

# Association between smoking burden and one-year mortality in ST-elevation and non-ST-elevation myocardial infarction: insights from a regional cohort

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## Abstract

**Introduction:** Cigarette smoking is a major modifiable risk factor for cardiovascular disease and acute myocardial infarction (MI). The prognostic impact of cumulative smoking exposure (pack-years) on post-MI outcomes remains uncertain. The controversial “smoker’s paradox” suggesting better short-term prognosis in smokers has been largely attributed to younger age and fewer comorbidities. Prior studies frequently failed to quantify smoking intensity, stratify by MI subtype (STEMI vs. NSTEMI), or adequately adjust for confounders such as age and renal function.

**Aim:** This study examined whether cumulative smoking burden is independently associated with one-year all-cause mortality after MI.

**Materials and methods:** In this retrospective cohort study from a tertiary center in Western Iran (December 2019–August 2020), 1,019 confirmed MI patients were classified as never-smokers (0 pack-years), moderate smokers ( $\leq 15$  pack-years), and heavy smokers ( $> 15$  pack-years). Cox proportional hazards models (crude, age-adjusted, and fully adjusted for age, sex, diabetes, hypertension, BMI, lipids, eGFR, reperfusion therapy, and systolic blood pressure) estimated hazard ratios for one-year mortality. Proportional hazards assumptions were confirmed (Schoenfeld residuals  $p > 0.05$ ). Bias was minimized through multivariable adjustment and sensitivity analyses.

**Results:** Smokers were younger, predominantly male, and had fewer comorbidities. In STEMI, heavy smokers exhibited lower crude mortality than never-smokers, but this vanished after adjustment. No differences emerged across smoking categories in NSTEMI. Age and reduced eGFR consistently predicted mortality in both subtypes.

**Conclusions:** Cumulative smoking burden showed no independent association with one-year post-MI mortality. The smoker’s paradox is explained by confounding, especially age and renal function. Smoking cessation remains essential for secondary prevention.

## Keywords

Cox regression, mortality, myocardial infarction, NSTEMI, renal function, smoker’s paradox, smoking burden, STEMI

## Introduction

Tobacco use remains one of the leading global causes of preventable morbidity and mortality, with cardiovascular disease representing its most devastating consequence. According to the World Health Organization, over seven million deaths annually are attributed to tobacco use, a substantial proportion from ischemic heart disease.<sup>[1]</sup> Both active smoking and exposure to secondhand smoke pose significant threats to cardiovascular health, emphasizing the pervasive nature of this public health challenge.

Cigarette smoking accelerates atherogenesis, impairs endothelial function, and promotes a prothrombotic state all of which increase the risk of acute myocardial infarction (AMI).<sup>[2,3]</sup> While smoking is a well-established risk factor for coronary artery disease, paradoxical findings in acute settings often termed the “smoker’s paradox” have suggested lower short-term mortality among smokers following AMI.<sup>[4,5]</sup> Several observational studies have reported lower in-hospital or early mortality among smokers compared to non-smokers presenting with AMI. This paradox is often attributed to confounding factors such as younger age, fewer comorbidities, or differences in therapeutic responsiveness among smokers.<sup>[6]</sup>

However, more recent evidence suggests that the perceived survival advantage dissipates after appropriate statistical adjustments for baseline disparities.<sup>[7,8]</sup>

Significant gaps remain in understanding the prognostic impact of smoking post-MI. Most studies dichotomize patients as smokers or non-smokers, overlooking cumulative exposure via pack-years, which may obscure dose-response relationships.<sup>[9]</sup> Additionally, few have stratified analyses by AMI subtype ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) despite their distinct pathophysiology, management, and prognosis. The lack of subtype-specific analyses limits insights into whether smoking’s impact varies across these conditions. Furthermore, prior studies often inadequately adjust for critical confounders like renal function, which strongly predicts post-MI outcomes.<sup>[10]</sup>

## Aim

This study addresses these gaps by evaluating the association between cumulative smoking burden (pack-years) and one-year all-cause mortality in a regional cohort of STEMI and NSTEMI patients from the Middle East, using robust statistical adjustments, subtype-specific analyses, and dose-response quantification a novel approach in non-Western populations where tobacco use patterns may differ. This provides a nuanced understanding of smoking’s prognostic role in contemporary MI management, contributing to global diversity in cardiovascular epidemiology.

