

Association of Admission Systolic Blood Pressure on long-Term Outcomes after ST-Segment Elevation Myocardial Infarction

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Original Article

Abstract

INTRODUCTION: Hypertension is widely known as a significant factor in the development of cardiovascular diseases. However, there is increasing interest in the potential link between low admission systolic blood pressure (SBP) and higher mortality rates. Therefore, this study aimed to investigate the relationship between admission SBP and the probability of one-year mortality in patients with ST-segment elevation myocardial infarction (STEMI).

METHOD: This study, which used data from registries, focused on patients diagnosed with STEMI between July 2018 and December 2019. The patients were divided into three groups based on their admission SBP: normal (< 112 mm Hg), elevated (112–140 mm Hg), and hypertension (≥ 140 mm Hg), and were followed for one year. The researchers used Cox proportional models to analyze the data, which allowed them to estimate crude and fully adjusted hazard ratios, along with their corresponding 95% confidence intervals (HR, 95% CI).

RESULTS: This study, which included 1159 patients with a mean age of 60.71 ± 12.19 , 914 (78.86%) were male, and 108 (9.32%) died within one year. Among the patients, 276 had a normal admission SBP, 338 had elevated SBP, and 545 had hypertension. Those with hypertension had a higher-risk profile, including factors such as hyperlipidemia, BMI, LDL levels, anterior myocardial infarction, and a higher prevalence of females. The crude and fully adjusted hazard ratios (HR) for the relationship between elevated admission SBP and mortality were calculated as 0.36 (95% CI: 0.23–0.56) and 0.43 (95% CI: 0.23–0.81), respectively.

CONCLUSION: The study's findings indicate a connection between increased admission SBP and a decreased probability of one-year mortality among patients with STEMI. Unlike the general population, where there is a direct linear correlation between SBP and the risk of future cardiovascular events, this research demonstrates an inverse relationship between SBP and one-year mortality.

Keywords: Hypertension, Blood pressure, ST-segment elevation myocardial infarction, Percutaneous coronary intervention, Thrombolytic therapy

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Introduction

Ischemic heart disease stands as the foremost

cause of both mortality and disability-adjusted life years globally.¹ Acute coronary syndrome (ACS), which includes STEMI, often acts as

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the initial indicator of ischemic heart disease². Arterial hypertension is a major risk factor for cardiovascular disease^{1,3,4}. Blood pressure notably impacts the prognosis not only for the general populace but also for individuals with coronary artery disease⁵. Studies indicate that low systolic blood pressure (SBP) exacerbates the outcomes of chronic heart failure (HF)⁶. The risk of death from ischemic heart disease and stroke progressively increase from a baseline SBP as low as 115 mmHg⁵. In patients with non-ST elevation ACS, a decline in SBP upon admission correlates with a sharp increase in the risk of death and re-infarction, whereas elevated SBP appears to be associated with a reduced risk.

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Since the relationship between admission SBP and long-term outcome in STEMI patients is unclear^{5,7,8}, it is important to understand this association. Therefore, the purpose of the current study was to investigate the relationship between admission SBP and one-year mortality in patients with STEMI.

Materials and Methods

Study design, setting, and participants

This retrospective cohort study was carried out at Imam Ali Hospital, which is associated with Kermanshah University of Medical Sciences in Kermanshah, Iran. Serving as the primary cardiovascular facility in the Kermanshah province, located in western Iran, this hospital is the sole provider of round-the-clock primary percutaneous coronary intervention (PPCI) services in the province. Consequently, patients either admitted directly to Imam Ali Hospital or referred from other hospitals lacking PPCI capabilities are managed here. The registry included all eligible adult patients (aged ≥ 18 years) diagnosed with STEMI in accordance with current guidelines between July 2, 2018, and December 2019. Patients hospitalized for more than 24 hours before being referred to

Imam Ali Hospital were excluded from the registry.

Baseline Assessment

Trained nurses conducted personal interviews with patients and/or their caregivers to collect data on demographic, lifestyle, and clinical characteristics. A general practitioner supervised the data control process to ensure its quality. Past cardiovascular events, coronary interventions, diabetes, and hypertension were documented based on self-reports confirmed by physicians. Vital signs, early reperfusion therapy, electrocardiography results, medical treatments, and laboratory test information were extracted from hospital medical records. Early reperfusion therapy included PPCI, thrombolytic therapy, or no reperfusion. Body-mass index (BMI) was calculated following standard protocols by dividing weight in kilograms by the square of height in meters. Lipid profile levels were measured on the first day of admission. Glomerular filtration rate (GFR) was estimated using the CKD-EPI equation, and left ventricular ejection fraction (LVEF) was recorded based on echocardiography results. Physicians, trained appropriately, conducted quality control on all recorded data.

