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Predictors of In-Hospital Mortality in ST-Segment Elevation Myocardial Infarction: A Prospective Multicenter Cohort from a Conflict-Affected, Resource-Limited Setting

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Abstract:

Background: ST-segment elevation myocardial infarction (STEMI) outcomes in conflict-affected, resource-limited settings remain critically understudied. We sought to identify predictors

of in-hospital mortality among STEMI patients in Yemen, a fragile healthcare system affected by protracted conflict.

Methods: This prospective multicenter cohort enrolled 920 consecutive STEMI patients from seven Yemeni cardiac centers in 2025. Independent predictors of in-hospital mortality were identified using bootstrap stability selection with least absolute shrinkage and selection operator penalization, followed by Bayesian mixed-effects logistic regression incorporating the treating center as a random intercept.

Results: The overall in-hospital mortality rate was 12.2% (112/920). In the final model, prior myocardial infarction (adjusted odds ratio [aOR] 5.436, 95% credible interval [CrI] 2.799–10.557), dyslipidemia (aOR 2.143, 95% CrI 1.262–3.641), higher Killip class (aOR 1.999 per class, 95% CrI 1.598–2.502), elevated serum creatinine (aOR 1.021 per μmol/L, 95% CrI 1.015–1.026), and lower left ventricular ejection fraction (aOR 0.972 per %, 95% CrI 0.954–0.981) independently predicted mortality. Smoking was inversely associated with mortality (aOR 0.481, 95% CrI 0.279–0.830). Beta-blockers (aOR 0.252, 95% CrI 0.137–0.465) and sodium-glucose cotransporter-2 inhibitors (aOR 0.214, 95% CrI 0.086–0.536) demonstrated strong independent protective associations. Total ischemic time was not independently associated with in-hospital mortality.

Conclusions: In this fragile healthcare system, the short-term prognosis for STEMI was mainly determined by baseline cardiovascular vulnerability and hemodynamic compromise at the time of presentation. These findings offer current evidence to enhance early risk assessment and improve management guidelines in conflict-affected, resource-limited healthcare systems.

Keywords: ST-elevation myocardial infarction, in-hospital mortality, resource-limited settings, conflict-affected settings, smoking paradox, prognostic assessment.

1. Introduction

Cardiovascular disease remains the leading cause of death worldwide, with ischemic heart disease accounting for a substantial share of premature mortality and disability [1, 2]. Among acute coronary syndromes (ACS), ST-segment elevation myocardial infarction (STEMI) represents a highly time-sensitive clinical emergency, in which survival depends critically on rapid diagnosis, timely reperfusion, and effective early care [3, 4]. When access, coordination, or treatment delivery fails, patients arrive later in the course of infarction, contributing to worse outcomes and greatly reducing the chances for saving heart tissue [5-8]. Under such circumstances, mortality reflects not only the biological severity of disease but also limitations in health system performance. Over the past few decades, improvements in regional care systems, primary percutaneous coronary intervention (PCI) and medical treatments have led to a significant drop in STEMI mortality rates in high-income countries [9]. Most existing STEMI outcome data and prognostic tools originate from organized emergency medical services with widespread access to revascularization [8, 10-13].

As a result, the traditional predictors of in-hospital mortality—such as older age [7, 10, 14, 15], female sex [14-16], cardiogenic shock (CS) [15], higher Killip class [7, 10, 13, 14, 17], renal dysfunction [7, 15, 18], and impaired left ventricular systolic function [10, 18, 19]—have been consistently recognized in these populations. Nevertheless, this advancement has not been uniform globally. In Low- and Middle-Income Countries (LMICs), STEMI outcomes are still impacted by

long pre-hospital delays, fragmented referral processes, limited cardiac catheterization labs, and a shortage of critical care services [5, 20-24].

However, critical evidence gaps persist regarding how established prognostic determinants operate in health systems affected by conflict and fragility. Armed conflict exacerbates existing challenges in LMICs by disrupting emergency medical care, driving the migration of healthcare personnel, damaging healthcare infrastructure, and interrupting medical supply chains [25, 26]. Rigorous multicenter evidence from these settings remains scarce, making Yemen a particularly important setting for investigation. Since 2015, prolonged armed conflict and economic collapse have profoundly weakened the Yemeni health system, while the burden of cardiovascular disease has continued to rise [27-30]. Because the relative importance and performance of established mortality predictors may differ substantially from those reported in well-resourced healthcare systems, locally generated evidence is essential to optimize pre-hospital referral pathways and guide pragmatic prognostic assessment.

To address these gaps, we sought to identify predictors of in-hospital mortality among patients presenting with STEMI across multiple governorates in Yemen. By analyzing a large contemporary multicenter cohort, this study provides clinically relevant evidence to inform prognostic assessment and quality improvement initiatives in one of the world's most fragile healthcare systems.

2. Patients and Methods

2.1.Study design and setting

This prospective, multicenter cohort study aimed to identify the independent predictors of in-hospital mortality among patients presenting with STEMI in Yemen. Between January 2025 and

December 2025, consecutive eligible patients were enrolled from seven cardiac centers spanning four major governorates: Sana'a (Al-Thawra Modern General Hospital, Al-Yemen Al-Saeed Hospital, Yemeni French Hospital, and the Cardiac Center), Aden (American Modern Hospital), Mukalla (Nabdh Al-Hayat Cardiac Center), and Ibb (Al-Badr International Hospital). These centers were selected using a purposive sampling approach to provide broad geographic representation across Yemen's governorates while ensuring 24-hour primary PCI capability. All participating centers had established cardiovascular diagnostic capabilities, including echocardiography, electrocardiography, cardiac biomarker assays, and routine biochemical testing. Intravenous fibrinolysis and primary PCI were available at all sites.

The study was conducted in accordance with the 2013 Declaration of Helsinki. Administrative permission to access hospital facilities and patient records was obtained from the relevant authorities at all participating hospitals. Written informed consent was obtained from all participants, who were informed of their right to withdraw at any time.

2.2.Study population and eligibility criteria

Adult patients hospitalized with a primary diagnosis of STEMI were eligible for inclusion. The diagnosis was established according to current clinical guidelines, requiring ischemic symptoms accompanied by ST-segment elevation in at least two contiguous leads (or equivalent electrocardiogram [ECG] patterns), with elevated cardiac biomarkers as supportive evidence [3].