## Materials and methods

### Study design and population

This retrospective cohort study was conducted at Imam Ali Hospital, a tertiary cardiovascular referral center located in Western Iran. We included all patients aged  $\geq 18$  years admitted with a confirmed diagnosis of either STEMI or NSTEMI between December 2019 and August 2020. STEMI and NSTEMI diagnoses were established based on standard clinical, electrocardiographic, and biochemical criteria. Patients with a history of prior myocardial infarction (MI) were excluded to minimize confounding from recurrent ischemic events and differences in baseline risk profiles, such as variations in treatment history or disease severity. Patients with incomplete clinical data or unavailable follow-up information at one year were also excluded from the analysis.

### Data collection and baseline variables

Demographic characteristics, medical history, and cardiovascular risk factors were collected at the time of hospital admission via structured interviews by trained nurses and validated against the hospital’s electronic medical records. Clinical data included prior myocardial infarction, revascularization history, presence of hypertension, diabetes mellitus, and hyperlipidemia. Vital signs, laboratory tests (lipid profile, serum creatinine), and body mass index (BMI) were recorded upon admission. Estimated glomerular filtration rate (eGFR) was estimated using the CKD-EPI formula. Blood pressure was categorized into three groups:  $< 112$  mmHg, 112–140 mmHg, and  $> 140$  mmHg based on prior literature.<sup>[10]</sup>

### Smoking burden

Smoking burden was assessed using the pack-year index, calculated by multiplying the number of cigarette packs smoked per day by the number of years the patient had smoked. Patients were categorized as never-smokers (0 pack-years), moderate smokers ( $\leq 15$  pack-years), or heavy smokers ( $> 15$  pack-years) based on prior literature.<sup>[11]</sup> Smoking status was self-reported at admission due to the absence of biochemical verification.

### Study outcome and follow-up

The primary outcome was all-cause mortality within one year of AMI diagnosis, including in-hospital and post-discharge deaths. In-hospital mortality was documented via hospital records. Contact information for patients or their family members was recorded at admission to facilitate follow-up. Patients were contacted by phone at one year. For reported deaths, clinical and hospital records, including cause of death, were reviewed. Loss to follow-up was

minimal (1.2%, 12/1,019), primarily due to outdated contact information. The follow-up period was defined as the time from AMI diagnosis to death, loss to follow-up, or 365 days, whichever occurred first.

### Addressing bias

To minimize bias, several measures were implemented. Selection bias was reduced by including all eligible patients during the study period and excluding those with prior MI to limit confounding from recurrent events. Information bias was addressed by validating self-reported data (e.g., smoking status, medical history) against electronic medical records where possible. For smoking status, structured interviews used standardized questions to reduce recall bias, though biochemical validation was not feasible. Missing data (<5% per variable) were handled via list wise deletion, with sensitivity analyses excluding cases with missing eGFR values to assess robustness. Multivariable adjustment in Cox models accounted for key confounders (age, sex, diabetes, hypertension, BMI, lipid profiles, eGFR, reperfusion therapy, SBP). No imputation was performed due to low missingness, but patterns of missing data were assessed to ensure they were not systematically related to outcomes.

### Ethical approval and consent for study

All patients signed a written informed consent before enrolling in the study. The Research Ethics Committee at the Deputy of Research of the Kermanshah University of Medical Sciences approved the study protocol (Ethics registration code: IR.KUMS.REC.1400.252).

