.003
Optimal medical therapy	−0.803±0.413	0.406	0.181–0.913	0.029
Previous stroke	0.870±0.391	2.626	1.218–5.662	0.014
White (vs black)	0.524±0.450	2.022	0.835–4.898	0.119
Diabetes mellitus	0.524±0.338	1.736	0.895–3.366	0.103
Dyslipidemia	−0.652±0.429	0.559	0.240–1.301	0.176
Previous AMI	0.293±0.453	1.407	0.577–3.426	0.452
Typical pain	0.003±0.383	1.122	0.529–2.378	0.765
Primary reperfusion	0.316±0.370	1.272	0.616–2.628	0.516
Killip class at admission (Ref: I)				
II	−0.113±0.440	0.893	0.377–2.120	0.798
III	0.494±0.661	1.640	0.448–6.001	0.454
IV	−0.123±1.089	0.884	0.102–7.648	0.910
6-mo period (Ref: Jan–Jun 2011)				
Jul–Dec 2011	0.267±0.404	1.306	0.592–2.884	0.509
Jan–Jun 2012	−1.267±0.544	0.282	0.097–0.817	0.020
Jul–Dec 2012	−0.100±0.450	0.905	0.374–2.185	0.824
Jan–Jun 2013	−1.497±0.573	0.224	0.073–0.688	0.009
Constant	−4.223±0.851	0.015	0.003–0.078	0.000

AMI indicates acute myocardial infarction; CI, confidence interval; CRC, cardiology reference center; GRACE, Global Registry of Acute Coronary Events; OR, odds ratio; SE, standard error.

onset-to-presentation time intervals (median time of 180 minutes), 15.5% of the patients were first seen by a healthcare provider >12 hours after the onset of symptoms. In the most recent international registries, this time interval was at least 60 minutes shorter.^{17,18} Furthermore, among those who presented within 12 hours of symptom onset, primary reperfusion could not be provided to 17.6% because of delay in time-to-first ECG (mean time of 150 minutes). A recent North American registry reported up to 90% use of reperfusion therapies among eligible patients.¹⁸ In our study, 30.4% of individuals with STEMI received medical therapy only, since primary reperfusion was not possible. This, in part, could be a possible explanation why optimal medical therapy was independently associated with mortality, but primary reperfusion was not.

The door-to-needle time in the public health network of Salvador, Bahia, was 178.5 minutes, far exceeding the