Patients were excluded if the diagnosis of STEMI could not be confirmed or if an alternative diagnosis was established, including non-ST-elevation ACS, clinically suspected myocarditis, or Takotsubo syndrome. For clinically suspected myocarditis, differentiation from STEMI was based on a comprehensive clinical assessment: the presence of a pericardial friction rub on auscultation,

atypical chest pain characteristics (pleuritic in nature, worsening with respiration and positional changes, rather than the typical ischemic pain of STEMI), and the absence of classical evolutionary ECG changes consistent with acute myocardial infarction. In equivocal cases, cardiac magnetic resonance imaging was recommended where available, though in this resource-limited setting, clinical judgment by the two independent cardiologists was the primary diagnostic tool. Patients with advanced malignancy or liver cirrhosis were also excluded, as these conditions could confound short-term mortality outcomes independent of the index STEMI event. In addition, patients lacking documented in-hospital outcomes were excluded. To minimize diagnostic misclassification, two experienced cardiologists independently verified all enrolled cases against ECG tracings and clinical records, resolving any discordance through consensus.

2.3.Sample size considerations

Sample size was determined a priori based on the anticipated number of candidate predictors in the multivariable logistic regression model. To prevent model overfitting, we adhered to the established statistical standard of a minimum of 10 outcome events per predictor variable (EPV); thus, a minimum of 100 deaths was required to reliably evaluate up to 10 candidate predictors. Assuming a conservative in-hospital mortality rate of approximately 10% among Yemeni patients with STEMI [31], we projected an initial target enrollment of 1,000 patients to achieve this threshold. Ultimately, the observed in-hospital mortality rate of 12.2% yielded 112 deaths in the final analytic cohort of 920 patients, exceeding the predefined target. This provided 11.2 EPV, ensuring adequate model stability.

2.4.Sampling and enrollment

We employed a consecutive sampling technique. All adult patients presenting with a confirmed STEMI diagnosis to the seven participating tertiary cardiac centers during the study period were prospectively screened. To minimize selection bias and capture a realistic estimate of the disease burden, enrollment included all consecutive admissions across all facilities without imposing fixed quotas per center. Screening continued until the a priori event-driven target was achieved.

Of the 953 initially screened individuals, 29 were excluded based on predefined criteria: 13 had an unconfirmed STEMI or an alternative diagnosis, 4 had advanced malignancy or liver cirrhosis, and 12 lacked essential diagnostic investigations or documented in-hospital outcomes. During data auditing, 4 duplicate records from inter-hospital transfers were identified and removed, retaining only the index admission. This process resulted in a final analytic cohort of 920 patients (Fig. 1).

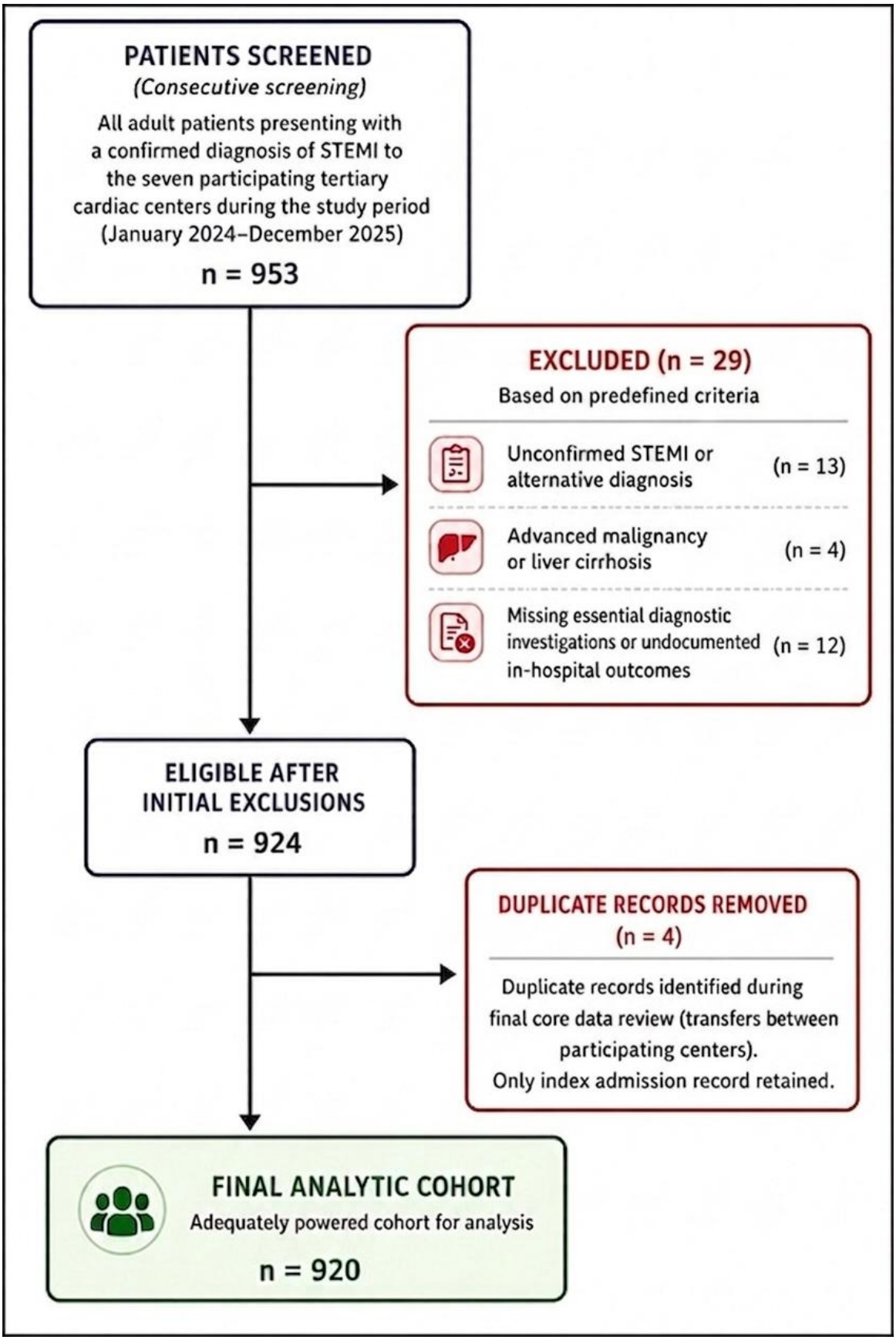

PATIENTS SCREENED
(Consecutive screening)
All adult patients presenting with a confirmed diagnosis of STEMI to the seven participating tertiary cardiac centers during the study period (January 2024–December 2025)
n = 953
EXCLUDED (n = 29)
Based on predefined criteria
Unconfirmed STEMI or alternative diagnosis (n = 13)
Advanced malignancy or liver cirrhosis (n = 4)
Missing essential diagnostic investigations or undocumented in-hospital outcomes (n = 12)
ELIGIBLE AFTER INITIAL EXCLUSIONS
n = 924
DUPLICATE RECORDS REMOVED
(n = 4)
Duplicate records identified during final core data review (transfers between participating centers).
Only index admission record retained.
FINAL ANALYTIC COHORT
Adequately powered cohort for analysis
n = 920

Fig. 1 Study flow diagram

Abbreviation: STEMI, ST-segment elevation myocardial infarction.

