Clinical Predictors of Heart Failure after STEMI: Data from a Middle-Income Country with Limited Access to Percutaneous Coronary Intervention

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Abstract

Background: **Heart failure (HF) is a common complication of ST-elevation myocardial infarction (STEMI) in low- and middle-income countries (LMICs), where cardiovascular mortality is disproportionately high. Primary percutaneous coronary intervention (PCI) has reduced post-STEMI HF incidence in high-income countries. However, access to this standard of care is poor in LMICs, and data in these settings remain scarce**

Objective: **To identify predictors of HF following STEMI in a LMIC with limited access to PCI, aiming at better management and outcomes.**

Methods: **This retrospective cohort study analyzed 2,467 STEMI patients admitted to two Brazilian public hospitals between January/2015 and February/2020. All participants received pharmacological thrombolysis and underwent coronarography within 48h post-admission. The primary outcome was symptomatic HF, defined as dyspnea with chest X-ray evidence of congestion, from 48h post-admission until discharge. Stepwise binary logistic regression was used to identify HF predictors. Significance was defined as p-values<0.05.**

Results: **The population was 61.9% male, mean age was 58.3±12.6 years, and 39.9% developed post-STEMI HF. HF was more common among older men with cardiovascular-kidney-metabolic (CKM) disease, larger infarcts, and left anterior descending artery involvement. Medications were often underprescribed at discharge, especially aldosterone antagonists (11.0%). HF was notably more frequent among individuals with failed thrombolysis (47.0%).**

Conclusions: **This regionally representative cohort from a LMIC with limited access to PCI showed that older men with CKM disease are particularly vulnerable to post-STEMI HF, and that HF pharmacotherapy at discharge needs optimization. The high HF incidence among patients with failed thrombolysis highlights the need to expand PCI availability.**

Keywords: **Heart Failure; ST Elevation Myocardial Infarction; Risk Factors; Pharmacological Thrombolysis.**

Introduction

ST-elevation myocardial infarction (STEMI) continues to be a major contributor to morbidity and mortality worldwide.[1,2] STEMI often leads to heart failure (HF), with high healthcare costs and a major impact on patient quality of life and productivity.[3,4]

In recent decades, advances in acute cardiovascular care and revascularization techniques, particularly primary percutaneous coronary intervention (PCI), have led to improved outcomes in high-income countries, such as United States, Sweden, Denmark, and Australia.[5-10] However, this gold-standard strategy is often unavailable in low- and middle-income countries (LMICs), and patients in these settings primarily receive pharmacological thrombolysis, or even no reperfusion therapy.

Recent articles have explored HF risk factors and/or STEMI outcomes after the advent of primary PCI.[11-13] Studies from the thrombolytic era also investigated those topics in high-income countries.[2] However, to our knowledge, there is no contemporary literature on HF after STEMI in LMICs with limited or no access to PCI.

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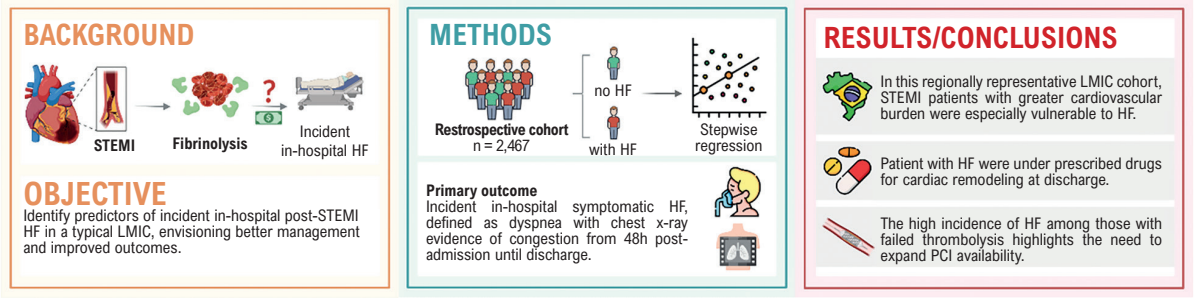
Central Illustration: Clinical Predictors of Heart Failure after STEMI: Data from a Middle-Income Country with Limited Access to Percutaneous Coronary Intervention



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Summarized design and results of the study. STEMI: ST-elevation myocardial infarction. HF: heart failure. LMIC: low- and middle-income countries. PCI: percutaneous coronary intervention

Therefore, this large multicenter study aims to identify and quantify predictors of HF post-STEMI in a typical LMIC with limited access to PCI. Identifying these predictors paves the way for more effective management strategies and improved outcomes in these resource-limited environments.

Methods

Study design, population, and ethics

This study used data from the Brasilia Cardiovascular Registry for Quality of Care and Outcomes (B-CaRe:QCO), a retrospective database of 6,341 patients admitted for acute coronary syndrome to two public tertiary hospitals of Brazil's Federal District, between January/2011 and February/2020.[14,15] We included only the subset of patients hospitalized for STEMI, and only those admitted after January/2015, as data on incident HF were not available for patients hospitalized beforehand (n=2,722). We also excluded 275 individuals with HF at baseline and patients with Killip class II-IV at hospital admission. The final cohort encompassed 2,467 eligible patients, as outlined in the STROBE flowchart (Figure 1).

All participants received pharmacological thrombolysis and underwent coronarography within 48h of admission, at either Hospital de Base do Distrito Federal (HBDF), or at Instituto de Cardiologia e Transplantes do Distrito Federal (ICTDF), both in Brasilia, Brazil. Between 2015 and 2019, these two institutions performed nearly 99% of all coronary angiographies in patients with STEMI in the public health system of Brazil's Federal District.

Research methodology followed the World Medical Association (WMA)'s Declaration of Helsinki, and was approved by the Institutional Review Board (IRB) of the Instituto de Gestão Estratégica de Saúde do Distrito Federal (IGESDF), which also granted a waiver for informed consent given the de-identified data collection (approval number 28530919.0.1001.8153).

Data collection and primary outcome

Data were collected through analysis of digital medical record using standardized collection forms. Data categories included: demographics, medical history, index STEMI characteristics, laboratory results, treatment details, and in-hospital outcomes. Laboratory testing followed standard clinical procedures. Coronary anatomy severity, atherosclerotic disease extent, angiographic treatments, TIMI flow grade, and myocardial blush grade (MBG) were determined by analysis of medical reports.

The primary outcome was in-hospital incident HF, defined as dyspnea with chest X-ray evidence of congestion, from 48h post-admission until discharge.

Statistical analysis

Population characteristics were compared between groups with or without HF. Categorical variables were represented as counts and percentages, and were compared using Pearson's chi-squared test (or Fisher's exact test for variables with less than 10 occurrences). Continuous variables were expressed as mean and standard deviation, and were compared using independent Student's t-test.