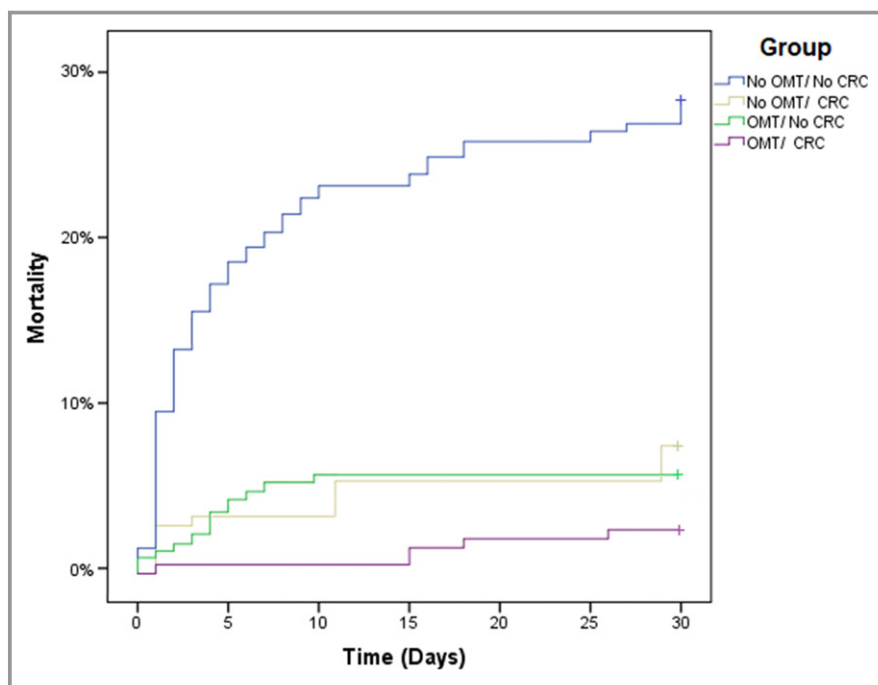


Figure 3. Thirty-day mortality rates according to transfer to the cardiology reference center (CRC) and use of optimal medical therapy (OMT), adjusted for Global Registry of Acute Coronary Events score, primary reperfusion, and previous stroke.

guideline recommendation of 30 minutes. In only 2 patients this time was <30 minutes, whereas in the National Cardiovascular Data Registry,¹⁵ 65.6% fulfilled this target in 2009, and in the Brazilian Registry of Acute Coronary Syndromes (ACCEPT),¹⁹ 33% did. In our study, no patients underwent primary PCI within 90 minutes from presentation (first door) at a nonspecialized health unit. The observation that the time required for primary PCI to be started was on average 4 hours longer than the time taken to initiate fibrinolytic therapy suggests that this type of reperfusion could be performed as an alternative reperfusion approach for cases when the expected time for transferring the patient for PCI is too long. The results of the CAPTIM (Comparison of Primary Angioplasty and Pre-hospital Fibrinolysis in Acute Myocardial Infarction) study indicated that prehospital fibrinolysis, particularly in the first 2 hours after symptoms onset, can be more effective than transfer for primary PCI.²⁰ In fact, 2 major registries—the Vienna STEMI Registry²¹ and the French Registry on Acute ST-Elevation and Non-ST-elevation Myocardial Infarction (FAST-MI) 2010²²—showed similar results for patients treated at an early stage.

The identification of modifiable factors with potential to improve quality of care for STEMI patients in the public health system is a remarkable opportunity to enhance professional training, implement public policies, improve the recognition of symptoms by the population, and facilitate mobility in urban areas with better public transport services. The impact of

these strategies was shown by Jollis et al¹⁰ in STEMI patients from 119 hospitals in North Carolina. Implementing an integrated regional network for STEMI reduced the time to primary reperfusion and improved survival. Importantly, in our study, the medical therapy provided in the acute stage was far from ideal. Except for P2Y12 inhibitors, all recommended medications are available in all emergency care facilities and general hospitals in Salvador. Accordingly, the BRIDGE-ACS (Brazilian Intervention to Increase Evidence Usage in Acute Coronary Syndromes)²³ randomized trial demonstrated the impact of a multifaceted educational intervention leading to a significant increase in the use of evidence-based therapies in patients with acute coronary syndromes in public hospitals in Brazil, which highlights another opportunity to improve care.

Some limitations of our study deserve consideration. First, our findings might not be applicable to private hospitals and institutions with higher adherence to evidence-based therapies. However, the Brazilian Unified Health System is used by 75% of the Brazilian population. The mortality rate observed in RESISST is consistent with the figures from the national medical databank¹⁴ regarding mortality by acute myocardial infarction in public hospitals of Salvador, Bahia. Second, this study was restricted to 1 location, and may not reflect the reality of care in other locations and centers of the country. Nevertheless, our study identified patients who had not been investigated in other registries—that is, patients who were