### Statistical analysis

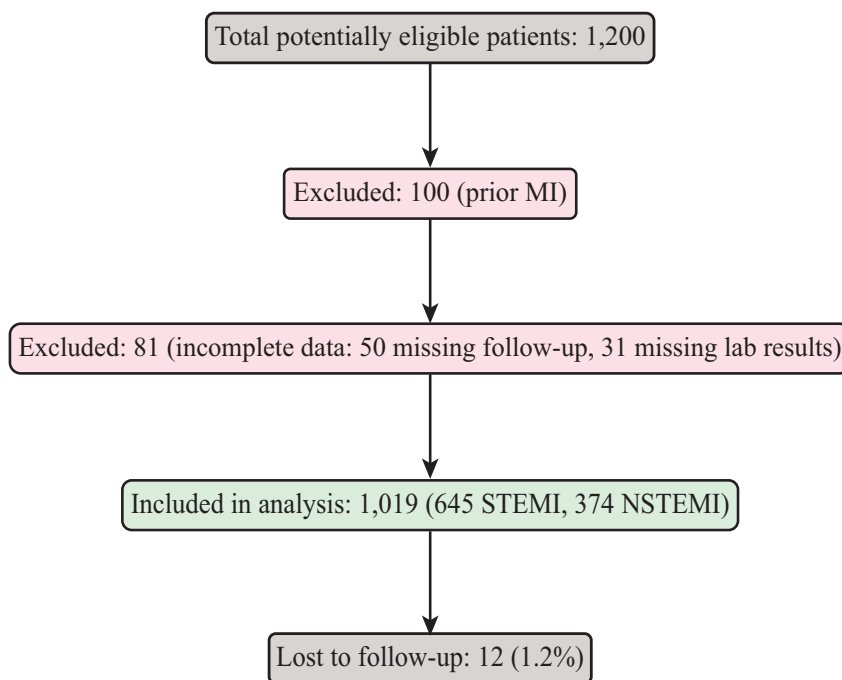
Continuous variables were presented as mean ± standard deviation (SD) and categorical variables as absolute value and percentage. Baseline characteristics were compared using chi-square and ANOVA as appropriate. Cox proportional hazards regression models were constructed separately for STEMI and NSTEMI to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality. Three models were assessed: crude, age-adjusted, and fully adjusted models including all covariates. To address potential sources of bias, we used multivariable adjustment for confounders and excluded patients with prior MI. Missing data were minimal (<5% per variable) and handled via listwise deletion in analyses. No formal interaction tests were performed, but subtype-specific models served as subgroup analyses. Sensitivity analyses were conducted by excluding cases with missing GFR values, yielding similar results.

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.<sup>[12]</sup>

### Results

#### Baseline characteristics of STEMI and NSTEMI patients

Of 1,200 potentially eligible patients, 1,019 were included after excluding 100 with prior MI and 81 with incomplete data (missing follow-up or lab results) (Fig. 1). Loss



**Figure 1.** Flow diagram of participant selection. The diagram illustrates the selection process of patients included in the analysis, with reasons for exclusions and loss to follow-up.

to follow-up was 12 (1.2%). Among the 1,019 patients, 645 (63.3%) had STEMI and 374 (36.7%) had NSTEMI. Missing data were minimal (<2% for age/sex, 4% for eGFR).

Among 645 STEMI patients (356 never-smokers, 124 moderate smokers, 165 heavy smokers), smokers were younger (mean age: 55.53±11.81 years for ≤15 pack-years, 57.63±9.89 years for >15 pack-years vs. 62.38±13.33 years for never-smokers;  $p<0.001$ ) and predominantly male (>95% vs. 63.2%;  $p<0.001$ ). Smokers had lower BMI (25.50±4.28 kg/m<sup>2</sup> for >15 pack-years vs. 26.81±4.68 kg/m<sup>2</sup>;  $p=0.034$ ), lower SBP and DBP ( $p=0.002$ ), and lower prevalence of hypertension (22.4% vs. 47.9%;  $p<0.001$ ) and diabetes (10.9% vs. 29.5%;  $p<0.001$ ). eGFR was higher among smokers ( $p<0.001$ ). Educational attainment was lower among smokers ( $p<0.001$ ). One-year mortality was lower among smokers (7.3% for ≤15 pack-years, 6.1% for >15 pack-years vs. 13.2%;  $p=0.021$ ). No differences were observed in income level or reperfusion therapy (Table 1).

Among 374 NSTEMI patients (253 never-smokers, 58 moderate smokers, 63 heavy smokers), age did not differ significantly ( $p=0.339$ ). Male sex was more prevalent among smokers (87.9% for ≤15 pack-years, 100% for >15 pack-years vs. 56.1%;  $p<0.001$ ). Hypertension (31.8% vs. 54.2%;  $p=0.003$ ) and diabetes (7.9% vs. 26.9%;  $p=0.002$ ) were less prevalent among smokers. eGFR was higher among smokers ( $p=0.029$ ). Educational attainment was lower among smokers ( $p<0.001$ ), but income level and reperfusion therapy did not differ. One-year mortality was similar across groups ( $p=0.761$ ) (Table 2).