2.5.Data collection, variable definitions, and quality assurance

Data from all participating centers were centralized using a standardized, cloud-based electronic case report form (eCRF). Before study initiation, investigators received standardized training on study procedures to ensure uniform data collection. To enhance data quality, the eCRF incorporated predefined drop-down menus, mandatory fields, and range restrictions. Regular audits of submitted eCRFs were performed throughout the study to verify data completeness and accuracy, and all patient-level data were anonymized at the source to protect confidentiality. To preserve the independence of observations, only the index STEMI admission was retained for analysis; subsequent inter-hospital transfers were excluded as redundant observations.

Baseline demographic parameters, including age, sex, and place of residence, were extracted directly from medical records at admission. Behavioral risk factors (smoking and khat chewing) and socioeconomic status (SES) were obtained via structured clinical interviews with patients or their families. Due to limited sample sizes, former smokers and former khat chewers were collapsed with current users during analysis. SES was categorized as low, intermediate, or high using a context-specific composite score based on education, employment, and estimated household income. A pilot-tested composite score was developed specifically for this setting, with tertiles (33^{rd} and 66^{th} percentiles) defining low, intermediate, and high SES categories. The score was weighted as follows: education (0-3 points), employment status (0-3 points), and household income estimated through a validated proxy questionnaire adapted for conflict settings (0-4 points). Baseline comorbidities included hypertension (HTN), diabetes mellitus (DM), and a

family history (FH) of premature coronary artery disease (CAD). Dyslipidemia was defined as a documented clinical history of abnormal lipid profiles or the active use of lipid-lowering therapy prior to admission, in accordance with the 2019 European Society of Cardiology and European Atherosclerosis Society guidelines [32]. Previous cardiovascular history encompassed prior myocardial infarction (MI), PCI, coronary artery bypass grafting (CABG), and heart failure (HF).

Clinical presentation was categorized as either typical ischemic chest pain or atypical symptoms [33]. Initial disease severity was assessed using admission vital signs, left ventricular ejection fraction (LVEF), baseline serum creatinine (SCr), and Killip class (I–IV). LVEF was assessed using transthoracic echocardiography within 24 hours of admission. All echocardiograms were performed by experienced cardiologists using the Simpson's biplane method of discs where feasible, or by visual estimation when image quality was suboptimal. The treating center's echocardiography laboratory performed the assessments according to standardized protocols, with 10% of studies randomly selected for blinded re-reading to assess inter-observer variability (kappa = 0.85 for LVEF categories). Baseline cardiac biomarkers (troponin and/or creatine kinase-MB [CK-MB]) were collected prior to reperfusion therapy. CS was defined according to the Shock Academic Research Consortium (SHARC) consensus as sustained systolic blood pressure (SBP) <90 mmHg or the requirement for hemodynamic support to maintain adequate tissue perfusion [34].

Treatment timelines and procedural characteristics were recorded in accordance with contemporary STEMI performance metrics [3], including symptom-to-door (S2D), door-to-ECG (D2ECG), door-to-needle (D2N), and door-to-wire (D2W) times. Reperfusion strategies were classified as primary PCI or rescue PCI (following failed fibrinolysis). Angiographic variables included the culprit vessel, arterial access site, and the presence of multi-vessel disease (MVD)

(≥70% stenosis in ≥2 major epicardial arteries). In-hospital management, including guideline-directed medical therapy (GDMT), was comprehensively documented. Finally, the primary endpoint (in-hospital mortality) and incident clinical complications were prospectively ascertained from daily cardiac care unit progress notes and discharge summaries.

2.6.Study endpoints

The primary clinical endpoint was all-cause in-hospital mortality. Secondary endpoints included major in-hospital complications, specifically CS, cardiac arrest, stroke (clinically evident or neuroimaging-confirmed), and procedural complications such as coronary perforation. Ischemic complications included reinfarction, defined according to the Fourth Universal Definition of Myocardial Infarction [33], and angiographic restenosis (≥50% luminal renarrowing at the treated lesion). Major bleeding was defined using the Bleeding Academic Research Consortium criteria (types 3 or 5) [35]. Finally, a composite of non-fatal complications (reinfarction, stroke, and restenosis) was also analyzed.

2.7.Statistical analysis

Continuous variables were summarized as means with standard deviations (SD) or medians with interquartile ranges (IQR), as appropriate according to their distribution, whereas categorical variables were presented as frequencies and percentages. Univariable logistic regression was initially performed to compare clinical characteristics between survivors and non-survivors, with results reported as crude odds ratios (CORs) and 95% confidence intervals (CIs). Because no in-hospital deaths occurred in one participating center (Ibb), resulting in complete data separation, Firth's penalized logistic regression was used to estimate the crude OR and corresponding 95% CI for this variable. To identify independent predictors of in-hospital mortality, we implemented a

rigorous multi-step analytical framework. Potential multicollinearity among candidate predictors was assessed using the variance inflation factor (VIF), with VIF < 5 considered indicative of acceptable collinearity. Based on both clinical reasoning and statistical assessment, CS was excluded from model development because it represents the most severe manifestation of the Killip classification (Killip class IV), and its inclusion would have introduced substantial collinearity and obscured the independent prognostic contribution of Killip class. To minimize overfitting and improve the stability of variable selection, we employed Bootstrap Stability Selection integrated with Least Absolute Shrinkage and Selection Operator (LASSO) logistic regression [36, 37]. The dataset underwent 500 bootstrap resamples with replacement. Within each bootstrap sample, a 5-fold cross-validated LASSO model was fitted using the more conservative penalty parameter (λ_{1se}). Predictors retaining non-zero coefficients in ≥70% of bootstrap iterations were considered stable and selected for subsequent multivariable modeling. The 70% threshold was chosen based on Meinshausen and Bühlmann's recommendation to control the per-family error rate (PFER) and minimize false positives in high-dimensional settings. The selected stable predictors were subsequently entered into a generalized linear mixed-effects logistic regression model. To account for institutional clustering and unmeasured between-center heterogeneity, participating hospital was incorporated as a random intercept. Given the limited number of participating centers (n = 7), conventional maximum-likelihood estimation of the random-effects variance can be unstable and biased. Therefore, the mixed-effects model was fitted using a Bayesian estimation approach with weakly informative Student-t priors on the random-effects standard deviation, thereby improving estimation stability and mitigating separation arising from the center with zero mortality events. Results are reported as adjusted odds ratios (aORs) with corresponding 95% Bayesian credible intervals (CrIs). Student-t priors with 3 degrees of freedom and scale parameter 2.5 were used for

the random-effects standard deviation. Convergence was assessed using the Gelman-Rubin diagnostic (Rhat < 1.01) and effective sample size > 1000 for all parameters. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed using R software version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria), and the study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

