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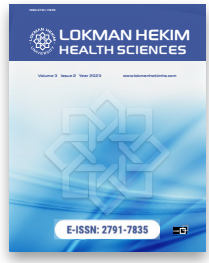

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ORIGINAL ARTICLE

Impact of Tobacco Use on 30-Day Mortality in Subjects Presenting with Spontaneous Intracerebral Hematoma: Retrospective Analysis of 335 Subjects

Spontan Intraserebral Hematom ile Başvuran Hastalarda Tütün Kullanımının 30 Günlük Mortalite Üzerindeki Etkisi: 335 Deneğin Retrospektif Analizi

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Abstract

Introduction: Spontaneous intracerebral hematoma (ICH) causes significant morbidity and mortality. Risk factors for early mortality still need to be clearly elucidated. This study aimed to identify factors associated with 30-day mortality, hematoma volume, and the presence of intravascular hematoma in subjects presenting with spontaneous ICH.

Methods: All consecutive subjects (>18 years) admitted to the intensive care unit between January 2013 and June 2021 with spontaneous ICH were analyzed retrospectively. Detailed systemic and neurological examinations were recorded and evaluated from files.

Results: A total of 335 subjects (51.3% male, median age 68 [55–77] years) with ICH were included in the study. Of these, 230 were smokers (68.7%), 105 were nonsmokers (31.3%). Compared to nonsmokers, smokers had a lower Glasgow Coma Scale score (p=0.036), larger hematoma volume (p=0.034), higher frequency of intraventricular hematoma (p=0.013). Multiple logistic regression revealed that smokers had 2.069-fold higher risk of death than nonsmokers (OR: 2.069, 95% CI: 1.115–3.839, p=0.021). Smoking was also independently associated with the presence of intraventricular hematoma (OR: 1.669, 95% CI: 1.027–2.711, p=0.039).

Discussion and Conclusion: The study showed that smokers have a 2.069-fold greater risk of 30-day mortality and a 1.669-fold higher likelihood of having intraventricular hematoma following spontaneous ICH than nonsmokers.

Keywords: Intracerebral hematoma; Intraventricular hematoma; Mortality; Smoking; Tobacco

Spontaneous intracerebral hematoma (ICH), which occurs due to the rupture of degenerated intracranial vessels, accounts for 10%–15% of all strokes in developed countries.[1] Excessive alcohol consumption, anticoagulant use, and poorly controlled hypertension are the most common underlying disorders leading to spontaneous ICH.[2]

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ICH leads to irreversible damage neuroglial tissue at the bleeding site and continues to cause adverse effects with the development of local hematoma, further deteriorating the clinical outcomes. Although the importance of adequate blood pressure control and prevention of excessive alcohol use have been well understood to reduce the likelihood of ICH, the widespread use of anticoagulants and antiaggregants as crucial therapies for patients with atrial fibrillation, pulmonary embolism, deep vein thrombosis, previous valvular surgery, and coronary artery disease has been suggested to increase the prevalence of ICH.[3]

The management of ICH consists of blood and intracranial pressure control, discontinuation of anticoagulants, head-of-bed elevation, mannitol infusion, therapeutic hypothermia, and surgical decompression in selected patients.[4] Re-bleeding and/or regrowth of the hematoma within the first few hours has been shown to be associated with poor prognosis. Advanced age, anticoagulant agent use, infratentorial localization, and spot sign on computed tomography (CT) are also factors that have been demonstrated to be associated with prognosis in patients with ICH.

Tobacco use is the most common cause of preventable deaths globally. Nicotine and other various agents included in the chemical mixture of cigarette smoke have been shown to promote cardiovascular and cerebrovascular diseases. A substantial amount of data has indicated that smoking is a major risk factor for the development of ICH.[5–7] However, data concerning the role of smoking on prognosis, especially in the short term, are lacking.

This study aimed to investigate whether smoking was associated with 30-day mortality, hematoma volume, or intraventricular hematoma presence in patients presenting with spontaneous ICH, as well as identifying other factors independently associated with these prognosis-related parameters.