Normality was tested using Kolmogorov-Smirnov test and confirmed with graphical inspection. Variables were also tested for absence of multicollinearity. Stepwise binary logistic regression (forward likelihood ratio method) was used to identify and quantify predictors of symptomatic in-hospital post-STEMI HF. The associated odds ratio (OR) and its respective 95% confidence interval (95%CI) were calculated for each predictor identified. The Hosmer-Lemeshow test was used to check if the model is a good fit for the data.

Statistical significance was defined as p-values<0.05. Microsoft Excel 2021 for Windows was used for data management. Statistical analyses were conducted on IBM SPSS 26 for Windows.

Results

From January/2015 to February/2020, 2,467 individuals were admitted for STEMI in two public tertiary hospitals in

Brazil's Federal District. Mean age of the population was 58.3±12.6 years, and most patients were male (61.9%, n=1,520 individuals). Post-STEMI HF was observed in 984 patients (39.9%).

Baseline population characteristics

HF was more frequent among males and older patients (Table 1). Notably, the odds of developing the condition were significantly lower for those under 60 years (OR: 0.581, 95%CI: 0.491-0.687) compared to those aged 60-79 years (OR: 1.500 (95%CI: 1.262-1.783)) and 80 years and above (OR: 2.241 (95%CI: 1.541-3.259)). Obesity was more prevalent in the HF group, as was hypertension, diabetes, hypothyroidism, chronic kidney disease (CKD), previous coronary arterial disease (CAD), previous myocardial infarction (MI), and previous PCI.

Characteristics of index STEMI

Regarding symptomatology at admission, patients who developed HF presented more often with syncope and cardiac arrest (Table 2). They also had lower systolic and diastolic blood pressures, as well as higher GRACE and CRUSADE scores. Furthermore, HF patients more often had anterior myocardial infarction and right bundle branch block (RBBB) on admission electrocardiogram (ECG). Pathological Q-waves were more common in leads V1-V4 (anterior), V1-V6 (anterolateral), and V4R (right), and less common in leads V5-V6 (lateral) and DII-DIII/AVF (inferior).

High-sensitivity cardiac troponin I (hs-cTnI) at admission was higher in the HF group, as was its peak levels and aspartate aminotransferase (AST), indicating more extensive myocardial injury. Renal impairment was also more common in the HF group, with higher creatinine and lower glomerular filtration rate (GFR). HF patients also had elevated blood glucose and hemoglobin A1c (HbA1c), and lower low-density lipoprotein cholesterol (LDL-C). Also, shorter prothrombin time (PT) and prolonged partial thromboplastin time (PTT) were seen among those with HF.

Treatment details

Pharmaco-invasive treatment strategy was strongly and inversely associated with incident post-STEMI HF (OR: 0.280, 95%CI: 0.235-0.334) (Table 3). In contrast, individuals who underwent rescue PCI after failing to meet reperfusion criteria more often developed HF (OR: 3.920, 95%CI: 3.269-4.699). Shorter times from symptom onset to hospital presentation and from thrombolysis to catheterization were seen in the HF group, likely reflecting the logistical prioritization of more severe presentations given limited capacity of our public healthcare system.

Regarding PCI details, incident HF was more common among those who received GPIIb/IIIa inhibitors and nitroprusside during catheterization, and those with more conventional stents implanted. Final TIMI-3 flow and myocardial blush grade 3 were less frequently achieved in the HF group.

HF patients had lower mean left ventricular ejection fraction (LVEF) and more frequent reduced ejection fraction (rEF) (LVEF <40%) on echocardiogram at 48-72h of admission. Motility changes in the HF group were mainly associated with left anterior descending artery (LAD) involvement.

At hospital discharge (or death), HF patients were less prescribed angiotensin receptor blockers (ARBs) and calcium channel blockers. On the other hand, this group more frequently received aldosterone antagonists, furosemide, prasugrel, ticagrelor, and anticoagulants.

In-hospital outcomes

Recurrent angina and MI occurred more often in the HF group (Table 4). Other cardiovascular complications were also associated with incident HF, including: atrial fibrillation, total atrioventricular block, mitral regurgitation, cardiac arrest, ischemic and hemorrhagic stroke, minor and major bleeding, and blood transfusion. Mean hospitalization stay was longer in the HF group, along with higher all-cause in-hospital mortality.

Predicting in-hospital HF post-STEMI

We conducted a stepwise binary logistic regression (forward likelihood ratio method) to identify and quantify significant predictors of incident in-hospital HF following STEMI (Table 5). This analysis resulted in a statistically significant model [Nagelkerke R^2=0.550, p=0.039] that correctly classified 82.3% of cases. The Hosmer-Lemeshow test indicated a good model fit (p=0.746).

Risk predictors of incident post-STEMI HF identified include: AST (in increments of 100U/L), V4R pathological Q-waves, anterior akinesia, rescue PCI, apical hypokinesia, septal akinesia, catheterization duration (in hours), hypothyroidism, prior MI, dorsal akinesia, blood glucose (in increments of 100mg/dL), RBBB, lateral hypokinesia, creatinine (mg/dL), smoking history, obesity, anterior MI, and apical akinesia.

As for protective predictors, the following factors were identified: higher systolic blood pressure (SBP) at admission, age <60 years, TIMI-3 flow after PCI, and PT (in seconds).

Discussion

To our knowledge, this is a pioneering study in identifying predictors of both risk and protection for HF after STEMI in a LMIC with limited access to primary PCI (Central Illustration). Patients who developed HF showed a clear profile of increased cardiovascular risk, marked by older age, male sex, metabolic dysfunction, and already established end-organ damage. Larger infarcts and LAD involvement were also found to be predictive of HF. Additionally, HF patients were notably underprescribed medications that improve cardiac remodeling, particularly aldosterone antagonists. Lastly, the high incidence of HF, especially among those with failed thrombolysis, underscore the imperative to expand primary PCI feasibility in LMICs like Brazil.

