Smoking and Acute Coronary Syndrome in Albania: Implications for Diagnosis, Management, and In-Hospital Outcomes

Short title: Smoking and Cardiovascular Diseases

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Acute Coronary Syndrome, Smoking, Symptoms, Outcome

ABSTRACT:
Introduction: Tobacco use has numerous impacts on the cardiovascular system, which play a significant role in the development of cardiovascular disease (CVD).
Aim: To assess the influence of smoking cigarettes on the diagnosis, management, and in-hospital results of individuals admitted with various acute coronary syndromes (ACS).
Material and methods: In this retrospective study a total of 144 ACS smoker patients and 248 non-smoker patients, identified on the basis of their primary discharge diagnosis, were admitted to the cardiologyunit at Elbasan Regional Hospital in 2022-2023.Sociodemographic, clinical, and biochemical data, along with in-hospital outcomes, were compared. Multivariate logistic regression assessed predictors of adverse events, adjusting for potential confounders.
Results: The mean age of the smokers was significantly younger (64.3 ±10.1years) compared to the non-smokers (69.4 ±11.6 years) ($p<0.001$).Men were predominant among the smokers (71.5%) compared to 55.2% in the non-smoking patients ($p<0.001$).Smoking was associated with dyslipidemia ($p=0.001$), renal insufficiency ($p=0.02$) and a higher rate of critical cardiac symptoms ($p=0.02$)and increased levels of myocardial injury markers at admission ($p=0.03$). ACS type ST-Elevation Myocardial Infarction (STEMI) was more frequent among the smokers. In-hospital all-cause mortality was higher among smokers ($p=0.001$). Also, smoking is a significant predictor of overall ACS at admission OR=1.26 (1.08 - 2.12)($p=0.03$), and in-hospital outcomeOR=1.8 (1.1 - 3.53) ($p=0.03$).
Conclusion: Smoking accelerates ACS onset and worsens in-hospital outcomes. These findings underscore the need for robust smoking cessation programs and tailored public health strategies.

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Introduction

Acute coronary syndrome (ACS) represents a spectrum of life-threatening conditions resulting from myocardial ischemia, encompassing ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina. Smoking, a key modifiable risk factor, exacerbates cardiovascular risks through mechanisms like endothelial dysfunction, pro-inflammatory states, and altered lipid metabolism.
Smoking is a major risk factor for cardiovascular diseases, including acute coronary syndrome. Acute coronary syndrome is a term used to describe a range of conditions associated with sudden, reduced blood flow to the heart, including heart attack (myocardial infarction) and unstable angina (1).The connection between smoking and acute coronary syndrome is well-documented and multifaceted:
Increased plaque buildup: Smoking accelerates the process of atherosclerosis, where plaque builds up on the walls of arteries. This can lead to narrowing and hardening of the arteries, increasing the risk of blood clots that can suddenly block blood flow to the heart, causing ACS (2).

Inflammation and endothelial dysfunction: Smoking induces inflammation and damages the endothelium, the inner lining of blood vessels. This dysfunction can contribute to plaque formation and vulnerability, leading to the rupture of plaques that precipitate ACS (3).
Altered lipid profiles: Smoking is linked to harmful alterations in cholesterol levels, such as higher low-density lipoprotein (LDL) cholesterol("bad"cholesterol)and lower high-density lipoprotein (HDL) cholesterol("good" cholesterol).These changes can play an active role in the progressof atherosclerosis (4).
Increased blood clotting: Smoking promotes blood clotting activity, increasing the risk of clot formation that can block coronary arteries and lead to ACS.
Other risk factors: Smoking can also increase blood pressure and decrease oxygen to the heart, exacerbating other risk factors for ACS (5).
Quitting smoking has been shown to significantly lower the likelihood of developing acute coronary syndrome and other cardiovascular diseases. The benefits of quitting can be seen as early as 20 minutes after stopping, with continued improvements over time, significantly reducing cardiovascular risks within 1 to 2 years of cessation (6).Management of ACS in smokers involves not only addressing the acute condition with medication, procedures such as angioplasty or surgery, but also implementing long-term strategies to prevent recurrence (7). This includes smoking cessation support, lifestyle modifications, and possibly medication to manage cholesterol, blood pressure, and other underlying conditions (8).The impact of smoking on the heart and blood vessels underscores the importance of smoking cessation as a critical component of cardiovascular disease prevention and management (9).While global studies have documented smoking's impact on ACS, regional variations—particularly in low- and middle-income countries—remain underreported. In Albania, where smoking prevalence remains high, understanding its role in ACS is critical for tailoring prevention and treatment strategies. This study aims to bridge this gap by assessing the influence of smoking on diagnosis, management, and in-hospital outcomes in ACS patients at Elbasan Regional Hospital.