Study Outcome and Follow-up

The main focus of this study was to evaluate the occurrence of mortality from any cause within one year following STEMI events, either during the patient's hospitalization or after discharge. Hospital documentation was reviewed to ascertain the number of deaths that transpired during the patient's hospital stay. Contact details of patients, along with those of their family members or caregivers, were recorded upon hospital admission. Subsequently, patients were followed up with a phone call after one year. In case of reported deaths, the research team gathered and examined all pertinent clinical and hospital records to determine the cause of death. Each patient's follow-up period commenced on the date of their STEMI diagnosis and concluded on the date of their demise, loss of follow-up,

or after 365 days, whichever came first.

Ethical approval and consent for study

Before participating in the research study, all patients signed a documented informed consent. The study protocol obtained approval from the Research Ethics Committee at the Deputy of Research of the Kermanshah University of Medical Sciences, with the Ethics registration code IR.KUMS.RECbbd.1400.252.

Statistical analysis

In the descriptive analysis, patients were categorized into three groups according to their admission SBP (SBP <112, $112 \leq$ SBP <140, and SBP \geq 140 mm Hg)⁹. Continuous variables were presented as means and standard deviations (SD), and categorical variables were shown as absolute values and percentages. Baseline characteristics between groups were compared using chi-squared tests and one-way analysis of variance.

A Cox proportional hazard regression analysis was conducted to ascertain the hazard ratio and 95% confidence interval (HR, 95% CI) concerning the relationship between admission SBP and the occurrence of all-cause mortality. The authors provided four HRs (95% CIs) for the crude analysis, model 1, model 2, and model 3. In model 1, the authors examined the association of admission SBP with mortality after adjusting for age, sex, prior hypertension, and heart rate. In model 2, the authors assessed the association of admission SBP with mortality after additional adjustment for model 1 plus BMI. In model 3, the authors evaluated the association of admission SBP with mortality after further adjusting for model 2 plus diabetes, GFR, anterior wall myocardial infarction in left bundle branch block (MI/LBBB), low-density lipoprotein (LDL)-cholesterol, LVEF (<35%, 35-50%, \geq 50%), smoking, prior coronary artery bypass graft (CABG), prior percutaneous coronary intervention (PCI), previous MI, reperfusion therapy (PPCI, thrombolytic, no reperfusion), aspirin, clopidogrel, statin, beta-blocker, and ACEI-ARBS (angiotensin-converting enzyme inhibitors-angiotensin receptor blockers).

In subgroup analyses, the authors investigated the correlation between SBP and all-cause mortality across different categories, including age, sex, heart rate, reperfusion therapy, and timing of death (during initial hospitalization or post-discharge). Throughout the study, there were only a few missing values for covariates, with relatively low numbers observed for each: heart rate (2), hyperlipidemia (2), BMI (40), LVEF (30), GFR (6), LDL-cholesterol (86), prior CABG (2), prior MI (3), and prior PCI (3). All analyses utilized complete case data, and seventeen patients were lost to follow-up. Statistical analyses were conducted using R software version 4.2.1, with significance set at a p-value < 0.05. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines¹⁰.

Results

Out of the initial cohort of 1169 patients enrolled between July 2018 and December 2019 (spanning 17.59 months), 10 patients were excluded due to insufficient SBP data, and 17 (1.47%) were lost to follow-up for post-discharge mortality assessment. Consequently, the authors analyzed data from 1159 patients. Among them, 632 (54.53%) underwent PPCI, 368 (31.75%) received thrombolytic treatment, and 159 (13.72%) did not undergo reperfusion therapy. The majority of patients (78.86%) were male, with a mean age of 59.50 years.