The increased cardiovascular-kidney-metabolic (CKM) risk observed among patients who developed HF after STEMI aligns with previous studies.[13,16-18] Interestingly, almost all cardiovascular (hypertension, prior CAD), kidney (chronic kidney disease), and metabolic (obesity, diabetes, hypothyroidism) components were more prevalent in the HF

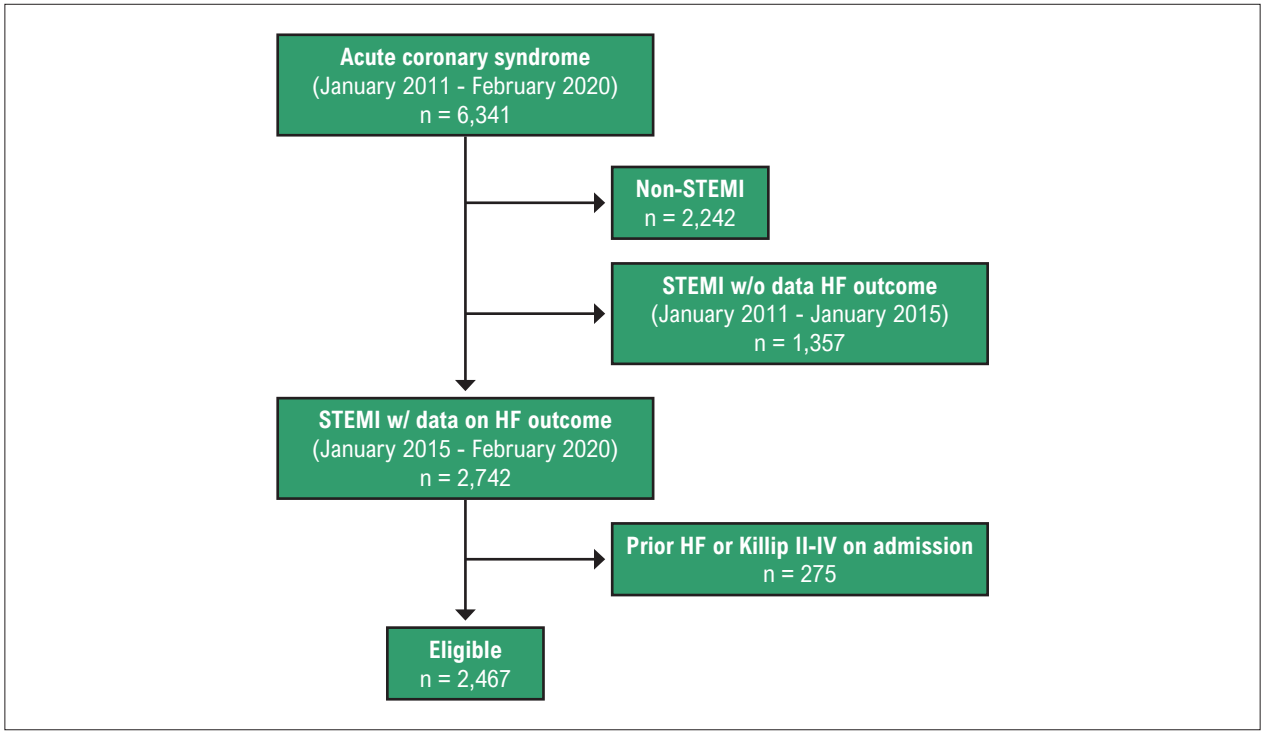

Figure 1 – *STROBE flowchart. STEMI: ST-elevation myocardial infarction. HF: heart failure.*

Table 1 – Baseline characteristics

Variable	Incident HF post-STEMI		p-value	OR(95%CI)
	No(n=1,483)	Yes(n=984)		
Demographics				
Male sex, n (%)	885(59.6)	635(64.5)	0.015*	1.229(1.040-1.452)
Age (years), μ±SD	57.5±13.3	59.5±11.4	<0.001†	-
Age <60 years, n (%)	1,026(69.2)	557(56.6)	<0.001*	0.581(0.491-0.687)
Age 60-79 years, n (%)	408(27.5)	357(36.3)	<0.001*	1.500(1.262-1.783)
Age ≥80 years, n (%)	49(3.3)	70(7.1%)	<0.001*	2.241(1.541-3.259)
BMI (kg/m^2), μ±SD	26.73±4.50	27.13±4.57	0.032†	-
Underweight (<18.5kg/m^2), n (%)	22(1.5)	7(0.7)	0.088‡	0.475(0.202-1.115)
Normal Weight (18.5-24.9kg/m^2), n (%)	559(37.8)	347(35.3)	0.204*	0.897(0.758-1.061)
Overweight (25-29.9kg/m^2), n (%)	613(41.5)	403(41.0)	0.814*	0.980(0.832-1.155)
Obese I (30-34.9kg/m^2), n (%)	219(14.8)	166(16.9)	0.166*	1.168(0.937-1.456)
Obese II (35-39.9kg/m^2), n (%)	45(3.0)	46(4.7)	0.035*	1.563(1.028-2.377)
Obese III (≥40kg/m^2), n (%)	20(1.4)	14(1.4)	0.882*	1.053(0.529-2.095)
Medical history				
Obesity, n (%)	260(17.5)	219(22.3)	0.004*	1.347(1.101-1.647)
Hypertension, n (%)	863(58.2)	614(62.4)	0.037*	1.192(1.011-1.406)
Diabetes, n (%)	387(26.1)	349(35.5)	<0.001*	1.557(1.307-1.853)
Dyslipidemia, n (%)	709(47.8)	507(51.5)	0.071*	1.160(0.988-1.363)

Smoking history, n (%)	960(64.7)	610(62.0)	0.166*	0.889(0.752-1.050)
Alcohol abuse history, n (%)	183(12.3)	118(12.0)	0.796*	0.968(0.756-1.239)
Illicit drugs abuse history, n(%)	64(4.3)	31(3.2)	0.141*	0.721(0.466-1.116)
CVD family history, n (%)	319(21.5)	197(20.0)	0.373*	0.913(0.748-1.115)
Hypothyroidism, n (%)	73(4.9)	72(7.3)	0.013*	1.525(1.090-2.134)
End-organ damage				
CKD, n (%)	68(4.6)	90(9.1)	<0.001*	2.095(1.512-2.902)
Prior CAD, (%)	399(26.9)	324(32.9)	0.001*	1.334(1.119-1.590)
Prior angina, n (%)	330(22.3)	243(24.7)	0.159*	1.146(0.948-1.385)
Prior MI, n (%)	105(7.1)	128(13.0)	<0.001*	1.962(1.495-2.575)
Prior PCI, n (%)	47(3.2)	70(7.1)	<0.001*	2.340(1.602-3.418)
Prior CABG, n (%)	26(1.8)	17(1.7)	0.962*	0.985(0.532-1.825)
Prior stroke, n (%)	51(3.4)	44(4.5)	0.192*	1.314(0.871-1.984)
Prior PAD, n (%)	57(3.8)	51(5.2)	0.111*	1.368(0.929-2.013)