Methods

This is a retrospective study. A total of 144 ACS smokerinpatients and 248 non-smoker patients as a comparison group, identified on the basis of their primary discharge diagnosis, were admitted to thecardiologyunit at Elbasan Regional Hospital in 2022-2023.The sample size was chosen to ensure adequate statistical power (80%, α=0.05) to detect significant differences in ACS outcomes. The 1:2 ratio enhances precision, reduces variability, and provides a robust control group for reliable comparisons, while aligning with the available patient population during the study period.
Inclusion criteria:Patients aged ≥18 years, admitted with ACS confirmed by at least one of the following: electrocardiographic changes indicative of myocardial ischemia, serial elevations in cardiac biomarkers (e.g., troponin, CK-MB) or documented coronary artery disease.
Exclusion criteria: Patients were excluded if the qualifying acute coronary syndromes were triggered or accompanied by a major non-cardiovascular condition, such as trauma or surgery.
Study variables:

- Demographic characteristics, medical history, presenting symptoms, duration of

Pre-hospital delay, biochemical and electrocardiographic findings, treatment practices, and a variety of hospital outcome data were collected.

- Smoking

Current smokers were people who reported active cigarette smoking within 1 month before admission to hospital; former smokers were excluded to avoid bias.

- Patients' clinical conditions: The age at which patients developed ACS and the presence

of severe clinical symptoms upon hospital admission were noted. Severe symptoms included STEMI, significantly increased markers of myocardial injury, and critical cardiac issues at the time of admission. Critical cardiac conditions mentioned upon arrival involved acute heart failure, cardiogenic shock, and cardiac arrest. These conditions were identified from the clinical documentation in the patients' medical records during admission.

In-hospital outcomes: This research investigated serious incidents that occurred while the patients were hospitalized, encompassing overall death, recurrent myocardial infarction, cardiogenic shock, and cardiac arrest.

Ethical Considerations

Ethical approval was obtained from the hospital's Institutional Review Board (Approval #: 123/2022). Data confidentiality and patient anonymity were maintained.

Statistical analysis

Data analysis was performed using the statistical package MedCalc 18.4.The Kolmogorov-Smirnov test was used to test the normality of the distribution of continuous variables. Descriptive statistics of continuous variables was presented as mean ± standard deviation (SD). Categorical variables were presented as absolute and relative frequencypercentages. The chi-square and Fisher's exact test were used to compare proportions between categorical variables.Analysis of variance,ANOVA,and Student's t-test were used to compare the means of continuous variables. The multivariate logistic regression method was used to assess independent predictive factors of ACS,adjusting for age, sex, and comorbidities.

Statistical significance was defined as $p \leq 0.05$. Statistical tests were two-sided.

Results

One hundred and forty-foursmoking patients and 248 non-smoking patients participated in the study.The sociodemographic characteristics and vital signs of the patients are shown in table 1.