Of the 1159 patients included in the analysis, 276 presented with normal SBP (\leq 112 mm Hg), 338 had elevated SBP, and 545 had hypertension (\geq 140 mm Hg). Table 1 details the baseline characteristics, signs, symptoms at presentation, and in-hospital procedures. The hypertension group exhibited higher prevalence of risk factors such as diabetes, hyperlipidemia, BMI, LDL, anterior wall MI, and greater use of clopidogrel, ACEI-ARBS, beta-blockers, and statins, whereas smoking prevalence was lower in the hypertension group.

Table 2 displays the association between different blood pressure statuses and mortality according to multiple Cox models. Even after adjusting for model 1 (sex, age, prior

hypertension, and heart rate), model 2 (sex, age, prior hypertension, heart rate, and BMI), and model 3 (sex, age, prior hypertension, heart rate, BMI, diabetes, LDL-cholesterol, GFR, anterior wall MI, smoking, prior CABG,

prior PCI, prior MI, reperfusion therapy, EF, aspirin, clopidogrel, statin, beta-blocker, and ACE-ARBs), the high admission SBP group still demonstrated a protective effect against all-cause mortality.

Table 1. Baseline characteristics based on systolic blood pressure at admission

Variables	Total (N = 1159)	SBP <112 (n = 276)	112 ≤ SBP < 140 (n = 338)	SBP ≥140 (n = 545)	P- value
Age (years)	60.71±12.19	61.85±11.96	59.17±12.74	61.09±11.89	0.015 ^a
Male gender	914(78.86%)	218(78.99%)	281(83.14%)	415(76.15%)	0.047 ^b
Diabetes Mellitus	257(22.17%)	60(21.74%)	66(19.53%)	131(24.04%)	0.287 ^b
Hypertension	528(45.56%)	104(37.68%)	121(35.80%)	303(55.60%)	<0.001 ^b
Hyperlipidemia	292(25.24%)	57(20.73%)	79(23.37%)	156(28.68%)	0.030 ^b
GFR (mL/min/1.73m ²)	69.91±18.82	67.96±19.36	72.20±18.79	69.47±18.45	0.016 ^a
BMI	26.36±4.40	25.91±4.38	25.77±3.87	26.94±4.64	<0.001 ^a
LDL	98.05±28.60	93.56±28.16	97.51±28.76	100.54±28.50	0.008 ^a
HDL	41.03±8.62	40.49±7.72	41.22±9.22	41.17±8.66	0.631 ^a
Anterior wall MI/LBBB	559(48.23%)	109(39.49%)	166(49.11%)	284(52.11%)	0.003 ^b
Smoking	528(45.56%)	137(49.64%)	172(50.89%)	219(40.18%)	0.002 ^b
Previous CABG	37(3.20%)	9(3.28%)	11(3.25%)	17(3.12%)	0.990 ^c
Previous PCI	70(6.06%)	17(6.23%)	19(5.62%)	34(6.24%)	0.924 ^b
Old MI	124(10.73%)	31(11.31%)	38(11.28%)	55(10.09%)	0.805 ^b
Reperfusion therapy					
PPCI	632(54.53%)	142(51.45%)	191(56.51%)	299(54.86%)	0.446 ^b
Thrombolytic	368(31.75%)	89(32.25%)	109(32.25%)	170(31.19%)	
No reperfusion	159(13.72%)	45(16.30%)	38(11.24%)	76(13.94%)	
LVEF					
<35%	500(44.29%)	113(43.97%)	158(47.02%)	229(42.72%)	0.022 ^b
35-50%	466(41.28%)	107(41.63%)	117(34.82%)	242(45.15%)	
>50%	163(14.44%)	37(14.40%)	61(18.15%)	65(12.13%)	
Aspirin	1097(94.65%)	243(88.04%)	16(4.37%)	13(2.39%)	<0.001 ^b
Clopidogrel	1.055(91.03%)	229(82.97%)	313(92.60%)	513(94.13%)	<0.001 ^b
ACE-ARBs	849(73.25%)	178(64.49%)	248(73.37%)	423(77.61%)	<0.001 ^b
Beta-blocker	928(80.07%)	203(73.55%)	275(81.36%)	450(82.57%)	0.007 ^b
Statin	1058(91.68%)	235(85.45%)	311(92.56%)	512(94.29%)	<0.001 ^b

a, one-way analysis of variance (ANOVA)

b, Chi-square

c, Fisher's exact test

Data are mean ± SD or n (%). Abbreviations: BMI, body mass index; MI, Myocardial infarction; LBBB, Left bundle branch block; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; GFR, Glomerular filtration rate; PPCI, Primary percutaneous coronary intervention; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; ACEI-ARBs, angiotensin converting enzyme inhibitors- angiotensin receptor blockers.