**Pearson's chi-squared test. †Independent Student's t-test; ‡Fisher's exact test; bolded p-values indicate statistical significance at a threshold of p<0.05; OR: odds ratio; CI: confidence interval; n: number of individuals; μ: mean value; SD: standard deviation; HF: heart failure; STEMI: ST-elevation myocardial infarction; BMI: body mass index; CVD: cardiovascular disease; CKD: chronic kidney disease; CAD: coronary arterial disease; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; PAD: peripheral artery disease.*

Table 2 – Characteristics of index ST-elevation myocardial infarction (STEMI)

Variable	Incident HF post-STEMI		p-value	OR(95%CI)
	No(n=1,483)	Yes(n=984)		
Symptomatology at admission				
Syncope, n (%)	12(0.8)	20(2.0)	0.009*	2.543(1.238-5.226)
Cardiac arrest, n (%)	4(0.3)	22(2.2)	<0.001‡	8.450(2.903-24.597)
Systolic BP (mmHg), μ±SD	136.3±25.1	129.7±30.0	<0.001†	-
Diastolic BP (mmHg), μ±SD	83.1±16.3	81.1±20.5	<0.001†	-
Risk stratification at admission				
GRACE score, μ±SD	99.2±24.5	141.9±43.1	<0.001†	-
CRUSADE score, μ±SD	21.6±12.2	33.7±15.0	<0.001†	-
Admission ECG				
Anterior wall MI, n (%)	495(33.4)	628(63.8)	<0.001*	3.521(2.974-4.169)
Right bundle branch block, n (%)	6(0.4)	16(1.6)	0.002‡	4.069(1.587-10.435)
Left bundle branch block, n (%)	4(0.3)	6(0.6)	0.211‡	2.268(0.638-8.059)
2nd/3rd-degree AV block, n (%)	5(0.3)	7(0.7)	0.240‡	2.118(0.670-6.692)
Septal (V1-V3) path. Q-waves, n (%)	80(5.4)	55(5.6)	0.835*	1.038(0.729-1.478)
Anterior (V1-V4) path. Q-waves, n (%)	191(12.9)	191(19.4)	<0.001*	1.629(1.309-2.029)
Anterolateral (V1-V6) path. Q-waves, n (%)	225(15.2)	383(38.9)	<0.001*	3.563(2.943-4.314)
Lateral (V5-V6) path. Q-waves, n (%)	80(5.4)	30(3.0)	0.006*	0.551(0.360-0.846)

Right (V4R) path. Q-waves, n (%)	129(8.7)	110(11.2)	0.041*	1.321(1.010-1.727)
Inferior (DI, DII, AVF) path. Q-waves, n (%)	649(43.8)	211(21.4)	<0.001*	0.351(0.292-0.421)
Laboratory results				
Admission hs-cTnI (ng/L), μ±SD	5,042±5,978	8,436±9,071	<0.001†	-
Peak hs-cTnI (ng/L), μ±SD	6,164±5,658	11,145±10,992	<0.001†	-
AST (U/L), μ±SD	167±139	267±198	<0.001†	-
ALT (U/L), μ±SD	49.4±48.5	95.7±185.7	<0.001†	-
Creatinine (mg/dL), μ±SD	0.92±0.40	1.11±0.87	<0.001†	-
GFR (mL/min), μ±SD	96.5±34.3	85.4±35.3	<0.001†	-
Blood glucose (mg/dL), μ±SD	132.6±56.5	166.0±85.6	<0.001†	-
HbA1c (%), μ±SD	6.55±1.81	6.95±2.23	<0.001†	-
TSH (mIU/L), μ±SD	2.16±3.99	2.81±6.21	0.007†	-
FT4 (ng/dL), μ±SD	1.29±0.63	1.30±0.62	0.744†	-
Total cholesterol (mg/dL), μ±SD	201.49±45.5	198.2±48.5	0.111†	-
HDL-C (mg/dL), μ±SD	41.5±12.3	41.3±12.5	0.637†	-
LDL-C (mg/dL), μ±SD	130.0±39.5	125.2±40.9	0.010†	-
Triglycerides (mg/dL), μ±SD	158.2±109.7	158.9±119.2	0.876†	-
Hemoglobin (g/dL), μ±SD	14.55±1.70	14.50±1.96	0.053†	-
Hematocrit (%), μ±SD	43.03±4.84	42.86±5.72	0.448†	-
PT (s), μ±SD	85.3±12.2	81.4±15.4	<0.001†	-
PTT (s), μ±SD	34.9±13.0	38.0±20.2	<0.001†	-

**Pearson's chi-squared test. †Independent Student's t-test. ‡Fisher's exact test. Bolded p-values indicate statistical significance at a threshold of p<0.05. OR: odds ratio. CI: confidence interval. n: number of individuals. μ: mean value. SD: standard deviation. STEMI: ST-elevation myocardial infarction. HF: heart failure. BP: blood pressure. AV: atrioventricular; hs-cTnI: high-sensitivity cardiac troponin I. AST: aspartate aminotransferase. ALT: alanine aminotransferase. GFR: glomerular filtration rate. HbA1c: hemoglobin A1c. TSH: thyroid-stimulating hormone. FT4: free thyroxine. HDL-C: high density lipoprotein cholesterol. LDL-C: low density lipoprotein cholesterol. PT: prothrombin time. PTT: partial thromboplastin time.*

Table 3 – Treatment details

Variable	Incident HF post-STEMI		p-value	OR(95%CI)
	No(n=1,483)	Yes(n=984)		
Treatment details				
Pharmaco-invasive, n (%)	1,164(78.5)	498(50.6)	<0.001*	0.280(0.235-0.334)
Rescue PCI, n (%)	273(18.4)	462(47.0)	<0.001*	3.920(3.269-4.699)
2nd cath., n (%)	110(7.5)	91(9.3)	0.106*	1.270(0.950-1.698)
Angioplasty on the 2nd cath., n (%)	81(7.6)	61(8.1)	0.669*	1.078(0.763-1.524)
Onset-primary hospital (min), μ±SD	158±135	146±126	0.036†	-
Door-needle (min), μ±SD	181±3,436	98±92	0.449†	-
Thrombolysis-cath. (min), μ±SD	1,392±1,220	1,059±1,186	<0.001†	-
Catheterization and PCI details				
Use of GPIIb/IIIa inhibitor, n (%)	50(3.4)	66(6.7)	<0.001*	2.061(1.414-3.003)