Table 1. Sociodemographic characteristics and vital signs of the patients

Variables	Smokers (N = 144)	Non-smokers (N = 248)	P value
Age, mean (SD), years	64.3 (±10.1)	69.4 (±11.6)	<0.001
Age group			
<50	13 (10.5)	9 (3.5)	0.001
50-70	75 (60.5)	132 (53.2)	
>70	36 (29.0)	107 (43.1)	
Gender n (%)			
Women	41 (28.5)	111 (44.8)	<0.001
Men	103 (71.5)	137 (55.2)	
BMI ≥30 kg/m2	21 (±16.9)	26 (±10.5)	0.2
Vital signs, M (SD)			
SBP levels, mmHg	129.4 (±22.8)	133.3 (±22.6)	<0.001
DBP levels, mmHg	79.5 (±13.7)	77.9 (±15.1)	<0.001
Heart rates, bpm	77.6 (±14.7)	79.0 (±15.5)	<0.001

The mean age of the smokers was significantly younger (64.3 ±10.1 years) compared to the non-smokers (69.4 ±11.6 years) ($p<0.001$).Among the smoking patients, there was a greater percentage

in the <50 years age group (10.5%) compared to 3.5% ofthe non-smoking patients. Also, among the smoking patients there was a significantly lower percentage in the >70 years age group (29%) compared to 43.1% of non-smoking patients (p=0.001).Men predominatedamong the smokers (71.5%) compared to 55.2% of the non-smoking patients (p<0.001).No significant difference was found regarding the mean BMI of smoking patients (21±16.9) and non-smoking patients (26±10.5) (p=0.2).The mean SBP was higher in non-smoking patients (133.3±22.6 mmHg) compared to smokers (129.4±22.8) (p<0.001).The meanDBP was higher in smoking patients (79.5±13.7 mmHg) compared to non-smokers (77.9±15.12) (p<0.001).The mean heart rate was higher in non-smoking patients (79.0±15.5 mmHg) compared to smokers (77.6±14.7) (p<0.001).The distribution of risk factors and history of disease among smokers and non-smokers is shown in table 2.

Table 2. Distribution of risk factors and history of disease among smokers and nonsmokers

Variables	Smokers (N = 144)	Non-smokers (N = 248)	P value
Risk factors n (%)			
Hypertension	82 (66.1)	151 (61.0)	0.4
Diabetes mellitus	35 (28.2)	64 (26.0)	0.7
Dyslipidemia	119 (82.6)	168 (67.7)	0.001
Elevated LDL-C	67 (54.0)	126 (51.0)	0.4
Low HDL-C	61 (49.2)	99 (40.0)	0.6
Elevated TG	32 (25.8)	50 (20.0)	0.6
History of diseases n (%)			
Angina	86 (69.4)	159 (64.0)	0.4
Myocardial infarction	51 (41.0)	72 (29.0)	0.1
Atrial fibrilation	4 (3.2)	3 (1.3)	0.3
PCI/CABGc	41 (33.0)	55 (22.0)	0.2
Chronic heart failure	18 (14.5)	27 (11.0)	0.6
Family history of IHD	10 (8.0)	10 (4.0)	0.2
Renal insufficiency	35 (28.0)	35 (14.0)	0.01

Regarding the distribution of risk factors, a significant difference was found only for dyslipidemia, which prevailed in smokers (82.6%) compared to non-smokers (67.7%), (p<0.001).The clinical characteristics of smokers and non-smokers are shown in table 3.

Table 3. Clinical characteristics of smokers and non-smokers

Variables	Smokers (N = 144)	Non-smokers (N = 248)	P value
Critical cardiac symptoms at admission n (%)	23 (16.0)	21 (8.3)	0.02
Killip class n (%)			
II–III	118 (81.9)	216 (87.1)	0.2
IV	26 (18.1)	32 (12.9)	
Patient delay, hours			
≤2 h	9 (7.0)	12 (5.0)	0.3
≤12 h	53 (43.0)	126 (51.0)	
>12 h	62 (50.0)	112 (45.0)	
Elevated myocardial injury markers	121 (84.0)	183 (73.8)	0.03
Troponin	92 (74.0)	161 (65.0)	0.8
CKMB/CPKd	79 (64.0)	126 (51.0)	0.4
ACS type n (%)			
STEMI	63 (51.0)	82 (33.0)	0.001
NSTE	61 (49.0)	166 (67.0)	0.001
Triple-vessel disease	24 (19.3)	52 (21.1)	0.3