Materials and Methods

All consecutive subjects (>18 years) admitted to the intensive care unit (ICU) of Lokman Hekim University Training Hospital between January 2013 and June 2021 with spontaneous ICH were analyzed in a retrospective manner. Those with tumor-related or traumatic ICH, hemorrhagic stroke, subarachnoid hemorrhage, malignant disease, active infection, hematological disorders, and those receiving steroid agents were excluded. Additionally, we excluded patients who were ex-smokers to limit potential confounding. The study was approved by the The Lokman Hekim University Ethics Committee (date: March 29, 2022; no: 2022/55) and was conducted in accordance with the Helsinki Declaration.

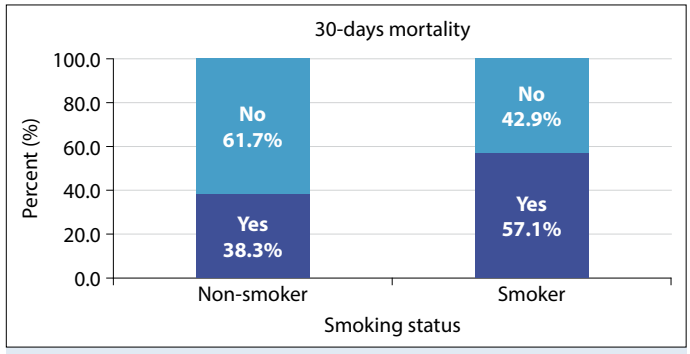

Figure 1. Thirty-day mortality with regard to smoking status.

Systemic and neurological examinations were performed for all subjects at the emergency department, and Glasgow Coma Scale (GCS) scores were recorded. Cranial CT was performed on all subjects at the emergency department prior to admission to the ICU. Venous blood samples for measurement of aPTT, PT, INR, albumin, C-reactive protein (CRP), and complete blood count were routinely obtained upon admission. Demographic characteristics, blood test results, imaging data, ICH etiology, and survival data were retrieved from the institutional digital database and patient charts. Hematoma site was recorded (frontal, temporal, parietal, occipital, cerebellum, basal ganglia, and brain stem). Patients' treatments were recorded in two categories, medical and surgical. Craniotomy and surgical drainage of hematomas had been performed in critical situations including large hematomas with mass effect and midline shift leading to progressive deterioration in consciousness and in subjects with delayed neurological deterioration. Smoking was categorized based on the patients' current smoking status (smoker vs nonsmoker).

The primary outcome measure of this study was to investigate smoking status, other demographic/clinical characteristics, and laboratory test results of patients to assess their independent associations with 30-day mortality among subjects with spontaneous ICH. Secondarily, we sought to perform similar analyses to identify factors that were independently associated with hematoma volume and the presence of intracerebral hematoma. Hematoma volumes were obtained according to the Cavalieri method.[8]

Statistical Analysis

All analyses were performed on IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). For the normality check, histogram and Q–Q plots were used. The data were summarized as mean±standard deviation (SD) or median (1st quartile–3rd quartile) for continuous variables according to the normality of distribution, while categorical variables were described with frequency (percentage). Continuous

Table 1. Summary of patients' characteristics and laboratory measurements with respect to smoking status