Use of nitroprusside, n (%)	5(0.3)	10(1.0)	0.034‡	3.035(1.034-8.906)
Use of adenosine, n (%)	38(2.6)	61(6.2)	<0.001*	2.513(1.662-3.800)
No. of conventional stents, μ±SD	0.83±0.73	0.93±0.75	0.001†	-
No. of drug-eluting stents, μ±SD	0.09±0.35	0.07±0.34	0.136†	-
TIMI-3 flow post-PCI, n (%)	1,058(83.4)	601(69.0)	<0.001*	0.444(0.361-0.545)
MBG grade 3 post-PCI, n (%)	845(69.7)	393(49.0)	<0.001*	0.418(0.348-0.503)
Cath. duration (min), μ±SD	90±1,181	62±29	0.460†	-
Echocardiography 48-72h after admission				
LVEF (%), μ±SD	54.9±7.4	41.0±9.8	<0.001†	-
LVEF <40%, n (%)	1(0.1)	367(42.7)	<0.001‡	851.8(119.3-6,080.8)
Hypokinesia anterior, n (%)	192(12.9)	254(25.8)	<0.001*	2.340(1.900-2.881)
Hypokinesia septal, n (%)	373(25.2)	257(26.1)	0.590*	1.052(0.875-1.265)
Hypokinesia lateral, n (%)	125(8.4)	160(16.3)	<0.001*	2.110(1.644-2.707)
Hypokinesia right, n (%)	3(0.2)	15(1.5)	<0.001‡	7.637(2.205-26.449)
Hypokinesia inferior, n (%)	396(26.7)	211(21.4)	0.003*	0.749(0.619-0.907)
Hypokinesia apical, n (%)	77(5.2)	91(9.2)	<0.001*	1.861(1.358-2.549)
Hypokinesia dorsal, n (%)	273(18.4)	130(13.2)	0.001*	0.675(0.538-0.846)
Akinesia anterior, n (%)	124(8.4)	373(37.9)	<0.001*	6.691(5.345-8.374)
Akinesia septal, n (%)	251(16.9)	467(47.5)	<0.001*	4.434(3.686-5.333)
Akinesia lateral, n (%)	39(2.6)	90(8.1)	<0.001*	3.277(2.215-4.848)
Akinesia right, n (%)	0(0.0)	2(0.2)	0.159‡	0.398(0.380-0.418)
Akinesia inferior, n (%)	382(25.8)	264(26.8)	0.554*	1.057(0.880-1.269)
Akinesia apical, n (%)	188(12.7)	431(43.8)	<0.001*	5.369(4.404-6.545)
Akinesia dorsal, n (%)	108(7.3)	105(10.7)	0.003*	1.521(1.148-2.016)
Pharmacotherapy at discharge (or death)				
ACE inhibitors, n (%)	661(44.6)	413(41.9)	0.202*	0.899(0.764-1.058)
Angiotensin receptor blockers, n (%)	351(23.7)	167(16.9)	<0.001*	0.659(0.537-0.809)
Beta-blockers, n (%)	1,003(67.6)	656(66.6)	0.616*	0.957(0.806-1.136)
Aldosterone antagonists, n (%)	64(4.3)	109(11.0)	<0.001*	2.762(2.005-3.803)
Furosemide, n (%)	86(5.8)	110(11.1)	<0.001*	2.044(1.522-2.744)
Calcium channel blockers, n (%)	320(21.6)	145(14.7)	<0.001*	0.628(0.506-0.779)
Statins, n(%)	1,226(82.7)	815(82.8)	0.920*	1.010(0.816-1.251)
Acetylsalicylic acid, n (%)	1,449(97.7)	965(98.8)	0.543*	1.191(0.675-2.101)
Clopidogrel, n (%)	1,035(69.8)	667(67.7)	0.291*	0.910(0.765-1.083)
Prasugrel, n (%)	214(14.4)	260(26.4)	<0.001*	2.129(1.738-2.607)
Ticagrelor, n (%)	33(2.2)	35(3.5)	0.047*	1.620(1.000-2.625)
Anticoagulants, n (%)	46(3.1)	56(5.6)	0.001*	1.885(1.265-2.808)

**Pearson's chi-squared test. †Independent Student's t-test. ‡Fisher's exact test. Bolded p-values indicate statistical significance at a threshold of p<0.05. OR: odds ratio. CI: confidence interval. n: number of individuals. μ: mean value. SD: standard deviation. STEMI: ST-elevation myocardial infarction. HF: heart failure. PCI: percutaneous coronary intervention. LVEF: left ventricular ejection fraction. ACE: angiotensin-converting-enzyme; MBG: myocardial blush grade.*

Table 4 – In-hospital outcomes

Variable	Incident HF post-STEMI		p-value	OR(95%CI)
	No(n=1,483)	Yes(n=984)		
Recurrent angina, n (%)	32(2.2)	35(3.6)	0.036*	1.672(1.028-2.720)
Recurrent MI, n (%)	12(0.8)	28(2.8)	<0.001*	3.590(1.817-7.095)
Atrial fibrillation, n (%)	31(2.1)	55(5.6)	<0.001*	2.773(1.772-4.339)
3rd degree atrioventricular block, n (%)	48(3.2)	70(7.1)	<0.001*	2.290(1.571-3.337)
Mitral regurgitation, n (%)	3(0.2)	9(0.9)	0.017‡	4.554(1.230-16.863)
Cardiac arrest, n (%)	5(0.3)	24(2.4)	<0.001‡	7.385(2.808-19.422)
Ischemic stroke, n (%)	6(0.4)	21(2.1)	<0.001‡	5.368(2.159-13.348)
Hemorrhagic stroke, n (%)	3(0.2)	13(1.3)	0.001‡	6.605(1.877-23.238)
Minor bleeding, n (%)	28(1.9)	38(3.9)	0.003*	2.087(1.272-3.424)
Major bleeding, n (%)	11(0.7)	51(5.2)	<0.001*	7.315(3.793-14.106)
Blood transfusion, n (%)	7(0.5)	31(3.2)	<0.001‡	6.859(3.008-15.639)
Hospitalization length (days), μ±SD	4.01±3.15	6.59±7.36	<0.001†	-
All-cause in-hospital death, n (%)	12(0.8)	110(11.2)	<0.001*	15.428(8.453-28.160)

**Pearson's chi-squared test. †Independent Student's t-test. ‡Fisher's exact test. Bolded p-values indicate statistical significance at a threshold of p<0.05. OR: odds ratio. CI: confidence interval. n: number of individuals. μ: mean value. SD: standard deviation. STEMI: ST-elevation myocardial infarction. HF: heart failure. MI: myocardial infarction.*

Table 5 – Predictors of incident in-hospital HF post-STEMI identified by stepwise binary logistic regression (forward likelihood ratio method)