2.8.Sensitivity and supplementary analyses

To evaluate the robustness of the primary mixed-effects model and explore clinically relevant secondary questions, several prespecified supplementary analyses were performed. First, to contextualize the observed smoker's paradox, baseline clinical characteristics and comorbidities were compared according to smoking status. Second, reperfusion strategies were compared with respect to treatment timelines, including S2D and total ischemic (TI) times, to explore potential system- and procedure-related delays. Third, a center-exclusion sensitivity analysis was performed to evaluate whether the complete data separation observed in the Ibb center disproportionately influenced the primary findings. Fourth, a clinical proxy substitution model was constructed by replacing Killip class with CS to evaluate the robustness of the identified predictors in the presence of potential collinearity between these two markers of hemodynamic severity. Finally, as a statistical sensitivity analysis, we fitted an alternative fixed-effects logistic regression model with cluster-robust standard errors, clustering on hospital and applying the Kauermann–Carroll small-sample bias correction (with degrees of freedom approximated as the number of clusters minus one), to verify that the primary findings were robust to the choice of modeling framework.

3. Results

Among the 920 included patients with STEMI, 112 died during hospitalization, yielding an in-hospital mortality rate of 12.2%.

3.1.Baseline demographic and clinical characteristics

Non-survivors presented with a significantly higher comorbid burden; they were more likely to have a history of HTN, DM, dyslipidemia, prior cardiovascular events (MI, PCI, and HF), and a FH of premature CAD. In terms of sociodemographic and geographic factors, low SES and khat chewing were more prevalent among non-survivors, and mortality varied significantly by treating location, with patients managed in Sana'a exhibiting higher mortality rates compared to those in other participating cities. Conversely, smoking was less frequent among non-survivors. At presentation, higher body mass index (BMI), lower LVEF, and advanced Killip class were strongly associated with mortality. There were no significant differences in age, sex, rural residence, anterior infarction location, or admission vital signs (heart rate [HR] and both SBP and diastolic blood pressure [DBP]) between survivors and non-survivors (Table 1).

Table 1 Baseline demographic, socioeconomic, clinical, and presentation characteristics according to in-hospital survival status

Characteristic / Clinical Presentation	Survivors (n = 808)	Non-survivors (n = 112)	COR (95% CI)	p-value
Demographic and socioeconomic characteristics				
Age (years), median (IQR)	55 (47, 65)	58 (50, 65)	1.012 (0.995 - 1.030)	0.164
Female sex, n (%)	138 (17.1)	22 (19.6)	1.187 (0.719 - 1.958)	0.503

Rural residence, n (%)	530 (65.6)	81 (72.3)	1.371 (0.884 - 2.125)	0.159
SES, n (%)				
Low	413 (51.1)	70 (62.5)	0.750 (0.572 - 0.982)	**0.036**
Intermediate	230 (28.5)	25 (22.3)		
High	165 (20.4)	17 (15.2)		
Treatment city, n (%)#				
Sana'a	550 (68.1)	105 (93.8)	4.536 (1.926 - 13.920)	**<0.001**
Mukalla	88 (10.9)	3 (2.7)	0.936 (0.205 - 3.945)	0.927
Ibb	64 (7.9)	0 (0.0)	0.183 (0.001 - 1.762)	0.164
Aden	106 (13.1)	4 (3.6)	Reference (1.00)	1.000
Cardiovascular risk factors				
Khat chewing, n (%)	564 (69.8)	92 (82.1)	1.990 (1.224 - 3.387)	**0.007**
Smoking, n (%)	605 (74.9)	57 (50.9)	0.348 (0.232 - 0.521)	**<0.001**
BMI (kg/m^2), median (IQR)	25.4 (23.0, 27.7)	25.6 (23.5, 29.0)	1.062 (1.011 - 1.116)	**0.016**
HTN, n (%)	316 (39.1)	65 (58.0)	2.153 (1.446 - 3.229)	**<0.001**

DM, n (%)	277 (34.3)	55 (49.1)	1.846 (1.239 - 2.750)	**0.002**
Dyslipidemia, n (%)	200 (24.8)	51 (45.5)	2.542 (1.692 - 3.808)	**<0.001**
FH of premature CAD, n (%)	127 (15.7)	33 (29.5)	2.240 (1.417 - 3.481)	**<0.001**
Prior Cardiovascular History, n (%)				
Prior MI	57 (7.1)	26 (23.2)	3.983 (2.353 - 6.612)	**<0.001**
Prior PCI	21 (2.6)	16 (14.3)	6.246 (3.110 - 12.340)	**<0.001**
Prior CABG	2 (0.2)	1 (0.9)	3.631 (0.327 - 40.368)	0.294
Prior HF	5 (0.6)	13 (11.6)	21.089 (7.776 - 66.878)	**<0.001**
Clinical Presentation at Admission				
Atypical chest pain presentation, n (%)	122 (15.1)	15 (13.4)	1.026 (0.591 - 1.781)	0.927
Anterior STEMI, n (%)	484 (59.9)	67 (59.8)	0.883 (0.587 - 1.327)	0.548
HR (bpm), median (IQR)	89.0 (80.0, 100.0)	88.0 (80.0, 100.0)	0.998 (0.990 - 1.007)	0.684

SBP (mmHg), median (IQR)	130.0 (110.0, 150.0)	120.0 (100.0, 140.0)	0.996 (0.990 - 1.002)	0.182
DBP (mmHg), median (IQR)	80.0 (70.0, 90.0)	80.0 (70.0, 90.0)	0.996 (0.987 - 1.005)	0.194
Killip class, n (%)				
I	609 (75.4)	42 (37.5)	2.030 (1.715 - 2.405)	**<0.001**
II	117 (14.5)	29 (25.9)		
III	26 (3.2)	9 (8.0)		
IV	56 (6.9)	32 (28.6)		
LVEF (%), median (IQR)	50.0 (44.0, 58.0)	45.0 (40.0, 55.0)	0.954 (0.928 - 0.980)	**<0.001**

Note: Statistically significant associations (P < 0.05) are highlighted in bold.

#Firth's penalized logistic regression was utilized to calculate the odds ratio and 95% CI for the 'Ibb' center to resolve the complete data separation caused by zero mortality events.

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; COR, crude odds ratio; DBP, diastolic blood pressure; DM, diabetes mellitus; FH, family history; HF, heart failure; HR, heart rate; HTN, hypertension; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SES, socioeconomic status; STEMI, ST-segment elevation myocardial infarction.