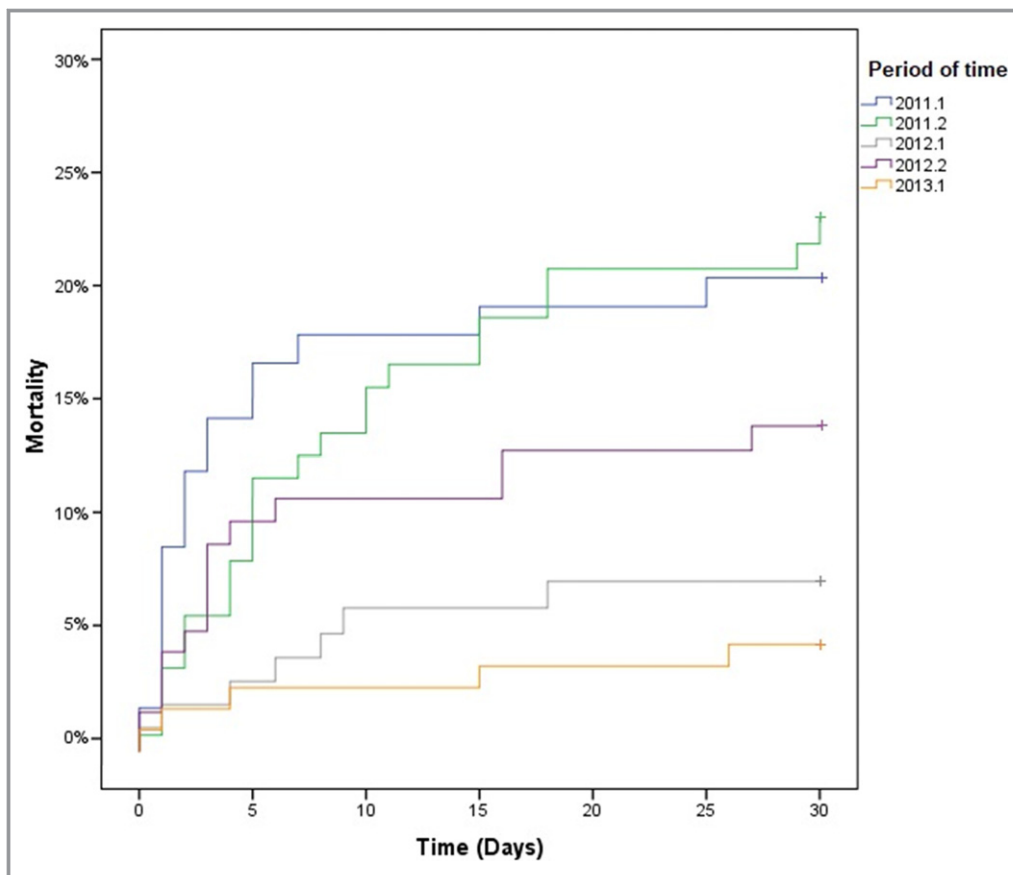


Figure 4. Thirty-day mortality according to different periods of time of health unit presentation, adjusted for Global Registry of Acute Coronary Events score, transfer to cardiology reference center, primary reperfusion, optimal medical therapy, and previous stroke.

assisted in fixed and mobile prehospital units and public hospitals. Third, the method we used to capture data on STEMI patients, through telemedicine reports, may not have comprised the total targeted population. It is possible that some patients using the public health system may have had STEMI but might not have undergone an ECG evaluation via telemedicine, despite the fact that all patients in emergency care units with complaint of chest pain were referred by their identification algorithm to ECG via the telemedicine center, which is the standard flow for this evaluation in the health network in Salvador. Fourth, detailed information about contraindications to therapies was not systematically collected in this study. Fifth, as our study was observational, unmeasured confounding could be responsible for some of the observed differences. Finally, despite the extensive statistical adjustment performed in our study, including for the GRACE score and Killip class at admission, one cannot exclude the presence of unmeasured confounders, which could have played a role in our findings. Thus, a cause-and-effect relationship between implementing an integrated regional network for STEMI patients and reducing mortality

cannot be established. Future studies testing this strategy are warranted.

Conclusion

In patients presenting with STEMI, absence of previous stroke, lower GRACE scores, transfer to a CRC, and receipt of optimal medical therapy were significantly associated with low rates of death at 30 days. The implementation of an integrated regional network to establish rapid reperfusion and use of evidence-based therapies for STEMI patients in Salvador might improve survival. However, this hypothesis still needs to be tested in a prospective well-powered randomized trial. Our findings highlight opportunities to improve clinical care for STEMI patients in underdeveloped geographic regions of the world.

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Disclosures

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