Variable	B	SE	Wald	p-value	OR(95%CI)
Risk predictors for in-hospital HF post-STEMI					
AST (increments of 100U/L)	0.373	0.061	37.398	<0.001*	1.453(1.289-1.637)
Right (V4R) path. Q-waves (on admission ECG)	1.770	0.318	30.920	<0.001*	5.868(3.145-10.950)
Anterior akinesia (48-72h after admission)	1.159	0.304	14.549	<0.001*	3.187(1.757-5.782)
Rescue PCI	0.787	0.215	13.400	<0.001*	2.197(1.441-3.348)
Apical hypokinesia (48-72h after admission)	1.260	0.349	13.005	<0.001*	3.524(1.777-6.987)
Septal akinesia (48-72h after admission)	0.869	0.249	12.207	<0.001*	2.384(1.464-3.880)
Cath. duration (h)	0.750	0.216	12.052	0.001*	2.117(1.386-3.233)
Hypothyroidism	1.114	0.361	9.547	0.002*	3.047(1.503-6.177)
Prior MI	0.915	0.307	8.875	0.003*	2.497(1.368-4.559)
Dorsal akinesia (48-72h after admission)	0.940	0.329	8.157	0.004*	2.560(1.343-4.880)
Blood glucose (increments of 100mg/dL)	0.371	0.147	6.351	0.012*	1.449(1.086-1.933)
Right bundle branch block (on admission ECG)	2.442	1.022	5.712	0.017*	11.501(1.552-85.245)
Lateral hypokinesia (48h after admission)	0.705	0.297	5.621	0.018*	2.023(1.130-3.622)
Creatinine (mg/dL)	0.566	0.249	5.168	0.023*	1.761(1.081-2.870)
Smoking history	0.478	0.211	5.142	0.023*	1.613(1.067-2.438)
Obesity	0.492	0.236	4.343	0.037*	1.636(1.030-2.600)

Anterior wall MI (on admission ECG)	0.553	0.267	4.286	0.038*	1.739(1.030-2.936)
Apical akinesia (48-72h after admission)	0.544	0.286	3.609	0.057*	1.722(0.983-3.017)
Protective predictors for in-hospital post-STEMI HF					
SBP (mmHg) (at admission)	-0.017	0.004	21.893	<0.001*	0.983(0.976-0.990)
Age <60 years	-0.868	0.204	18.131	<0.001*	0.420(0.282-0.626)
TIMI-3 flow post-PCI	-0.880	0.285	9.522	0.002*	0.415(0.237-0.726)
PT (s)	-0.018	0.007	7.161	0.007*	0.982(0.969-0.995)

**Stepwise binary logistic regression (forward likelihood ratio method). Bolded p-values indicate statistical significance at a threshold of p<0.05. SE: standard error. OR: odds ratio. CI: confidence interval. STEMI: ST-elevation myocardial infarction. HF: heart failure. ECG: electrocardiogram. AST: aspartate aminotransferase. PCI: percutaneous coronary intervention. MI: myocardial infarction. hs-cTnI: high-sensitivity cardiac troponin I. SBP: systolic blood pressure. PT: prothrombin time.*

group. The exception was dyslipidemia, where HF patients exhibited lower LDL-C levels. This result was also observed in other studies and is mostly explained by the acute inflammatory response associated with the infarction.[13,18,19]

Our findings also corroborate the well-established associations of infarct size and anterior MI with post-MI HF.[13,18,20,21] Upon hospital admission, a lower blood pressure suggests myocardial injury severe enough to cause some degree of hemodynamic impairment. Higher serum levels of hs-cTnI and AST, which correlate with a larger infarcted area, were also observed in the HF group.[22-25] LAD involvement played a significant role in our predictive model, encompassing several components, such as anterior akinesia, apical hypokinesia, septal akinesia, anterior wall MI on admission ECG, and apical akinesia. Lastly, RBBB is associated with both a large infarct area and LAD lesion.[26-29]

An analysis of pharmacotherapy at hospital discharge revealed that HF patients were undertreated, particularly for mineralocorticoid receptor antagonist (MRAs), a class of medication that improve cardiac remodeling and cardiovascular outcomes. Only 11.0% of HF patients, among whom 42.7% were diagnosed with rEF, were prescribed spironolactone, raising concerns about the underprescribing of evidence-based therapy and a deviation from guideline recommendations.[30] It is worth mentioning that spironolactone was the only aldosterone antagonist approved for use in Brazil up until 2021. Despite the limited literature on this topic, a recent study suggests that concerns regarding hyperkalemia, hypotension and gynecomastia are plausible explanations for the underprescribing of MRAs.[31] It is also important to highlight that the data used in this study precede the recommendation for the use of SGLT2 inhibitors in patients with HF.[32]

In the settings of limited access to primary PCI, as seen in LMICs, new features, particularly the role of failed thrombolysis, take a key predictive role. The high incidence of post-STEMI HF in the studied population (39.9%), especially among individuals with failed thrombolysis (47.0%), highlights the ongoing need for rescue PCI despite the systematic pharmaco-invasive approach, as 29.8% still depended on this strategy to survive after STEMI. In high-income countries, such as United States, Sweden, Denmark, and Australia, the incidence of HF complicating MI has dramatically declined from 20-46% in the thrombolytic era to 4-28% in the PCI era.[5-10] In contrast, LMICs still face significant challenges with limited primary PCI availability. Our results emphasize the critical need to expand primary PCI capacity in healthcare systems of LMICs like Brazil. Additionally, delays in the time from symptom onset to hospital arrival and from hospital arrival to thrombolysis also contribute to suboptimal adherence to guidelines.[33] Improving pre-hospital care networks and reducing these delays could enhance the likelihood of successful thrombolysis.[34]

The importance of our study may go beyond Brazil, resonating in LMICs globally, where more than 75% of cardiovascular deaths disproportionally occur.[35] The identified predictors of post-STEMI HF, within the context of limited access to PCI, could be used as a start template, potentially applicable for developing strategies in numerous LMICs facing similar challenges. This study also highlights the need to expand primary PCI availability and to enforce evidence-based pharmacotherapy guidelines in LMICs. As a benchmark for improving STEMI care, our findings provide important information for strategic interventions and healthcare policies, addressing the high burden of cardiovascular diseases across LMICs.

Strengths and limitations

The main strength of this study is the fact that it provides up-to-date data, from January 2015 to February 2020. Additionally, all participants underwent coronarography within 24h of thrombolysis, providing a contemporary perspective despite the limited resources of a LMIC. Furthermore, our study focused exclusively on STEMI patients, a notable distinction from several previous studies.[1,5-10,12,17,18,20,21] Lastly, the substantial sample size, of 2,622 participants, drawn from a regionally-representative cohort, bolsters statistical power and internal validity.