3.2.Ischemic time intervals and reperfusion management

Non-survivors experienced significantly prolonged D2ECG, D2N, and D2W intervals. Conservative therapy and rescue PCI were more prevalent among non-survivors, whereas primary

PCI showed a non-significant trend toward lower mortality. Of note, TI time and S2D delay were not significantly associated with mortality in univariable analyses (Table 2).

Table 2 Ischemic delays, reperfusion strategies, and treatment timelines according to in-hospital survival status

Variable	Survivors (n = 808)	Non-survivors (n = 112)	COR (95% CI)	p-value
Ischemic Delays				
TI time (min), median (IQR)	660.0 (360.0, 1140.0)	720.0 (360.0, 1425.0)	0.995 (0.982 - 1.009)	0.416
S2D time (min), mean (SD)	785.5 (425.1)	829.9 (430.5)	1.003 (0.991 - 1.015)	0.823
D2ECG time (min), mean (SD)	16.9 (10.4)	22.0 (8.0)	1.029 (1.014 - 1.043)	**<0.001**
Management Strategy, n (%)				
Primary PCI	598 (74.0)	74 (66.1)	0.684 (0.449 - 1.042)	0.076
Thrombolysis alone	84 (10.4)	6 (5.4)	0.488 (0.208 - 1.145)	0.093
Rescue PCI	46 (5.7)	12 (10.7)	1.988 (0.977 - 3.765)	**0.040**
Conservative therapy	80 (9.9)	20 (17.9)	1.978 (1.133 - 3.325)	**0.011**
Treatment Delays				

D2W time[a] (min), median (IQR)	120.0 (60.0, 240.0)	180.0 (60.0, 263.7)	1.035 (1.000 - 1.071)	**0.047**
D2N time[b] (min), mean (SD)	92.4 (41.4)	202.3 (149.4)	1.025 (1.008 - 1.050)	**0.003**

Note: Statistically significant associations (P < 0.05) are highlighted in bold.

[a] Among patients undergoing PCI (n = 644 survivors, 86 non-survivors).

[b] Among patients receiving thrombolysis (n = 90).

Abbreviations: CI, confidence interval; COR, crude odds ratio; S2D, symptom-to-door; D2ECG, door-to-electrocardiogram; D2N, door-to-needle; D2W, door-to-wire; PCI, percutaneous coronary intervention; SD, standard deviation; TI, total ischemic time.

3.3.Angiographic, procedural, and treatment-related characteristics

Table 3 summarizes the laboratory, angiographic, and procedural characteristics, alongside in-hospital treatment protocols. Non-survivors presented with significantly elevated baseline SCr levels and a higher angiographic disease burden, evidenced by increased rates of MVD and triple-vessel disease (TVD). Procedural characteristics, particularly the higher utilization of femoral arterial access, were also more prevalent among this cohort.

Regarding in-hospital pharmacological management, foundational therapies such as aspirin and statins were administered at exceptionally high rates across both groups. However, non-survivors received significantly lower rates of beta-blockers (BB) and sodium-glucose cotransporter-2 inhibitors (SGLT2i). In contrast, the administration of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARBs) was comparable between survivors and non-

survivors. Conversely, the utilization of Glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors was markedly higher among non-survivors.

Table 3 Laboratory, angiographic, procedural, and treatment-related characteristics according to in-hospital survival status

Variable	Survivors (n = 808)	Non-survivors (n = 112)	COR (95% CI)	p-value
Laboratory Findings				
Troponin positive, n (%)	550 (68.1)	67 (59.8)	0.698 (0.466 - 1.048)	0.082
CK-MB positive, n (%)	676 (83.7)	89 (79.5)	0.756 (0.461 - 1.239)	0.266
SCr (μmol/L), median (IQR)	88.0 (74.8, 113.4)	115.7 (88.0, 193.0)	1.019 (1.015 - 1.024)	**<0.001**
Angiographic Characteristics & Procedures	**(n = 644)**	**(n = 86)**		
Culprit vessel territory, n (%)				0.089#
Right system (right coronary artery)	188 (29.2)	18 (20.9)	Reference (1.00)	

Left system*	456 (70.8)	68 (79.1)	1.584 (0.932 - 2.690)#	
Left anterior descending artery	370 (57.5)	55 (64.0)	-	
Left circumflex artery	84 (13.0)	11 (12.8)	-	
Left main coronary artery	2 (0.3)	2 (2.3)	-	
Vessel disease, n (%)				
Single-vessel disease	431 (66.9)	38 (44.2)	0.449 (0.297 - 0.680)	**<0.001**
Double-vessel disease	150 (23.3)	26 (30.2)	1.326 (0.826 - 2.129)	0.158
TVD	63 (9.8)	22 (25.6)	2.891 (1.669 - 4.861)	**<0.001**
MVD	213 (33.1)	48 (55.8)	2.095 (1.392 - 3.138)	**<0.001**
Arterial access site, n (%)				
Radial	209 (32.5)	6 (6.9)	Reference (1.00)	**<0.001**
Femoral	435 (67.5)	80 (93.0)	6.406 (2.749 - 14.926)	
Drug-coated balloon	15 (1.9)	3 (2.7)	1.455 (0.415 - 5.107)	0.558
In-Hospital Pharmacological	**(n = 808)**	**(n = 112)**		

Management, n (%)				
Aspirin (24 hrs)	806 (99.8)	110 (98.2)	0.136 (0.019 - 0.979)	**0.048**
Clopidogrel (24 hrs)	786 (97.3)	106 (94.6)	0.494 (0.196 - 1.247)	0.136
Unfractionated heparin	715 (88.5)	104 (92.9)	1.691 (0.798 - 3.583)	0.166
Low molecular weight heparin	80 (9.9)	8 (7.1)	0.700 (0.329 - 1.490)	0.355
GPIIb/IIIa inhibitors	310 (38.4)	62 (55.4)	1.992 (1.337 - 2.968)	**<0.001**
Statin therapy	799 (98.9)	109 (97.3)	0.409 (0.109 - 1.535)	0.185
ACEI/ARBs	227 (28.1)	32 (28.6)	1.024 (0.661- 1.586)	0.916
BB	728 (90.1)	70 (62.5)	0.183 (0.117 - 0.287)	**<0.001**
SGLT2i	151 (18.7)	10 (8.9)	0.427 (0.218 - 0.836)	**0.013**
Oral anticoagulants	57 (7.1)	9 (8.0)	1.151 (0.553 - 2.395)	0.706
Planned referral for CABG	99 (12.3)	9 (8.1)	0.626 (0.307 - 1.277)	0.204

Notes: Statistically significant associations ($P < 0.05$) are highlighted in bold. Angiographic characteristics are reported among patients undergoing PCI (total n = 730).