	Total (n=335)	Nonsmoker (n=230)	Smoker (n=105)	p
Age (years)	68 (55–77)	68 (55–77)	70 (55–77)	0.464
Sex				0.622
Male	172 (51.3%)	116 (50.4%)	56 (53.3%)	
Female	163 (48.7%)	114 (49.6%)	49 (46.7%)	
Glasgow Coma Scale score	10 (6–13)	10 (7–13)	10 (4–12)	**0.036**
Ischemic infarct	14 (4.2%)	7 (3.0%)	7 (6.7%)	0.145
Hypertension	209 (62.4%)	140 (60.9%)	69 (65.7%)	0.396
Arrhythmia	8 (2.4%)	6 (2.6%)	2 (1.9%)	1.000
Aneurysm	11 (3.3%)	9 (3.9%)	2 (1.9%)	0.513
Bleeding disorder	3 (0.9%)	2 (0.9%)	1 (1.0%)	1.000
Anticoagulant use	74 (22.1%)	47 (20.4%)	27 (25.7%)	0.280
Smoking pack years	27.98±15.11	–	27.98±15.11	N/A
Volume of hematoma (cm^3)	9.0 (4.5–21.0)	7.75 (4.5–20.0)	13.1 (5.3–23.25)	**0.034**
Location of hematoma				0.942
Frontal lobe	38 (11.4%)	27 (11.8%)	11 (10.6%)	
Temporal lobe	62 (18.7%)	41 (18.0%)	21 (20.2%)	
Parietal lobe	70 (21.1%)	51 (22.4%)	19 (18.3%)	
Occipital lobe	7 (2.1%)	5 (2.2%)	2 (1.9%)	
Cerebellum	31 (9.3%)	21 (9.2%)	10 (9.6%)	
Basal ganglia	115 (34.6%)	78 (34.2%)	37 (35.6%)	
Brain stem	9 (2.7%)	5 (2.2%)	4 (3.8%)	
Intraventricular hematoma	136 (40.6%)	83 (36.1%)	53 (50.5%)	**0.013**
Etiology[a]				
Idiopathic	83 (24.8%)	64 (27.8%)	19 (18.1%)	0.076
Hypertension	205 (61.2%)	137 (59.6%)	68 (64.8%)	0.365
Anticoagulant use	68 (20.3%)	41 (17.8%)	27 (25.7%)	0.096
Aneurysm	8 (2.4%)	7 (3.0%)	1 (1.0%)	0.443
Trauma	23 (6.9%)	16 (7.0%)	7 (6.7%)	1.000
Other	7 (2.1%)	5 (2.2%)	2 (1.9%)	1.000
Treatment				
Surgical	86 (25.7%)	62 (27.0%)	24 (22.9%)	0.508
Medical	249 (74.3%)	168 (73.0%)	81 (77.1%)	
Hemoglobin	12.59±2.29	12.56±2.37	12.66±2.10	0.696
WBC ($\times10^3$)	12.10 (9.30–15.44)	11.83 (9.24–15.00)	12.87 (9.62–16.06)	0.129
Neutrophil ($\times10^3$)	9.64 (6.90–13.02)	9.50 (6.55–12.93)	9.85 (7.24–13.33)	0.143
Lymphocyte ($\times10^3$)	1.20 (0.83–1.96)	1.17 (0.79–1.96)	1.24 (0.87–1.98)	0.573
Platelet ($\times10^3$)	223 (175–282)	229.5 (180–290)	215 (175–265)	0.209
Albumin	3.59±0.69	3.59±0.71	3.61±0.66	0.788
PT	14.7 (13.5–17.2)	14.6 (13.5–17.0)	15.0 (13.8–17.6)	0.176
aPTT	29.1 (25.9–33.9)	29.1 (25.9–33.2)	29.2 (26.8–35.8)	0.164
INR	1.15 (1.06–1.38)	1.14 (1.05–1.35)	1.19 (1.09–1.45)	0.147
CRP	10.69 (4.28–38.37)	11.36 (4.28–36.10)	8.88 (4.43–43.87)	0.906
30-day mortality	148 (44.2%)	88 (38.3%)	60 (57.1%)	**0.001**
Time of mortality (days)	9 (4.5–13)	9 (4–13)	8.5 (5–13.5)	0.674

The data are summarized as mean±standard deviation or median (1st quartile–3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. N/A: Not applicable; WBC: White blood cell; CRP: C-reactive protein; PT: Prothrombin time; aPTT: Activated partial thromboplastin time; INR: International normalized ratio; a: Patients may have more than one etiology. P<0.05 value is shown to be significant.

variables demonstrating normal distribution were analyzed with the independent samples t-test. Nonnormally distributed continuous variables were analyzed using the Mann–Whitney U test. Categorical variables were analyzed using the Chi-squared tests or Fisher's exact tests (or the Fisher–Freeman–Halton test when necessary). Linear and logistic regres-

Table 2. Factors associated with the volume of hematoma, linear regression analysis