### Association between smoking and one-year mortality in STEMI and NSTEMI patients

In the unadjusted model, patients with a smoking history >15 pack-years had a significantly lower risk of one-year mortality compared to never-smokers (HR: 0.46; 95% CI: 0.23–0.91). Those with <15 pack-years also showed a lower, though non-significant, risk (HR: 0.54; 95% CI: 0.26–1.19). After adjusting for age, the protective association was attenuated and no longer statistically significant (HR for >15 pack-years: 0.58; 95% CI: 0.29–1.16). In the full-adjusted model, which controlled for age, sex, diabetes, hypertension, BMI, lipid profiles, estimated eGFR, reperfusion therapy, and SBP, the association remained non-significant (HR: 0.75; 95% CI: 0.24–2.31 for >15 pack-years). Among the covariates, age was consistently associated with increased mortality risk across models (full-adjusted HR: 1.07; 95% CI: 1.02–1.12). Diabetes was a significant predictor in the crude and age-adjusted models but not in the full-adjusted model. eGFR was inversely associated with mortality in unadjusted (HR: 0.97; 95% CI: 0.96–0.98) and age-adjusted models (HR: 0.98; 95% CI: 0.96–0.99), though the association lost significance after full adjustment. SBP >140 mmHg was associated with reduced mortality in unadjusted (HR: 0.43; 95% CI: 0.23–0.78) and age-adjusted models (HR: 0.42; 95% CI: 0.23–0.77), but this effect was

not observed in the full-adjusted model (HR: 1.31; 95% CI: 0.36–4.78). Reperfusion therapy was significantly associated with reduced mortality in the crude model (HR: 0.50; 95% CI: 0.29–0.85), but this association was not sustained after full adjustment (Table 3).

Among NSTEMI patients, no significant association was observed between smoking and one-year mortality across all models. In the crude model, the HR for <15 pack-years was 0.49 (95% CI: 0.11–2.15) and 1.00 (95% CI: 0.33–2.97) for >15 pack-years. These estimates remained non-significant after age adjustment (HR: 0.56 and 1.12, respectively) and in the full-adjusted model (HR: 0.14; 95% CI: 0.00–3.90 for <15 pack-years and HR: 1.10; 95% CI: 0.27–4.46 for >15 pack-years). Age was a significant predictor of mortality in the unadjusted model (HR: 1.06; 95% CI: 1.03–1.10), though this association weakened in the full-adjusted model (HR: 1.05; 95% CI: 0.98–1.14). eGFR remained a robust inverse predictor of mortality in all models, including the full-adjusted model (HR: 0.95; 95% CI: 0.90–0.99). Reperfusion therapy was associated with significantly reduced mortality in both the crude (HR: 0.12; 95% CI: 0.01–0.92) and age-adjusted (HR: 0.13; 95% CI: 0.017–0.96) models, though this effect was attenuated in the full-adjusted model (HR: 0.86; 95% CI: 0.08–8.41). Lower systolic blood pressure (<112 mmHg) was associated with increased mortality compared to higher SBP categories in unadjusted and age-adjusted models; however, these associations lost significance after full adjustment (Table 4).

Figs 2 and 3 show the survival curves for heavy and moderate smokers versus never-smokers based on the full-adjusted Cox regression model.

## Discussion

In this retrospective cohort study of patients presenting with STEMI and NSTEMI, we found that smoking burden, as measured in pack-years, was not independently associated with one-year all-cause mortality following adjustment for key clinical variables. Although heavy smoking initially appeared to be linked to reduced mortality among STEMI patients in unadjusted analyses, this association was nullified after adjusting for confounders. These results cast doubt on the concept of the “smoker’s paradox” and reaffirm the well-documented deleterious cardiovascular effects of tobacco use.<sup>[13,14]</sup>

Our results are consistent with prior studies demonstrating that the apparent protective effects of smoking in AMI patients are largely attributable to confounding by younger age, lower burden of comorbidities, and potential differences in clinical management.<sup>[6,15,16]</sup> Gao et al. similarly reported that, in an unadjusted model, smoking history appeared protective, but after adjusting for age and the number of cigarettes smoked, smoking was associated with worse outcomes.<sup>[7]</sup> Moreover, a meta-analysis of PCI trials also found that smoking was linked to higher risks