***** Left system includes left main, left anterior descending, and left circumflex arteries.

#P-value represents the comparison between right and left coronary systems.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; BB, beta-blockers; CABG, coronary artery bypass grafting; CI, confidence interval; CK-MB, creatine kinase-MB; COR, crude odds ratio; GPIIb/IIIa inhibitors, glycoprotein IIb/IIIa inhibitors; MVD, multi-vessel disease; SCr, serum creatinine; SGLT2, sodium-glucose cotransporter-2 inhibitors; TVD, triple-vessel disease.

3.4.In-Hospital clinical complications

Table 4 details incident in-hospital complications and their univariable associations with mortality. As expected, in-hospital mortality was strongly associated with major adverse clinical events sustained post-admission. Specifically, incident CS and cardiac arrest (CA) were the strongest correlates of death. Reinfarction and restenosis were also significantly more frequent among non-survivors, whereas cerebrovascular accidents (CVA) and bleeding complications were rare and showed no significant association with mortality.

Table 4 Incidence of in-hospital complications and association with mortality

Outcome / Complication	**Survivors (n = 808)**	**Non-survivors (n = 112)**	**COR (95% CI)**	**p-value**
Severe Events & Mortality Context, n (%)				
CA	36 (4.5)	17 (15.2)	3.837 (2.032 - 7.003)	**<0.001**
CS	108 (13.4)	47 (42.0)	4.687 (3.051 - 7.172)	**<0.001**
Non-Fatal Ischemic Complications, n (%)				
Non-Fatal Complications Composite[a]	57 (7.1)	22 (19.6)	3.221 (1.849 - 5.453)	**<0.001**

Reinfarction	45 (5.6)	17 (15.2)	3.034 (1.631 - 5.424)	**<0.001**
Stroke/CVA	6 (0.7)	1 (0.9)	1.204 (0.144 - 10.096)	0.864
Restenosis	7 (0.9)	5 (4.5)	5.347 (1.559 - 17.048)	**0.002**
Procedural and Bleeding Complications, n (%)				
Procedural/Bleeding Complications Composite[b]	9 (1.1)	2 (1.8)	1.614 (0.344 - 7.568)	0.540
Coronary perforation	1 (0.1)	0 (0.0)	Not applicable (NA)	1.000
Access-site bleeding	7 (0.9)	2 (1.8)	2.081 (0.427 - 10.142)	0.354
Retroperitoneal bleeding	2 (0.2)	0 (0.0)	NA	1.000

Note: Statistically significant associations ($P < 0.05$) are highlighted in bold. Percentages are calculated from the total cohorts (808 and 112).

[a] Composite of reinfarction, stroke/CVA, and restenosis.

[b] Composite of all bleeding types and coronary perforation.

Abbreviations: CA, cardiac arrest; CI, confidence interval; COR, crude odds ratio; CS, cardiogenic shock; CVA, cerebrovascular accident; NA, not applicable.

3.5.Independent predictors of in-hospital mortality

The final multivariable Bayesian mixed-effects logistic regression model identified multiple independent predictors of in-hospital mortality (Fig. 2). Prior MI was the strongest predictor, increasing mortality odds by more than fivefold (aOR 5.436, 95% CrI 2.799–10.557, $P < 0.001$). Dyslipidemia was also associated with increased mortality (aOR 2.143, 95% CrI 1.262–3.641, P =

0.005). Conversely, smoking exhibited an independent, inverse association with mortality (aOR 0.481, 95% CrI 0.279–0.830, P = 0.009).

At admission, advanced Killip class (aOR 1.999 per class increase, 95% CrI 1.598–2.502, P < 0.001) and elevated baseline SCr (aOR 1.021, 95% CrI 1.015–1.026, P < 0.001) were robust predictors of death. Conversely, higher LVEF was independently protective (aOR 0.972, 95% CrI 0.954–0.981, P = 0.015).

Regarding in-hospital pharmacological therapy, both SGLT2i (aOR 0.214, 95% CrI 0.086–0.536, P < 0.001) and BB (aOR 0.252, 95% CrI 0.137–0.465, P < 0.001) were independently associated with improved survival.

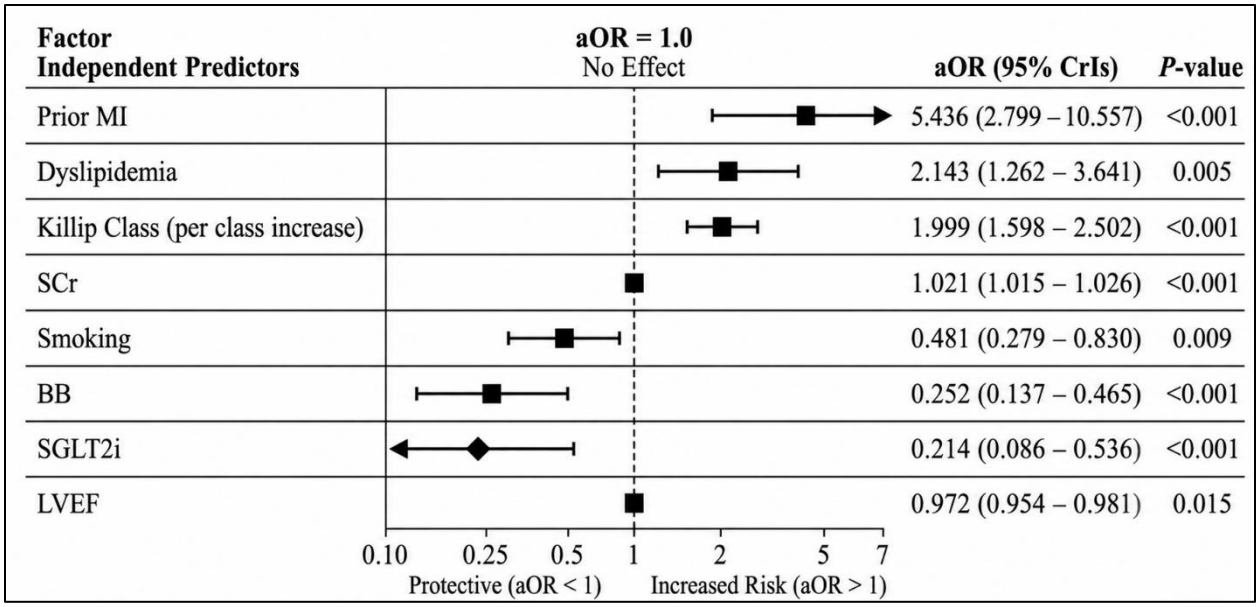


Fig. 2 Forest plot of factors independently associated with in-hospital mortality

Notes: Estimates were obtained from a Bayesian multivariable mixed-effects logistic regression model with treating center included as a random intercept. Killip class was modeled as an ordinal variable; the reported effect represents the increase in mortality risk per one-class increment.