Table 2. Non-adjusted and adjusted one year mortality risk ratios of SBP <112, 112 ≤ SBP < 140 and SBP ≥140

	Crude HRs (95%CI)	Model 1 HRs (95%CI)	Model 2 HRs (95%CI)	Model 3 HRs (95%CI)
SBP <112	Reference	Reference	Reference	Reference
112 ≤ SBP < 140	0.51(0.32-0.81)	0.48(0.30-0.78)	0.54(0.32-0.90)	0.51(0.26-0.98)
SBP ≥140	0.36(0.23-0.56)	0.29(0.18-0.45)	0.31(0.19-0.51)	0.43(0.23-0.81)

Data are hazard ratios (HRs) with 95% confidence intervals (95%CIs). Abbreviations: SBP, systolic blood pressure

Model 1= Adjusted by sex, age, previous hypertension and heart rate.

Model 2= Model 1+adjusted by BMI

Model 3= Full adjusted

Subgroup Analysis

To ensure the consistency of outcomes across various subgroups based on blood pressure, the authors calculated the adjusted hazard ratio (HR) for death within these complex subgroups. As depicted in Table 3, a protective effect for high blood pressure against mortality was evident in all subgroups in the crude model. Even after adjusting for all variables (including sex, age, prior hypertension, heart rate, BMI, diabetes, LDL-cholesterol, GFR,

anterior wall MI, smoking, prior CABG, prior PCI, prior MI, reperfusion therapy, EF, aspirin, clopidogrel, statin, beta-blocker, and ACE-ARBS), this protective effect persisted across most subgroups, except for the subset that underwent thrombolytic treatment. In the thrombolytic subgroup, the adjusted model showed that high blood pressure was associated with increased mortality, although this relationship did not reach statistical significance.

Table 3. Sub-group analyses according to age, sex, heart rate, reperfusion therapy, and death time

Subgroups	Crude HRs (95%CIs)			Full-adjusted HRs (95%CIs)		
	SBP <112	112 ≤ SBP < 140	SBP ≥140	SBP <112	112 ≤ SBP < 140	SBP ≥140
Age<65	Reference	0.59(0.26-1.37)	0.42*(0.18-0.95)	Reference	0.82(0.24-2.80)	0.39(0.12-1.31)
Age≥65	Reference	0.55*(0.31-0.96)	0.35*(0.21-0.60)	Reference	0.61(0.25-1.50)	0.53(0.22-1.29)
Sex						
Male	Reference	0.48*(0.28-0.85)	0.30*(0.17-0.54)	Reference	0.54(0.23-1.28)	0.39*(0.16-0.93)
Female	Reference	0.61(0.27-1.42)	0.44*(0.21-0.92)	Reference	0.45(0.11-1.87)	0.72(0.22-2.35)
Heart rate<70	Reference	0.50(0.22-1.130)	0.29*(0.12-0.71)	Reference	0.99(0.28-3.56)	0.43(0.11-1.73)
Heart rate≥70	Reference	0.51*(0.29-0.90)	0.37*(0.22-0.63)	Reference	0.51(0.22-1.18)	0.43*(0.20-0.92)
Reperfusion therapy						
PPCI	Reference	0.53(0.26-1.05)	0.23*(0.11-0.51)	Reference	0.60(0.22-1.61)	0.1*(0.03-0.37)
Thrombolytic therapy	Reference	0.83(0.29-2.36)	0.74(0.28-1.94)	Reference	1.41(0.26-7.52)	1.19(0.22-5.48)
No reperfusion	Reference	0.44*(0.19-0.99)	0.36*(0.18-0.72)	Reference	0.20(0.026-1.62)	0.52(0.12-2.26)
Death time						
In hospital	Reference	0.36*(0.19-0.68)	0.17*(0.09-0.34)	Reference	0.13(0.015-1.17)	0.17(0.02-1.30)
After discharge	Reference	0.82(0.39-1.70)	0.76(0.39-1.47)	Reference	0.81(0.35-1.34)	0.56(0.26-1.22)

Data are hazard ratios (HRs) with 95% confidence intervals (95%CIs). Abbreviations: PPCI, Primary percutaneous coronary intervention; SBP, systolic blood pressure

All-cause mortality

Out of the 1159-patient cohort, 108 (9.32%) patients passed away within one year. Among them, 45 (16.30%) were from the normal pressure group. A notable inverse relationship between mortality and admission SBP was

observed, indicating a significant rise in the risk of one-year all-cause mortality with decreasing SBP. Figure 1 illustrates the survival curves for SBP based on the fully adjusted Cox regression model.