**Table 1.** Demographic and clinical characteristics of STEMI patients by pack-years of cigarette smoking status.

Characteristics	All (n=645)	Never-smoker (n=356)	≤15 Pack-Years (n=124)	>15 pack-years (n=165)	P-value
Age (years)	59.58±12.57	62.38±13.33	55.53±11.81	57.63±9.89	<0.001
Sex, n (%)					
Male	503 (77.98%)	225 (63.20%)	119 (95.97%)	159 (96.63%)	<0.001
Female	142 (22.02%)	131 (36.80%)	5 (4.03%)	6 (3.64%)	
BMI (kg/m <sup>2</sup> ),	26.35±4.53	26.81±4.68	26.31±4.34	25.50±4.28	0.034
Systolic pressure (mmHg)	135.37±26.84	138.54±28.57	130.71±24.21	132.15±24.06	0.002
Diastolic pressure (mmHg)	83.30±14.82	85±16.02	80.40±12.90	81.90±13.00	0.002
SBP<112	137 (21.88%)	69 (20.13%)	31 (25.62%)	37 (22.84%)	0.015
112<SBP<140	212 (33.87%)	101 (29.45%)	46 (38.02%)	65 (40.12%)	
SBP>140	277 (44.25%)	173 (50.44%)	44 (36.36%)	60 (37.04%)	
Hypertension, n (%)					<0.001
Yes	246 (38.20%)	170 (47.89%)	39 (31.45%)	37 (22.42%)	
No	398 (61.80%)	185 (52.11%)	85 (68.55%)	128 (77.58%)	
Diabetes, n (%)					<0.001
Yes	143 (22.17%)	105 (29.49%)	20 (16.13%)	18 (10.91%)	
No	502 (77.83%)	251 (70.51%)	104 (83.87%)	147 (89.09%)	
Total cholesterol, mmol/l	167.50±41.55	168.41±42.75	171±44.66	162.90±36.01	0.228
HDL-C, mg/dL	38.48±14.65	38.56±12.53	40.78±20.84	36.55±12.87	0.105
eGFR, ml/min	72.23±21.95	67.58±22.67	76.90±21.92	78.83±17.66	<0.001
Education					<0.001
Illiterate	206 (32.04%)	147 (41.29%)	26 (21.31%)	33 (20%)	
Primary school	146 (22.71%)	71 (19.94%)	23 (18.85%)	52 (31.52%)	
Secondary school	121 (18.82%)	51 (14.33%)	35 (28.69%)	32 (21.21%)	
Diploma	106 (16.49%)	51 (14.33%)	24 (19.67%)	31 (18.79%)	
Post-diploma and higher	64 (9.95%)	36 (10.11%)	14 (11.48%)	14 (8.48%)	
Income					0.265
Very low	327 (51.01%)	182 (51.27%)	61 (50.41%)	84 (50.91%)	
Low	137 (21.37%)	74 (20.85%)	30 (24.79%)	33 (20%)	
Moderate	117 (18.25%)	64 (18.03%)	17 (14.05%)	36 (21.82%)	
Good	55 (8.58%)	34 (9.58%)	10 (8.26%)	11 (6.67%)	
Very good	5 (0.78%)	1 (0.28%)	3 (2.48%)	1 (0.61%)	
Reperfusion					0.102
Yes	531 (82.33%)	283 (79.49%)	105 (84.68%)	143 (86.67%)	
No	114 (17.67%)	73 (20.51%)	19 (15.32%)	22 (13.33%)	
One year mortality					0.021
Yes	66 (10.23%)	47 (13.20%)	9 (7.26%)	10 (6.06%)	
No	579 (89.77%)	309 (86.80%)	115 (92.74%)	155 (93.94%)	

BMI: body mass index; HDL-C: high density lipoprotein-cholesterol; eGFR: estimated glomerular filtration rate

of all-cause mortality and heart failure when appropriate adjustments were applied.<sup>[8]</sup>

Interestingly, despite a higher incidence of recurrent myocardial infarction among smokers reported in some studies<sup>[7,17]</sup>, we did not observe a significant association between smoking burden and increased one-year mor-

tality. Several factors could account for this finding. First, improvements in acute cardiac care and early revascularization strategies may mitigate the adverse effects of recurrent ischemic events. Second, the urban structure and efficient healthcare system in the studied region may allow faster access to medical care, potentially improving sur-