A core limitation of this study was its retrospective design. To address selection bias, we sequentially included all patients admitted for STEMI to the participating centers

during the study period. To minimize problems arising from data accuracy and completeness, a standardized and objective collection form was used, and an adjudication committee reviewed the data. Lastly, the identification of risk factors cannot establish causality, limiting potential interventions targeted to reduce incident post-STEMI HF.

Conclusions

Our study, based on a regionally-representative cohort from a typical LMIC with limited access to PCI, revealed that older men with increased CKM risk face greater vulnerability to HF following STEMI. The observed high incidence of HF, particularly among individuals with failed thrombolysis, highlights the need to expand primary PCI availability in regions where primary thrombolysis remains the standard of care. Our findings also emphasize the need to optimize HF pharmacotherapy, as this measure would significantly improve the clinical outcome of this population, especially in resource-limited settings.

The insights gained from our pioneering study on post-STEMI HF predictors in an LMIC with limited PCI access may hold important implications for future research, clinical practice, and health policies. The identified risk factors, including CKM components and failed thrombolysis, call for further investigations to refine risk prediction models tailored to resource-constrained settings. This study also underscores pharmacological undertreatment of HF patients at hospital discharge after STEMI in LMICs, advocating for targeted educational initiatives to improve adherence to evidence-based guidelines. Policy interventions aimed at expanding primary PCI availability in LMICs, as emphasized by our findings, could significantly reduce the incidence of post-STEMI HF. Ultimately, these efforts contribute to enhanced STEMI care and improved patient outcomes in these resource-limited environments.

Author Contributions

Conception and design of the research: Carvalho LSF; Acquisition of data: Alexim GA, Carvalho LSF; Analysis and interpretation of the data: Fiusa VC, Carvalho LSF; Statistical analysis: Fiusa VC, Carvalho LSF; Obtaining financing: Carvalho LSF, Bilevicius E, Batista V; Writing of the manuscript: Fiusa VC; Critical revision of the manuscript for content: Stephanus AD, Couto VF, Staffico A, Sposito AC, Carvalho LSF, Guimarães AJBA, Bilevicius E, Batista V; Administrative, technical, and/or logistic support: Alexim GA, Severino TMM, Nogueira ACC, Soares A.

Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

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Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Instituto de Gestão Estratégica de Saúde do DF under the protocol number 28530919.0.1001.8153. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013.

References

1. Johansson S, Rosengren A, Young K, Jennings E. Mortality and Morbidity Trends after the First Year in Survivors of Acute Myocardial Infarction: A Systematic Review. BMC Cardiovasc Disord. 2017;17(1):53. doi: 10.1186/s12872-017-0482-9.
2. Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'Agostino RB, Kannel WB, et al. Lifetime Risk for Developing Congestive Heart Failure: The Framingham Heart Study. Circulation. 2002;106(24):3068-72. doi: 10.1161/01.cir.0000039105.49749.6f.
3. Roger VL. Epidemiology of Heart Failure. Circ Res. 2013;113(6):646-59. doi: 10.1161/CIRCRESAHA.113.300268.
4. Mosterd A, Hoes AW. Clinical Epidemiology of Heart Failure. Heart. 2007;93(9):1137-46. doi: 10.1136/hrt.2003.025270.
5. Gerber Y, Weston SA, Berardi C, McNallan SM, Jiang R, Redfield MM, et al. Contemporary Trends in Heart Failure with Reduced and Preserved Ejection Fraction after Myocardial Infarction: A Community Study. Am J Epidemiol. 2013;178(8):1272-80. doi: 10.1093/aje/kwt109.
6. Ali AS, Rybicki BA, Alam M, Wulbrecht N, Richer-Cornish K, Khaja F, et al. Clinical Predictors of Heart Failure in Patients with First Acute Myocardial Infarction. Am Heart J. 1999;138(6 Pt 1):1133-9. doi: 10.1016/s0002-8703(99)70080-3.
7. Shah RV, Holmes D, Anderson M, Wang TY, Kontos MC, Wiviott SD, et al. Risk of Heart Failure Complication during Hospitalization for Acute Myocardial Infarction in a Contemporary Population: Insights from the National Cardiovascular Data ACTION Registry. Circ Heart Fail. 2012;5(6):693-702. doi: 10.1161/CIRCHEARTFAILURE.112.968180.
8. Desta L, Jernberg T, Löfman I, Hofman-Bang C, Hagerman I, Spaak J, et al. Incidence, Temporal Trends, and Prognostic Impact of Heart Failure Complicating Acute Myocardial Infarction. The SWEDEHEART Registry (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies): A Study of 199,851 Patients Admitted with Index Acute Myocardial Infarctions, 1996 to 2008. JACC Heart Fail. 2015;3(3):234-42. doi: 10.1016/j.jchf.2014.10.007.
9. Gjesing A, Gislason GH, Køber L, Gustav Smith J, Christensen SB, Gustafsson F, et al. Nationwide Trends in Development of Heart Failure and Mortality after First-Time Myocardial Infarction 1997-2010: A Danish Cohort Study. Eur J Intern Med. 2014;25(8):731-8. doi: 10.1016/j.ejim.2014.08.009.
10. Hung J, Teng TH, Finn J, Knuiman M, Briffa T, Stewart S, et al. Trends from 1996 to 2007 in Incidence and Mortality Outcomes of Heart Failure after Acute Myocardial Infarction: A Population-Based Study of 20,812 Patients with First Acute Myocardial Infarction in Western Australia. J Am Heart Assoc. 2013;2(5):e000172. doi: 10.1161/JAHA.113.000172.

11. Lenselink C, Ricken KWLM, Groot HE, Bruijne TJ, Hendriks T, van der Harst P, et al. Incidence and Predictors of Heart Failure with Reduced and Preserved Ejection Fraction after ST-Elevation Myocardial Infarction in the Contemporary Era of Early Percutaneous Coronary Intervention. Eur J Heart Fail. 2024;26(5):1142-9. doi: 10.1002/ejhf.3225.

12. Cahill TJ, Kharbanda RK. Heart Failure after Myocardial Infarction in the Era of Primary Percutaneous Coronary Intervention: Mechanisms, Incidence and Identification of Patients at Risk. World J Cardiol. 2017;9(5):407-15. doi: 10.4330/wjc.v9.i5.407.

13. Gho JMIH, Postema PG, Conijn M, Bruinsma N, Jong JSSG, Bezzina CR, et al. Heart Failure Following STEMI: A Contemporary Cohort Study of Incidence and Prognostic Factors. Open Heart. 2017;4(2):e000551. doi: 10.1136/openhrt-2016-000551.