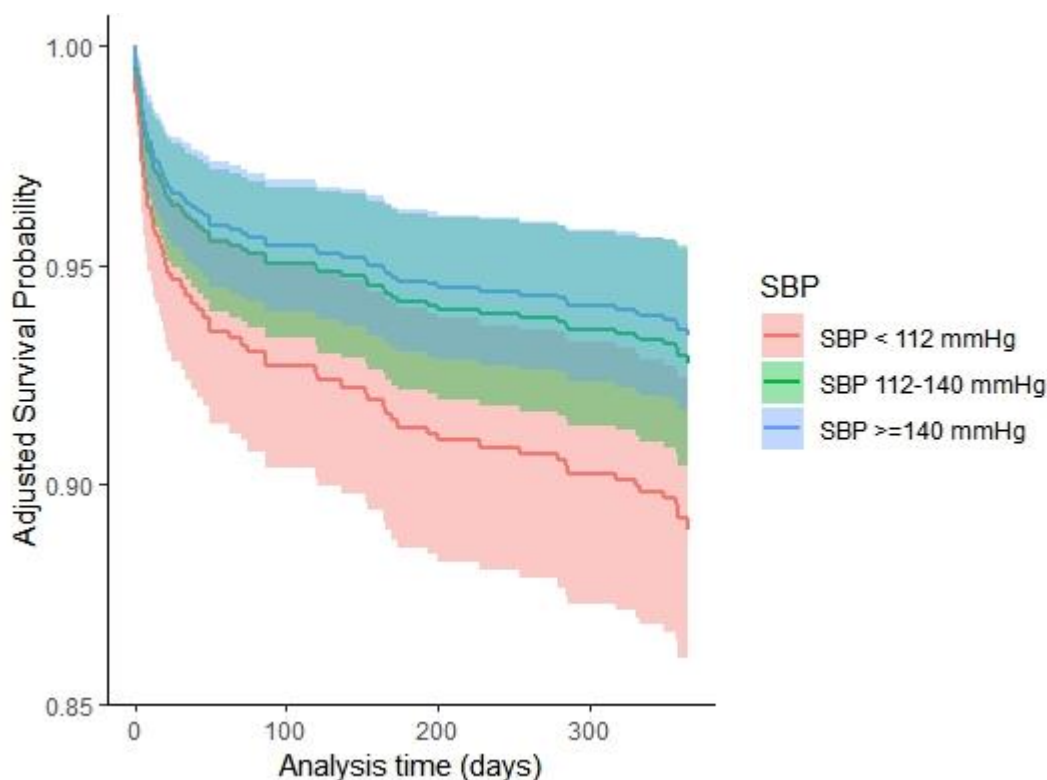


Figure 1. The adjusted survival curves for systolic blood pressure. Survival curves of the three groups, SBP: systolic blood pressure.

Discussion

The present research investigates the relationship between admission SBP and mortality among patients diagnosed with STEMI. Results reveal an inverse association between admission SBP and mortality, suggesting that higher SBP levels correspond to lower mortality rates (BP paradox). Moreover, the study suggests that the most favorable outcomes are not linked with the intermediate blood pressure range of 112-140 mmHg, but rather with SBP values surpassing 140 mmHg. Even after adjusting for confounding variables in three distinct models, the association between admission SBP and clinical outcomes remained consistent. However, uncertainties persist regarding the

causal nature of this relationship. Certain studies have noted that patients with lower SBP tended to be older and frailer.⁸ However, in this study, advanced age couldn't account for the poorer prognosis, as patients with lower admission SBP were even younger. Previous research has yielded inconsistent findings regarding the prognostic influence of elevated blood pressure on mortality in myocardial infarction (MI) patients. For instance, De Luca et al.,⁹ discovered that hypertension among STEMI patients undergoing primary angioplasty was significantly associated with increased mortality, reinfarction, stent thrombosis, and target-vessel revascularization over a median follow-up period of 1200 days. Abrignani et al.,¹⁰ suggested that individuals