**Table 2.** Demographic and clinical characteristics of NSTEMI patients by pack-years of cigarette smoking status

Characteristics	All (n=374)	Never-smoker (n=253)	≤15 pack-years (n=58)	>15 pack-years (n=63)	P-value
Age (years)	59.73±12.75	60.12±13.35	57.46±12.57	60.24±10.12	0.339
Sex, n (%)					
Male	231 (61.76%)	117 (46.25%)	51 (87.93%)	63 (100%)	<0.001
Female	143 (38.24%)	136 (53.57%)	7 (12.07%)		
BMI (kg/m <sup>2</sup> ),	26.48±4.40	26.79±4.48	26.07±4.12	25.72±4.32	0.253
Systolic pressure (mmHg)	141.93±27.34	144.23±27.31	136.98±27.83	137.02±26.15	0.064
Diastolic pressure (mmHg)	85.25±15.35	86.07±14.48	83.02±19.02	83.97±15.00	0.318
SBP<112	56 (15.51%)	33 (13.41%)	12 (21.43%)	11 (18.64%)	0.331
112<SBP<140	109 (30.19%)	71 (28.86%)	19 (33.93%)	19 (32.20%)	
SBP>140	196 (54.29%)	142 (57.72%)	25 (46.64%)	29 (49.15%)	
Hypertension, n (%)					
Yes	181 (48.40%)	137 (54.15%)	24 (41.38%)	20 (31.75%)	0.003
No	193 (51.60%)	116 (45.85%)	34 (58.62%)	43 (68.25%)	
Diabetes, n (%)					
Yes	82 (21.93%)	68 (26.88%)	9 (15.52%)	5 (7.94%)	0.002
No	292 (78.07%)	185 (73.12%)	49 (84.48%)	58 (92.06%)	
Total cholesterol, mmol/l	159.24±45.77	160.45±46.59	152.57±40.91	160.19±46.66	0.517
HDL-C, mg/dL	38.92±17.77	38.63±15.63	38.89±12.94	40.16±27.46	0.833
eGFR (mL/min/1.73 m <sup>2</sup> )	68.95±20.71	66.99±20.72	73.56±22.06	72.56±18.41	0.029
Education					
Illiterate	144 (38.61%)	116 (46.03%)	11 (18.97%)	17 (26.98%)	<0.001
Primary school	90 (24.13%)	51 (20.24%)	19 (32.76%)	20 (31.75%)	
Secondary school	67 (17.96%)	34 (13.49%)	18 (31.03%)	15 (23.8%)	
Diploma	44 (11.80%)	28 (11.11%)	5 (8.62%)	11 (17.46%)	
Post-diploma and higher	28 (7.51%)	23 (9.13%)	5 (8.62%)		
Income level					
Very low	216 (57.91%)	147 (58.33%)	30 (51.72%)	39 (61.90%)	0.450
Low	64 (17.16%)	39 (15.48%)	13 (22.41%)	12 (19.05%)	
Moderate	57 (15.28%)	40 (15.87%)	9 (15.52%)	8 (12.70%)	
Good	29 (7.77%)	31 (9.13%)	3 (5.17%)	3 (4.76%)	
Very good	7 (1.88)	3 (1.19%)	3 (5.17%)	1 (1.59%)	
Reperfusion therapy					
Yes	95 (25.40%)	63 (24.90%)	18 (31.03%)	14 (22.33%)	0.512
No	279 (74.60%)	190 (75.10%)	40 (68.97%)	49 (77.78%)	
One-year mortality					
Yes	23 (6.15%)	17 (6.72%)	2 (3.45%)	4(6.35%)	0.761
No	351 (93.85%)	236 (93.28%)	56 (96.55%)	59 (93.65%)	

BMI: body mass index; HDL-C: high density lipoprotein-cholesterol; eGFR: estimated glomerular filtration rate

vival despite adverse risk profiles. Third, our sample size, although relatively large, may still have limited power to detect small differences in mortality across smoking categories.

Renal dysfunction (GFR <60 mL/min/1.73 m<sup>2</sup>) and older age emerged as the strongest independent predictors of

one-year mortality, consistent with prior literature.<sup>[18,19]</sup> These findings highlight the importance of comprehensive risk stratification in AMI patients beyond traditional risk factors like smoking status alone.