Abbreviations: aOR, adjusted odds ratio; BB, beta-blockers; CrI, credible interval; LVEF, left ventricular ejection fraction; MI, myocardial infarction; SCr, serum creatinine; SGLT2i, sodium-glucose cotransporter-2 inhibitors.

3.6.Sensitivity and supplementary analyses

Five prespecified supplementary analyses elucidated key clinical findings and verified the final model's robustness (Supplementary Materials). First, subgroup analysis by smoking status (Table S1) explained the observed "smoker's paradox." Smokers had a significantly more favorable baseline risk profile than non-smokers, being younger and exhibiting a lower prevalence of major comorbidities (HTN, DM, and dyslipidemia), as well as better initial hemodynamic parameters (higher LVEF and lower Killip class). Second, an evaluation of reperfusion pathways (Table S2) highlighted substantial in-hospital procedural delays; patients undergoing primary PCI experienced significantly longer median TI times compared to those receiving alternative strategies (713 vs. 551 minutes, $P = 0.003$), despite having markedly shorter S2D delays (420 vs. 1200 minutes, $P < 0.001$). Furthermore, three statistical sensitivity analyses confirmed model stability. A center-exclusion analysis (Table S3) omitting the 'Ibb' center (which had zero mortality events) did not significantly alter the aORs, confirming that the identified predictors were not disproportionately influenced by this specific institutional cluster. Similarly, a clinical proxy substitution model (Table S4) replacing Killip classification with CS yielded highly consistent prognostic weights for all other independent variables, reaffirming model stability against potential multicollinearity. Finally, a statistical sensitivity analysis using an alternative frequentist fixed-effects model with Kauermann-Carroll bias correction (Table S5) yielded prognostic weights highly consistent with the primary Bayesian mixed-effects model, confirming the robustness of the identified predictors against the choice of inferential framework.

4. Discussion

To our knowledge, this is the first study to comprehensively identify independent predictors of in-hospital mortality among patients with STEMI within a fragile, conflict-affected, resource-limited healthcare system. Using a robust statistical methodology that minimized overfitting and accounted for between-center heterogeneity, we identified prior MI, dyslipidemia, advanced Killip class, elevated SCr, and reduced LVEF as independent predictors of in-hospital mortality. Conversely, smoking, as well as BB and SGLT2i therapies, were independently associated with improved survival. This study provides important evidence from an underrepresented Middle Eastern population and offers clinically relevant insights for early prognostic assessment in fragile settings.

The heightened vulnerability to adverse outcomes observed in our cohort is likely rooted in the cumulative effects of prolonged healthcare disruption and socioeconomic hardship. In Yemen, prolonged conflict has resulted in fragmented healthcare infrastructure, an almost complete absence of organized pre-hospital emergency medical services, delayed inter-hospital transfers, and substantial out-of-pocket healthcare expenditures, all of which contribute to delayed presentation and limited access to definitive reperfusion [26]. These structural barriers are compounded by documented sex-related disparities in STEMI care, where women frequently experience delayed presentation and lower utilization of invasive therapies [38]. These healthcare-system constraints likely influenced disease severity at presentation and consequently shaped the prognostic profile observed in our cohort.

Prior MI emerged as the strongest independent predictor of mortality, conferring a more than five-fold increase in adjusted risk. This reflects the vulnerability of myocardium already compromised

by previous ischemic injury, ventricular remodeling, and reduced contractile reserve [39, 40]. Although secondary prevention and complete revascularization substantially attenuate recurrent risk in high-income settings [9, 41], these interventions remain inconsistently available in resource-constrained environments. Consequently, prior MI in our cohort likely indicates both advanced underlying coronary disease and missed opportunities for long-term cardiovascular management, emphasizing the need for aggressive secondary prevention in this high-risk population.

Markers of acute hemodynamic deterioration also demonstrated strong prognostic significance. Killip class remained a potent bedside predictor, with each incremental increase nearly doubling the odds of in-hospital mortality, consistent with extensive previous literature [7, 13]. Likewise, elevated admission SCr independently predicted mortality, reflecting impaired renal perfusion, cardiorenal syndrome, and early multiorgan dysfunction during acute STEMI [7, 42, 43]. These findings highlight the continued value of Killip classification and admission renal function as pragmatic bedside indicators for early prognostic assessment in resource-limited, conflict-affected healthcare settings.

In our cohort, reduced LVEF independently predicted in-hospital mortality, underscoring the central role of ventricular systolic dysfunction in determining early clinical outcomes following STEMI. Reduced LVEF reflects the cumulative burden of irreversible myocardial injury and diminished cardiac reserve, predisposing patients to pulmonary edema, CS, and progressive circulatory collapse [3, 44, 45]. Similar findings have been reported previously; contemporary registry data demonstrated that patients with an LVEF below 40% experienced approximately a 3.6-fold higher mortality than those with preserved systolic function [17]. Importantly, the

prognostic value of LVEF persisted in the final multivariable Bayesian mixed-effects model, confirming that echocardiographic assessment provides independent prognostic information beyond bedside clinical evaluation alone.

Dyslipidemia also remained independently associated with increased in-hospital mortality after multivariable adjustment. Although dyslipidemia is a well-established causal driver of atherosclerotic cardiovascular disease through prolonged exposure to atherogenic lipoproteins that promote plaque formation and progression [32, 46], our findings suggest that it also serves as a marker of more advanced coronary pathology at the time of STEMI presentation (a concept indirectly supported by the significantly higher prevalence of MVD and TVD among non-survivors in our cohort). Individuals with dyslipidemia frequently exhibit diffuse coronary atherosclerosis, endothelial dysfunction, impaired coronary microvascular perfusion, and a chronic pro-inflammatory and pro-thrombotic milieu, all of which may contribute to larger infarct size and impaired myocardial recovery [47-49]. In resource-limited settings such as Yemen, dyslipidemia may additionally serve as a surrogate marker for prolonged exposure to untreated lipid abnormalities and inadequate primary prevention, reflecting advanced atherosclerotic burden before the index infarction. Supporting this concept, prior large-scale analyses reported that each unit reduction in high-density lipoprotein cholesterol increased mortality risk by 3% [17], emphasizing the adverse prognostic implications of persistent lipid abnormalities [50, 51].

An unexpected observation was the persistence of the so-called "smoker's paradox," whereby current smokers exhibited lower adjusted in-hospital mortality despite the established harmful cardiovascular effects of tobacco [3]. Similar findings have been reported in several STEMI registries [52-54]. In our cohort, smokers were substantially younger and had fewer traditional

cardiovascular comorbidities. Crucially, as demonstrated in our supplementary analyses, they also presented with a more favorable baseline hemodynamic profile, including a higher median LVEF and a lower proportion of advanced Killip classes at admission. These findings suggest that differences in baseline clinical characteristics and physiological reserve likely explain much of the apparent survival advantage. Previous large-scale investigations have likewise demonstrated that this association is substantially attenuated after comprehensive adjustment, supporting the concept of a "pseudo-paradox" rather than any genuine protective effect of smoking [53-55]; therefore, the observed association in our cohort most likely reflects differences in baseline risk profiles.