14. Alexim GA, Rocha LF, Dobri GP, Rosa ADS Jr, Reis RTB, Nogueira ACC, et al. Clinical and Economic Impact of Coronary Artery Bypass Graft and Percutaneous Coronary Intervention in Young Individuals with Acute Coronary Syndromes and Multivessel Disease: A Real-World Comparison in a Middle-Income Country. Front Cardiovasc Med. 2022;9:1000260. doi: 10.3389/fcvm.2022.1000260.

15. Carvalho LSF, Alexim G, Nogueira ACC, Fernandez MD, Rezende TB, Avila S, et al. The Framing of Time-Dependent Machine Learning Models Improves Risk Estimation Among Young Individuals with Acute Coronary Syndromes. Sci Rep. 2023;13(1):1021. doi: 10.1038/s41598-023-27776-0.

16. Khan SS, Coresh J, Pencina MJ, Ndumele CE, Rangaswami J, Chow SL, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement from the American Heart Association. Circulation. 2023;148(24):1982-2004. doi: 10.1161/CIR.0000000000001191.

17. Velazquez EJ, Francis GS, Armstrong PW, Aylward PE, Diaz R, O'Connor CM, et al. An International Perspective on Heart Failure and Left Ventricular Systolic Dysfunction Complicating Myocardial Infarction: The VALIANT Registry. Eur Heart J. 2004;25(21):1911-9. doi: 10.1016/j.ehj.2004.08.006.

18. Lewis EF, Moye LA, Rouleau JL, Sacks FM, Arnold JM, Warnica JW, et al. Predictors of Late Development of Heart Failure in Stable Survivors of Myocardial Infarction: The CARE Study. J Am Coll Cardiol. 2003;42(8):1446-53. doi: 10.1016/s0735-1097(03)01057-x.

19. Henkin Y, Crystal E, Goldberg Y, Friger M, Lorber J, Zuili I, et al. Usefulness of Lipoprotein Changes During Acute Coronary Syndromes for Predicting Postdischarge Lipoprotein Levels. Am J Cardiol. 2002;89(1):7-11. doi: 10.1016/s0002-9149(01)02154-3.

20. Gerber Y, Weston SA, Enriquez-Sarano M, Berardi C, Chamberlain AM, Manemann SM, et al. Mortality Associated with Heart Failure after Myocardial Infarction: A Contemporary Community Perspective. Circ Heart Fail. 2016;9(1):e002460. doi: 10.1161/CIRCHEARTFAILURE.115.002460.

21. Santoro GM, Carrabba N, Migliorini A, Parodi G, Valenti R. Acute Heart Failure in Patients with Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention. Eur J Heart Fail. 2008;10(8):780-5. doi: 10.1016/j.ejheart.2008.06.004.

22. Ladenson JH. A Personal History of Markers of Myocyte Injury [Myocardial Infarction]. Clin Chim Acta. 2007;381(1):3-8. doi: 10.1016/j.cca.2007.02.039.

23. Tzivoni D, Koukoui D, Guetta V, Novack L, Cowing G; CASTEMI Study Investigators. Comparison of Troponin T to Creatine Kinase and to Radionuclide Cardiac Imaging Infarct Size in Patients with ST-Elevation Myocardial Infarction Undergoing Primary Angioplasty. Am J Cardiol. 2008;101(6):753-7. doi: 10.1016/j.amjcard.2007.09.119.

24. Nguyen TL, Phan JA, Hee L, Moses DA, Otton J, Terreblanche OD, et al. High-Sensitivity Troponin T Predicts Infarct Scar Characteristics and Adverse Left Ventricular Function by Cardiac Magnetic Resonance Imaging Early after Reperfused Acute Myocardial Infarction. Am Heart J. 2015;170(4):715-25.e2. doi: 10.1016/j.ahj.2015.06.022.

25. Hassan AK, Bergheanu SC, Hasan-Ali H, Liem SS, van der Laarse A, wolterbeek R, et al. Usefulness of Peak Troponin-T to Predict Infarct Size and Long-Term Outcome in Patients with First Acute Myocardial Infarction after Primary Percutaneous Coronary Intervention. Am J Cardiol. 2009;103(6):779-84. doi: 10.1016/j.amjcard.2008.11.031.

26. Xiang L, Zhong A, You T, Chen J, Xu W, Shi M. Prognostic Significance of Right Bundle Branch Block for Patients with Acute Myocardial Infarction: A Systematic Review and Meta-Analysis. Med Sci Monit. 2016;22:998-1004. doi: 10.12659/msm.895687.

27. Vivas D, Pérez-Vizcayno MJ, Hernández-Antolín R, Fernández-Ortiz A, Bañuelos C, Escaned J, et al. Prognostic Implications of Bundle Branch Block in Patients Undergoing Primary Coronary Angioplasty in the Stent Era. Am J Cardiol. 2010;105(9):1276-83. doi: 10.1016/j.amjcard.2009.12.044.

28. Melgarejo-Moreno A, Galcerá-Tomás J, Garcia-Alberola A. Prognostic Significance OF Bundle-Branch Block In Acute Myocardial Infarction: The Importance of Location and Time of Appearance. Clin Cardiol. 2001;24(5):371-6. doi: 10.1002/clc.4960240505.

29. Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Hata T, et al. Right Bundle-Branch Block In Anterior Acute Myocardial Infarction In The Coronary Intervention Era: Acute Angiographic Findings And Prognosis. Int J Cardiol. 2007;116(1):57-61. doi: 10.1016/j.ijcard.2006.02.010.

30. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063.

31. Henrysson J, Thunström E, Chen X, Fu M, Basic C. Hyperkalaemia as a Cause of Undertreatment with Mineralocorticoid Receptor Antagonists in Heart Failure. ESC Heart Fail. 2023;10(1):66-79. doi: 10.1002/ehf2.14137.

32. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. Eur Heart J. 2021;42(36):3599-726. doi: 10.1093/eurheartj/ehab368.

33. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the Management of Acute Coronary Syndromes. Eur Heart J. 2023;44(38):3720-826. doi: 10.1093/eurheartj/ehad191.

34. Koh HP, Redzuan AM, Mohd Saffian S, Hassan H, Nagarajah JR, Ross NT. Mortality Outcomes and Predictors of Failed Thrombolysis Following STEMI Thrombolysis in a Non-Pci Capable Tertiary Hospital: A 5-Year Analysis. Intern Emerg Med. 2023;18(4):1169-80. doi: 10.1007/s11739-023-03202-1.

35. Gheorghe A, Griffiths U, Murphy A, Legido-Quigley H, Lamptey P, Perel P. The Economic Burden of Cardiovascular Disease and Hypertension in Low- and Middle-Income Countries: A Systematic Review. BMC Public Health. 2018;18(1):975. doi: 10.1186/s12889-018-5806-x.