Notably, smoking burden did not appear to differentially impact outcomes between STEMI and NSTEMI patients,

**Table 3.** Unadjusted and adjusted association between smoking and clinical outcomes in STEMI patients

Variables	Crude model, HRs (95% CIs)	Age-adjusted HRs (95% CIs)	Full-adjusted HRs (95% CIs)
Never-smoker	Reference	Reference	Reference
<15	0.54 (0.26-1.19)	0.64 (0.30-1.38)	0.23 (0.02-1.87)
>15	0.46 (0.23-0.91)	0.58 (0.29-1.16)	0.75 (0.24-2.31)
Age (years)	1.04 (1.02-1.06)		1.07 (1.02-1.12)
Sex (female vs. male)	1.92 (1.16-3.19)	1.51 (0.89-2.54)	1.22 (0.42-3.51)
Diabetes	2.63 (1.61-4.30)	2.47 (1.50-4.06)	1.10 (0.38-3.21)
Hypertension	1.46 (0.90-2.36)	1.12 (0.68-1.84)	0.71 (0.27-1.82)
HDL-C (mg/dL)	1 (0.98-1.01)	1 (0.98-1.02)	1 (0.97-1.03)
Cholesterol (mg/dL)	1 (0.99-1.02)	1 (0.99-1)	1 (0.99-1.01)
BMI (kg/m <sup>2</sup> )	1.00 (0.93-1.10)	1.03 (0.95-1.13)	1.02 (0.93-1.12)
eGFR (mL/min/1.73 m <sup>2</sup> )	0.97 (0.96-0.98)	0.98 (0.96-0.99)	1.02 (0.99-1.05)
Reperfusion therapy	0.50 (0.29-0.85)	0.64 (0.37-1.12)	1.67 (0.46-6.05)
SBP<112	Reference	Reference	Reference
112-140	0.57 (0.31-1.04)	0.55 (0.30-1.00)	0.99 (0.25-3.96)
SBP>140	0.43 (0.23-0.78)	0.42 (0.23-0.77)	1.31 (0.36-4.78)

BMI: body mass index; HDL-C: high-density lipoproteins-cholesterol; SBP: systolic blood pressure; eGFR: glomerular filtration rate

**Table 4.** Unadjusted and adjusted association between smoking and clinical outcomes in NSTEMI patients

Variables	Crude model, HRs (95% CIs)	Age-adjusted, HRs (95% CIs)	Full-adjusted, HRs (95% CIs)
Never-smoker	Reference	Reference	Reference
<15	0.49 (0.11-2.15)	0.56 (0.13-2.46)	0.14 (0-3.90)
>15	1 (0.33-2.97)	1.12 (0.37-3.36)	1.10 (0.27-4.46)
Age (years)	1.06 (1.03-1.10)		1.05 (0.98-1.14)
Sex	1.05 (0.45-2.42)	1.03 (0.44-2.38)	0.59 (0.06-5.28)
Diabetes	2 (0.85-4.72)	1.71 (0.72-4.03)	3.87 (0.58-25.92)
Hypertension	2.61 (1.07-6.35)	1.84 (0.74-4.55)	3.35 (0.37-29.93)
HDL-C (mg/dL)	1 (0.99-1.02)	1 (0.98-1)	0.99 (0.96-1)
Cholesterol (mg/dL)	0.99 (0.98-1)	0.99 (0.98-1)	0.99 (0.96-1)
BMI (kg/m <sup>2</sup> )	0.95 (0.81-1.12)	0.97 (0.81-1.16)	0.96 (0.76-1.20)
eGFR	0.95 (0.93-0.97)	0.98 (0.96-0.99)	0.95 (0.90-0.99)
Reperfusion therapy	0.12 (0.01-0.92)	0.13 (0.017-0.96)	0.86 (0.08-8.41)
SBP<112	Reference	Reference	Reference
112-140	0.30 (0.98-0.92)	0.33 (0.11-1.01)	0.36 (0.02-5.82)
SBP>140	0.33 (0.13-0.84)	0.31 (0.12-0.78)	0.20 (0.02-1.77)