Among therapeutic variables, BB therapy was independently associated with an approximately 74% lower adjusted odds of mortality. In environments characterized by prolonged reperfusion delays, BB therapy may act as a crucial "pharmacological bridge" by reducing myocardial oxygen demand, suppressing malignant arrhythmias, and preserving myocardial viability prior to definitive reperfusion. This observation warrants further evaluation in prospective trials within resource-constrained systems. Similarly, SGLT2i therapy was independently associated with markedly lower in-hospital mortality. Although residual confounding cannot be completely excluded in this observational study, the association is biologically plausible and aligns with the expanding body of evidence supporting the cardiovascular benefits of SGLT2i beyond glycemic control [56, 57]. Proposed mechanisms include improved myocardial energetics, attenuation of oxidative stress and inflammation, preservation of renal function, reduction of adverse ventricular remodeling, and favorable modulation of neurohormonal activation [58, 59]. Emerging evidence from contemporary randomized trials has renewed interest in the early use of SGLT2i after acute MI. While DAPA-MI and EMPACT-MI, the two largest randomized trials of SGLT2i in the acute MI setting, did not demonstrate a definitive mortality benefit at 12 months [60, 61], both studies

demonstrated the safety of early initiation and suggested favorable cardiometabolic effects, including reductions in heart failure hospitalizations. Although the profound protective association observed in our cohort is likely influenced by immortal time bias and non-randomized treatment allocation, our findings strongly support the conduct of future randomized trials specifically designed for resource-limited settings, where baseline cardiovascular risk is higher and the potential benefits of early SGLT2i initiation may be more pronounced.

The lack of an independent association between TI time and in-hospital mortality, despite numerically longer delays among non-survivors, warrants careful interpretation. This observation is likely multifactorial. First, substantial pre-hospital survivor bias likely exists in conflict-affected settings, whereby patients experiencing the most catastrophic infarctions may die before reaching hospital care. Second, the median TI time in our cohort exceeded 11 hours, a duration at which myocardial necrosis has largely plateaued; consequently, prognosis becomes increasingly determined by baseline physiological reserve and the severity of hemodynamic compromise rather than incremental ischemic delay. Finally, much of the adverse prognostic impact of delayed reperfusion appears to be mediated through downstream manifestations of infarct severity—including Killip class, renal dysfunction, and ventricular systolic impairment—which remained independent predictors in the final model. Consistent with this interpretation, our supplementary analyses demonstrated that patients undergoing primary PCI paradoxically experienced longer TI times than those receiving alternative reperfusion strategies despite earlier presentation, reflecting unavoidable in-hospital delays related to catheterization laboratory activation, inter-hospital transfer, and centralized PCI services within a fragmented healthcare system.

Ultimately, because patients were enrolled from seven independent cardiac centers with varying resources and referral patterns, we incorporated the treating center as a random intercept using Bayesian hierarchical mixed-effects modeling. This approach accounted for institutional clustering while preserving patient-level inference. Although crude mortality differed substantially across centers, these geographic differences disappeared after adjustment, indicating that the observed variation was largely attributable to differences in case-mix and referral complexity rather than intrinsic differences in hospital performance. Importantly, the stability of these predictors was rigorously confirmed under an alternative frequentist framework using small-sample bias corrections, ensuring that our findings were not artifacts of the limited number of institutional clusters. The persistence of our identified predictors after accounting for center-level heterogeneity further strengthens the robustness and generalizability of the study findings, highlighting the urgent need to integrate these validated metrics into routine clinical evaluation to improve STEMI survival in similarly resource-limited and fragile healthcare environments.

Limitations

This study has several limitations. First, the observational design precludes definitive causal inference. While our Bayesian multivariable mixed-effects models rigorously adjusted for clinical severity and institutional clustering, residual confounding from unmeasured factors—such as angiographic complexity, detailed pre-hospital care, or prior medication adherence—cannot be entirely excluded. Specifically, the observed protective association of SGLT2i therapy should be interpreted cautiously. Because these agents were initiated after hospital admission rather than before STEMI presentation, the analysis is susceptible to treatment-selection and immortal time biases, whereby patients who survived long enough to receive therapy may have had a more

favorable underlying prognosis. Although multivariable adjustment for baseline severity likely reduced this bias, it cannot eliminate it completely. Second, the cohort is inherently subject to pre-hospital survivor bias. In a conflict-affected environment with prolonged transport times, patients experiencing the most catastrophic STEMI events likely died before reaching a PCI-capable center. Furthermore, excluding inter-hospital transfers by retaining only the index hospitalization may have modestly underestimated the true population-level mortality burden. Third, our primary endpoint was restricted to in-hospital mortality, precluding the assessment of long-term post-discharge survival. Finally, findings from this specific national setting may lack direct generalizability to well-resourced healthcare systems with integrated emergency medical services and rapid primary PCI networks. Nevertheless, the prospective design, standardized electronic data collection, and rigorous machine-learning-based analytical framework strengthen the validity of the identified predictors, offering crucial evidence from one of the world's most fragile healthcare environments.

5. Conclusions

This prospective multicenter study provides critical contemporary evidence on STEMI outcomes from a conflict-affected, resource-limited healthcare system. In-hospital mortality in this vulnerable population is principally determined by the interaction between baseline cardiovascular vulnerability—most notably prior MI—and the severity of acute hemodynamic compromise at presentation, as reflected by higher Killip class, elevated SCr, and reduced LVEF. While systemic infrastructure deficits inevitably contribute to significant treatment delays, the independent protective associations observed with in-hospital BB and SGLT2i therapy highlight the importance of optimizing GDMT. These findings underscore the value of incorporating readily available

clinical predictors into early prognostic assessment to facilitate timely identification of high-risk patients and improve STEMI care in fragile healthcare settings.

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Research Ethics Committee (REC) at Al-Razi University (Approval Ref: RU/27/FMHS/2024, dated 02/09/2024). Written informed consent was obtained from all individual participants included in the study.

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Author Contributions

I.A. and A.A.M. conceptualized and designed the study. I.A., T.A., A.S.H., T.A.B., A.A.F., A.Su., A.A.S., and S.A. acquired the clinical data. I.A. and A.A. performed the formal statistical analysis, methodology design, and data curation. I.A. and A.A. drafted the main manuscript text. I.A. and A.A. prepared the tables and figures. A.A.M. provided clinical supervision and critical revision of the manuscript for important intellectual content. All authors reviewed and approved the final manuscript.

Clinical trial number

Not applicable.

Competing interests

The authors declare no competing interests.

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