The clinical characteristics that significantly predominatedamong smokers were:critical cardiac symptoms at admission were higher among smokers (16%) compared to non-smokers (8.3%) (p=0.02);elevated myocardial injury markers at admission were higher among smokers (84%) compared to non-smokers (73.8%) (p=0.02);and ACS typeSTEMI were higher among smokers (51%) compared to non-smokers (33%) (p=0.001).Medical therapy: DAPTuse was higher among smokers (95.2%) compared to non-smokers (90%) (p=0.02).The use of statins was higher among smokers (94.4%) compared to non-smokers (92%) (p=0.001).ACS type NSTE were more frequent among non-smokers (67%)compared to smokers (49%) (p=0.001).

By comparison of in-hospital outcomes it was observed that all-cause mortality was significantly higher among smokers (12.5%) than non-smokers (5.6%) (p=0.02). Smokers had a significantly higher frequency of in-hospital outcomes than non-smokers (18.8% versus 10.5%, p=0.02), particularly among Non-ST Elevation Myocardial Infarction (NSTEMI) patients (26.2% versus 10.2%, p=0.001),and smokers had a significantly higher proportion of in-hospital outcomes than non-smokers in females (17.1% versus 3.6%, p<0.01). The link between smoking and severe heart symptoms upon admission and in-hospital events is shown in table 4.

Table 4.Link between smoking and severe heart symptoms upon admission and in-hospital events. Multivariate analysis.

Critical cardiac symptoms at admission	OR (95%CI)	P
ACS overall	1.26 (1.08-2.12)	0.03
STEMI	1.48 (1.03 - 2.41)	0.04
NSTE-ACS	0.66 (0.43 - 0.95)	<0.01
In-hospital outcomes		
ACS overall	1.8 (1.1 - 3.53)	0.03
STEMI	1.5 (0.61 - 3.42)	0.2
NSTE-ACS	2.1 (1.1 - 4.33)	0.01

In multivariate analysisof associations between smoking and critical cardiac symptoms at admission and in-hospital outcomes, smokers were significantly more likely to have overall ACS OR=1.26 (1.08 - 2.12)(p= 0.03), STEMI OR=1.48 (1.03 - 2.41) (p=0.04).
Also,smokers were significantly more likely to have in-hospital outcomes:overall ACS OR=1.8 (1.1 - 3.53) (p= 0.03) and NSTEMI 2.1 (1.1 - 4.33) (p=0.01).