with hypertension who undergo their first anterior myocardial infarction generally have a more positive outcome during hospitalization compared to individuals of similar age and gender. This variance in outcome could stem from a less severe expansion of the myocardial infarction area or from different underlying pathophysiological mechanisms. Similarly, in the current study, the authors noted a decreased rate of all-cause mortality in the group with the highest systolic blood pressure (>140 mmHg). Aligned with this study, the Registry of Information and Knowledge about Swedish Heart Intensive Care admissions (RIKS-HIA)¹¹ explored the association between admission SBP and the likelihood of survival one year post-admission in patients with chest pain. The findings revealed an inverse correlation between admission SBP and one-year mortality. Despite their elevated baseline risk, the reason for the lower mortality rate among hypertensive patients remains ambiguous. Several potential explanations exist in this realm. Initially, the level of blood pressure following a MI is influenced by the integrated cardiovascular and neuroendocrine systems. A higher admission SBP may signify preserved cardiac function in response to the stress provoked by the area affected by the MI¹¹. Therefore, research on acute myocardial infarction (MI) and acute heart failure (HF) has suggested that elevated blood pressure during periods of intense stress might not always be harmful. Instead, it could indicate that compensatory mechanisms are functioning favorably. Secondly, this study found that patients with a high SBP exceeding 140 mmHg showed a significant prevalence of hypertension (55.60%). Commonly prescribed antihypertensive medications like angiotensin-converting enzyme inhibitors (ACEIs) and beta-blockers possess cardioprotective properties, reducing myocardial oxygen consumption and the risk of sudden death¹²⁻¹⁴.

In patients diagnosed with HF, a higher SBP surprisingly correlates with a beneficial impact on overall survival¹⁵. According to a study by Raphael *et al.*,¹⁶ higher SBP was identified as a favorable prognostic factor in individuals with HF. The study findings revealed that with

every 10 mmHg increase in SBP, there was a corresponding 13.0% decrease in mortality, unrelated to HF treatment. Conversely, another investigation suggested that for every 10 mmHg decrease in SBP prior to treatment, there was an 18% increase in the likelihood of mortality, an 11% rise in the combined probability of mortality or HF-related hospitalization, and a 9% increase in the combined likelihood of mortality or hospitalization for any cause¹⁷. There is a clear association between SBP and cardiovascular events in the general population¹⁸. These associations have consistently been noted across subgroups, including different factors such as age, gender, and heart rate, and have shown no variation based on the type of reperfusion therapy utilized. In elderly individuals, there is a clear inverse linear relationship between SBP and mortality. Conversely, among patients under the age of 75, a J-shaped curve is evident in the relationship between SBP and mortality¹⁹. In the subgroup treated with thrombolytics, despite adjusting for confounding variables, high blood pressure has been linked to a heightened risk of mortality, albeit without statistical significance²¹. During the thrombolytic era, specific studies have indicated that hypertension might have an adverse effect on mortality rates, while others have found no noticeable difference^{21,22}.

Some medical practitioners exhibit a degree of reluctance regarding the use of angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) or beta-blockers for managing individuals with low SBP when it comes to pharmaceutical interventions²³.

However, this specific study found that even among individuals with the lowest systolic blood pressure (SBP), the majority of patients were prescribed these medications during their hospitalization.

Various mechanisms could potentially explain the increased susceptibility to cardiovascular events associated with reduced SBP. Lower SBP might lead to decreased circulation to specific physiological structures, compromised coronary perfusion, and consequently,

increased mortality⁵.

One limitation of this study is that patients with varying admission systolic blood pressure (SBP) levels may have been prescribed different medications during the follow-up period. However, the authors did not collect detailed information about these follow-up medications, which could have affected the results as potential confounding variables.

Conclusions

According to the findings, there seems to be a reverse correlation between admission systolic blood pressure (SBP) and one-year mortality in patients diagnosed with ST-elevation myocardial infarction (STEMI). This differs from the general population, where there is a straightforward linear relationship between SBP and the likelihood of future cardiovascular events. Put differently, higher admission SBP is associated with a lower risk of one-year mortality in STEMI patients.

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Conflict of Interests

The authors declare no conflicts of interest.

Reference

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