	Univariable		Multivariable	
	Unstandardized coefficient (95% CI)	**p**	**Unstandardized coefficient (95% CI)**	**p**
Age	0.082 (-0.024 to 0.188)	0.127		
Sex, male	2.246 (-1.062 to 5.554)	0.183		
Glasgow Coma Scale score	-1.785 (-2.155 to -1.416)	<**0.001**	-1.538 (-1.943 to -1.134)	<**0.001**
Ischemic infarct	4.358 (-4.152 to 12.867)	0.314		
Hypertension	-3.197 (-6.603 to 0.208)	0.066		
Arrhythmia	5.099 (-5.666 to 15.864)	0.352		
Aneurysm	-3.405 (-12.633 to 5.823)	0.468		
Bleeding disorder	1.947 (-15.519 to 19.414)	0.827		
Anticoagulant use	3.261 (-0.737 to 7.260)	0.110		
Smoking	2.513 (-1.045 to 6.072)	0.166		
Location of hematoma, occipital lobe	-6.408 (-17.791 to 4.976)	0.269		
Intraventricular hematoma	5.820 (2.508–9.132)	**0.001**	3.765 (0.681–6.850)	**0.017**
Etiology, idiopathic	2.825 (-0.999 to 6.650)	0.147		
Treatment, surgery	3.433 (-0.355 to 7.220)	0.076		
Hemoglobin	-0.582 (-1.312 to 0.148)	0.118		
WBC ($\times 10^3$)	0.632 (0.316–0.948)	<**0.001**	0.310 (-0.806 to 1.427)	0.585
Neutrophil ($\times 10^3$)	0.602 (0.276–0.928)	<**0.001**	-0.078 (-1.229 to 1.072)	0.893
Lymphocyte ($\times 10^3$)	1.057 (-0.460 to 2.574)	0.171		
Platelet ($\times 10^3$)	-0.004 (-0.022 to 0.014)	0.681		
Albumin	-2.696 (-5.080 to -0.311)	**0.027**	-1.622 (-4.034 to 0.791)	0.187
INR	2.674 (0.893–4.455)	**0.003**	0.473 (-1.217 to 2.163)	0.582
CRP	0.027 (0.003–0.051)	**0.027**	0.003 (-0.021 to 0.028)	0.782

WBC: White blood cell; INR: International normalized ratio; CI: Confidence interval; CRP: C-reactive protein. Multivariable model adjusted R^2=0.225; F=14.651; p<0.001.

sion analyses were performed to determine factors that were independently associated with hematoma volume, presence of intraventricular hematoma, and 30-day mortality. Variables were initially analyzed using univariable linear/logistic regression analyses, and those with significance were included in the multivariable linear/logistic regression analyses. Values of p<0.05 were accepted as statistically significant.

Results

A total of 335 subjects (51.3% male, median age 68 [55–77] years) with ICH were included in the study. Of these, 230 were smokers (68.7%) and the remaining 105 subjects were nonsmokers (31.3%). The two groups were similar with respect to age, sex, etiology, presence of ischemic infarct, history of hypertension, arrhythmia, intracerebral aneurysm, bleeding disorder, anticoagulant agent use, hematoma site, type of treatment received (surgical or medical), and laboratory measurements including complete blood count indices, albumin, aPTT, PT, INR, and CRP. Compared to nonsmokers, smokers had lower GCS scores (10 [4–12] vs 10 [7–13], p=0.036), larger hematoma volume (13.1 [5.3–23.25] cm^3 vs 7.75 [4.5–20.0] cm^3, p=0.034), higher frequency of intraventricular hematoma (50.5% vs 36.1%, p=0.013). Thirty-day mortality was significantly higher among smokers compared to nonsmokers (57.1% vs 38.3%, p=0.001) (Table 1, Fig. 1).

Multivariable linear regression analysis revealed that low GCS score (p<0.001) and intraventricular hematoma presence (p=0.017) were independently associated with greater hematoma volume (Table 2).

Multivariable logistic regression analysis revealed that low GCS score (p<0.001), smoking (p=0.039), and high albumin level (p=0.001) were independently associated with the presence of intraventricular hematoma (Table 3).

Multivariable logistic regression analysis revealed that smokers had a 2.069-fold higher risk of death than nonsmokers (OR: 2.069, 95% CI: 1.115–3.839, p=0.021). Patients with intraventricular hematoma had a 1.844-fold higher risk of death than those without (OR: 1.844, 95% CI: 1.016–3.346, p=0.044). In addition, we found that patients with higher GCS scores had a lower risk of death (OR: 0.695, 95% CI: 0.631–0.764, p<0.001) (Table 4).