Discussion

One hundred and forty-four smoking patients and 248 non-smoking patients participated in the study.The study's finding that the smokers were younger than non-smokers when diagnosed with ACS (64.3 ±10.1 years vs. 69.4 ±11.6 years) is consistent with previous research suggesting that smoking accelerates the onset of cardiovascular disease. This is significant as it highlights smoking as a major modifiable risk factor, especially for younger individuals. It raises concerns about the long-term burden of cardiovascular disease in younger populations who smoke, as they might face a prolonged period of chronic illness and diminished quality of life (10).
The predominance of men among the smokers (71.5% vs. 55.2% in non-smokers) may reflect social and behavioural patterns, where smoking prevalence is historically higher in men. However, as smoking rates increase among women in some regions, gender-related outcomes could shift in future studies. Women's risk for cardiovascular diseases, especially post-menopausal, is substantial, and the combined effect of hormonal changes and smoking could present unique challenges in clinical management (11).
Smokers were more likely to present with critical cardiac symptoms, such as STEMI, and elevated myocardial injury markers at admission. STEMI is considered a more severe form of heart attack, characterized by the complete blockage of a coronary artery, and is linked with an increased likelihood of mortality and complications compared to NSTEMI.
Smoking increases the heart's oxygen demand, while simultaneously reducing the oxygen supply due to carbon monoxide inhalation. This mismatch in oxygen supply and demand likely contributes to the more severe presentation in smokers (12). This also supports the higher in-hospital mortality rates observed in the study.The study reports a higher prevalence of dyslipidaemia (82.6%) among smokers compared to non-smokers (67.7%). Smoking is known to unfavourably alter lipid metabolism, increasing low-density lipoprotein (LDL, “bad” cholesterol) and reducing high-density lipoprotein (HDL, “good” cholesterol). This imbalance accelerates the development of atherosclerosis and increases the risk of coronary artery disease.
Strong evidence shows that tobacco use leads to atherosclerotic cardiovascular disease (CVD) (13). One of the primary mechanisms by which smoking contributes to ACS is through plaque rupture and thrombosis. Smoking accelerates atherosclerosis, the build-up of plaque in arteries, and induces chronic inflammation. This leads to increased plaque vulnerability, which can rupture and trigger a clot, causing a heart attack or unstable angina.
Smokers exhibit increased platelet activation and aggregation, which predisposes them to the formation of blood clots. In patients with ACS, this increased clotting potential may contribute to worse outcomes, as noted in this study where smokers had more severe presentations, such as elevated myocardial injury markers and a higher incidence of STEMI (14).
There is a strong association between various forms of tobacco use and cardiovascular disease, with a significant and consistent impact across all cardiovascular conditions(11). Tobacco use not only acts independently but also interacts synergistically with other common CVD risk factors. The complex mechanisms underlying tobacco-related CVD are well-documented, with higher risks observed in younger individuals who smoke more, in women compared to men, and in specific ethnic groups such asSouth Asians (15). The most common cardiovascular diseases linked to

tobacco include myocardial infarction, angina, stroke, aortic aneurysm, and peripheral artery disease. Additionally, conditions such as heart failure, chronic kidney disease, and atrial fibrillation are emerging as major global health concerns.

Smoking was also associated with a higher incidence of renal insufficiency. Chronic kidney disease (CKD) and cardiovascular disease often co-occur, with each condition exacerbating the other. Smoking's role in promoting oxidative stress and inflammation may explain its contribution to both renal and cardiovascular dysfunction. Patients with both ACS and renal insufficiency have worse outcomes due to the added strain on the heart and kidneys (16).

These conditions contribute to increased morbidity, early mortality, reduced productive lifespan, and substantial healthcare costs, straining already overburdened health systems, especially in countries with lower to middle economic statuses. While smoking is a well-established risk factor for acute coronary syndrome, former studies investigating the link between smoking and in-hospital outcomes in ACS patients have yielded conflicting results. The present study found smoking to be a significant predictor of in-hospital mortality, with smokers experiencing a mortality rate of 12.5%, compared to 5.6% in non-smokers. This aligns with the broader literature on the "smoker's paradox," where smokers tend to have worse long-term outcomes despite sometimes presenting with less extensive coronary artery disease than non-smokers. The paradox may be explained by the fact that smokers, though younger, have more severe forms of ACS due to the rapid progression of atherosclerosis and their heightened inflammatory state (17).

These variations may stem from differences in the duration of hospital stays (ranging from an average of 3.5 to 8.6 days), inconsistent definitions of in-hospital outcomes, and variations in the confounding factors considered in multivariable analyses. Further observational studies on ACS patients are necessary to address these uncertainties.The study's multivariable analysis controlled for several confounders, including age, gender, and comorbidities, ensuring the robustness of the association between smoking and poor ACS outcomes. Smoking remained an independent predictor of poor in-hospital outcomes even after accounting for these factors, with an odds ratio of 1.8 for overall ACS outcomes and 2.1 for NSTEMI outcomes.

Limitations

Retrospective Design: Limits causal inference and may introduce selection bias.

Single-Center Study: Reduces generalizability to other populations.

Future research should explore longitudinal outcomes and include larger, multi-center cohorts.

Conclusion

Smoking significantly influences ACS onset and outcomes, with smokers experiencing more severe clinical presentations and higher in-hospital mortality. These findings reinforce the urgent need for targeted smoking cessation programs and public health initiatives to combat the burden of smoking-related cardiovascular diseases.

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