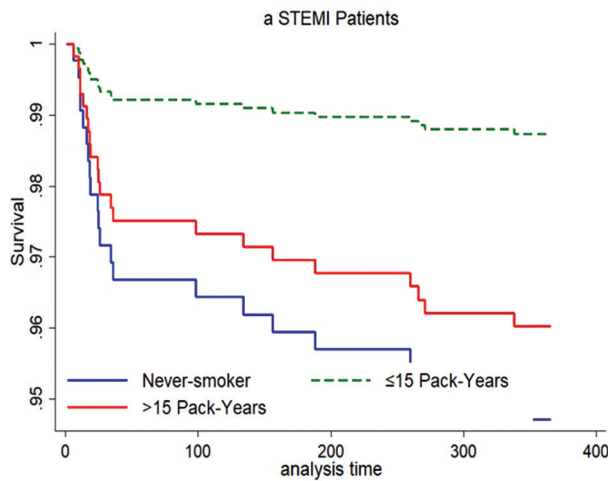
BMI: body mass index; HDL-C: high-density lipoproteins-cholesterol; SBP: systolic blood pressure; eGFR: glomerular filtration rate

suggesting that cumulative tobacco exposure may exert similar biological effects across AMI subtypes once acute management is optimized.

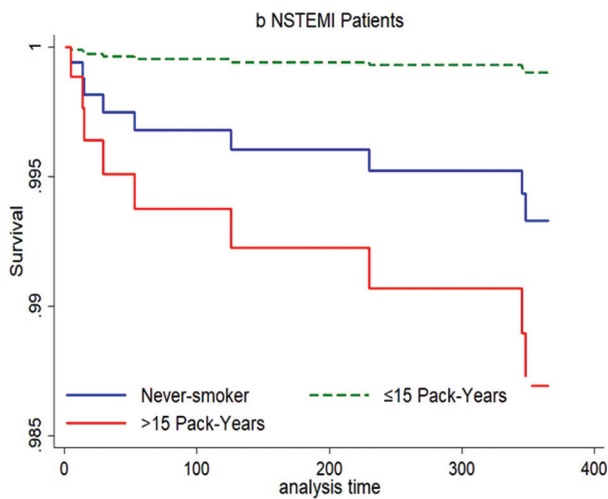
## Limitations

This study has several limitations. First, the retrospective design may introduce selection and information bias. Sec-

ond, smoking status was self-reported without biochemical validation, raising the possibility of misclassification. Third, the study population was derived from a single tertiary care center, potentially limiting the generalizability of our findings to broader populations. Furthermore, the pack-year cutoff of 15, while based on prior literature<sup>[11]</sup>, was arbitrary and may not capture the nuanced effects of smoking intensity. Finally, residual confounding cannot be fully excluded despite comprehensive adjustments.



**Figure 2.** The full-adjusted Cox regression survival curves for heavy and moderate smokers and never-smokers in STEMI patients.



**Figure 3.** The full-adjusted Cox regression survival curves for heavy and moderate smokers and never-smokers in NSTEMI patients.

## Conclusions

In this large, real-world cohort of patients with STEMI and NSTEMI, cumulative smoking burden was not an independent predictor of one-year all-cause mortality after adjustment for key confounders. These results challenge the validity of the smoker’s paradox and underscore the importance of incorporating renal function and age into risk assessment models. Efforts to promote smoking cessation should remain a cornerstone of secondary prevention strategies in AMI care, regardless of initial mortality trends. Future studies should employ prospective designs with biochemical validation, multi-center cohorts, and biomarkers (e.g., cotinine or genetic modifiers) to confirm dose-response in diverse populations.

## Ethical approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Kermanshah University of Medical Sciences (protocol No. IR.KUMS.REC.1400.252). The declarations can be accessed through the institutional Ethics Review Board archives at Kermanshah University of Medical Sciences, Kermanshah, Iran where they are deposited.

## Ethical statement

- The authors declared that no clinical trials were used in the present study.
- The authors declared that no experiments on humans or human tissues were performed for the present study.
- The authors declared that informed consent was obtained from all individual participants included in the study.
- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalized human and animal cell lines were used in the present study.

## Competing interests

The authors declare no conflicts of interest.

## Use of AI

No use of AI was reported.

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The authors have no funding to report.

## Author contributions

PJ: conceptualization, methodology, formal analysis, writing–original draft; SM: data curation, investigation, writing–original draft; NA: supervision, validation, writing–review and editing; MR: data curation, formal analysis, visualization; HJ: investigation, resources, writing–review and editing; AA: methodology, project administration, writing–review and editing; NS: supervision, funding acquisition, writing–review and editing.

## Data availability

All data used are referenced or included in the article.

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