Table 3. Factors associated with the presence of intraventricular hematoma, logistic regression analysis

	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.998 (0.984–1.012)	0.744		
Sex, male	1.502 (0.968–2.331)	0.069		
Glasgow Coma Scale score	0.908 (0.859–0.961)	**0.001**	0.900 (0.849–0.954)	<**0.001**
Ischemic infarct	1.102 (0.374–3.250)	0.860		
Hypertension	0.907 (0.579–1.422)	0.671		
Arrhythmia	0.203 (0.025–1.671)	0.138		
Aneurysm	0.315 (0.067–1.482)	0.144		
Bleeding disorder	2.955 (0.265–32.918)	0.378		
Anticoagulant use	1.235 (0.733–2.079)	0.428		
Smoking	1.805 (1.131–2.882)	**0.013**	1.669 (1.027–2.711)	**0.039**
Location of hematoma, temporal lobe	1.403 (0.805–2.445)	0.233		
Etiology, idiopathic	1.243 (0.753–2.052)	0.395		
Treatment, surgery	1.300 (0.793–2.133)	0.299		
Hemoglobin	1.030 (0.936–1.133)	0.546		
WBC ($\times 10^3$)	1.020 (0.978–1.064)	0.352		
Neutrophil ($\times 10^3$)	1.028 (0.984–1.074)	0.221		
Lymphocyte ($\times 10^3$)	0.914 (0.742–1.126)	0.399		
Platelet ($\times 10^3$)	1.001 (0.999–1.004)	0.225		
Albumin	1.615 (1.159–2.250)	**0.005**	1.780 (1.258–2.519)	**0.001**
INR	0.990 (0.780–1.255)	0.932		
CRP	0.997 (0.993–1.000)	0.085		

OR: Odds ratio; WBC: White blood cell; INR: International normalized ratio; CI: Confidence interval; CRP: C-reactive protein. Multivariable model Nagelkerke R^2=0.106.

Discussion

This study sought to find the role of tobacco use on prognosis and outcomes in patients presenting with spontaneous ICH. Compared to nonsmokers, smokers had lower GCS scores, larger hematomas, and a higher frequency of intraventricular hematoma. Thirty-day mortality was significantly higher among smokers compared to nonsmokers. Multiple logistic regression analysis revealed that smokers (2.069-fold) and those with intraventricular hematoma (1.844-fold) had a higher risk of death compared to nonsmokers.

Spontaneous ICH, which accounts for 10%–15% of all strokes, constitutes a major public health problem not only as a consequence of high mortality but also owing to the neurological sequela caused by ICH. Spontaneous ICH is the most disabling and least treatable form of stroke with estimated 30-day mortality rates ranging between 25% to 52%.[9] Recent data indicate that only 20% of the subjects with spontaneous ICH can acquire functional independency within the first 3 months of the hemorrhage.[10] Given the high frequency of mortality and morbidity rate from spontaneous ICH, risk stratification and early management are critical to prevent excessive morbidity and mortality. Despite the limitations in available therapeutic options, risk stratification based on clinical features, demographic characteristics, and imaging findings may still provide clues concerning the cause of the ICH and the estimation of its prognosis, thereby facilitating accurate decision-making and identifying patients with the need for intensive treatment or surgery.

Several risk scores have been developed to estimate the prognosis in spontaneous ICH. The "ICH score" is one of the most accepted and validated scores used to predict prognosis in patients with spontaneous ICH.[11] It comprises GCS score, ICH volume (≥30 cm^3 or <30 cm^3), presence of intraventricular hemorrhage, infratentorial origin, and age (≥80 or <80 years). The FUNC score, another validated and accepted scoring system used to assess prognosis in spontaneous ICH, is primarily used to estimate functional independence at 90 days.[12] It comprises ICH volume (<30 cm^3, 30–60 cm^3, >60 cm^3), age (<70 years, 70–80 years, >80 years), ICH site (lobar, deep, infratentorial), GCS score (≥9, <9), and presence of pre-ICH cognitive impairment. The intracerebral hemorrhage grading scale

Table 4. Factors associated with 30-day mortality (logistic regression analysis)

	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.019 (1.004–1.034)	**0.010**	1.018 (0.998–1.038)	0.087
Sex, male	1.050 (0.682–1.617)	0.824		
Glasgow Coma Scale score	0.674 (0.621–0.732)	<**0.001**	0.695 (0.631–0.764)	<**0.001**
Ischemic infarct	1.724 (0.585–5.082)	0.324		
Hypertension	0.983 (0.630–1.534)	0.939		
Arrhythmia	2.145 (0.504–9.123)	0.302		
Aneurysm	1.055 (0.316–3.526)	0.931		
Bleeding disorder	2.548 (0.229–28.375)	0.447		
Anticoagulant use	1.667 (0.992–2.801)	0.054		
Smoking	2.152 (1.346–3.439)	**0.001**	2.069 (1.115–3.839)	**0.021**
Volume of hematoma	1.044 (1.027–1.061)	<**0.001**	1.000 (0.978–1.022)	0.999
Location of hematoma, frontal lobe	1.647 (0.835–3.251)	0.150		
Intraventricular hematoma	2.234 (1.432–3.487)	<**0.001**	1.844 (1.016–3.346)	**0.044**
Etiology, idiopathic	1.022 (0.620–1.683)	0.933		
Treatment, surgery	1.766 (1.077–2.895)	**0.024**	1.323 (0.666–2.628)	0.424
Hemoglobin	0.848 (0.768–0.935)	**0.001**	0.907 (0.790–1.041)	0.164
WBC ($\times10^3$)	1.072 (1.026–1.121)	**0.002**	0.951 (0.760–1.189)	0.658
Neutrophil ($\times10^3$)	1.070 (1.022–1.120)	**0.004**	1.057 (0.840–1.330)	0.637
Lymphocyte ($\times10^3$)	1.076 (0.883–1.311)	0.469		
Platelet ($\times10^3$)	0.998 (0.996–1.001)	0.205		
Albumin	0.688 (0.501–0.945)	**0.021**	0.922 (0.558–1.521)	0.749
INR	2.049 (1.403–2.992)	<**0.001**	1.425 (0.899–2.258)	0.131
CRP	1.004 (1.001–1.007)	**0.018**	0.999 (0.994–1.004)	0.785

OR: Odds ratio; WBC: White blood cell; INR: International normalized ratio; CI: Confidence interval; CRP: C-reactive protein. Nagelkerke R^2=0.497.

(ICH-GS) is another validated and accepted scoring system used to estimate in-hospital mortality, 30-day mortality, and good 30-day functional recovery.[13] The ICH-GS score includes age (<45 years, 45–64 years, >64 years), GCS score at admission (3–8, 9–12, 13–15), ICH site (supratentorial or infratentorial), ICH volume (≥30 cm^3, <30 cm^3), and extension into ventricles.

All risk-stratifying models have advantages and disadvantages; however, they have been shown to predict outcomes in subjects with spontaneous ICH with acceptable sensitivity and specificity. There is still a need for simpler indices and markers to evaluate short-term outcomes in patients with spontaneous ICH. Tobacco use is the most common cause of preventable deaths worldwide. Nicotine and other various toxic agents included in cigarette smoke have been shown to promote cardiovascular and cerebrovascular diseases. Accumulating data show that smoking facilitates the development of ICH.[2] An increasing number of cigarettes consumed daily has been shown to correlate with the increased risk of spontaneous ICH.[14,15] However, the data concerning the role of smoking on outcomes and prognosis after spontaneous ICH are limited. Several earlier clinical studies revealed that hematoma expansion was more frequent among smokers after spontaneous ICH. The study of Yao and colleagues reported that the risk of hematoma expansion (>6 mL increase in hematoma volume or an increase of >33% of volume detected by CT) in patients with spontaneous ICH within the first 72 h was more prevalent among smokers compared to nonsmokers.[16] Another study conducted by Zhou et al.[17] revealed that hematoma volume in subjects with spontaneous ICH was significantly correlated with the number of cigarettes smoked daily. In our study, the presence of intraventricular hematoma was more frequent among smokers compared to nonsmokers, supporting the role of smoking on the development of intraventricular hematoma, which has been previously shown to influence outcomes significantly.

There are also limited data concerning the role of smoking on mortality following spontaneous ICH. Faigle and colleagues reported that smoking was predictive for mortality after spontaneous ICH in both the black and

white populations, with data drawn from the Johns Hopkins clinical stroke database and the Nationwide Inpatient Sample.[18] Another study by Saloheimo et al.[19] reported that the relative risk of death at long-term follow-up in subjects who survived the acute phase of spontaneous ICH was higher among smokers compared to nonsmokers. The prospective study by Neaton et al.[20] also reported that tobacco use was related to mortality following spontaneous ICH. Our findings confirm the results of the mentioned studies by revealing increased short-term mortality among smokers after spontaneous ICH. In our study group, the rate of 30-day mortality was 57.1% among smokers compared to the relatively lower (38.3%) mortality rate among nonsmokers. Our findings show that smokers have a 2.069-fold higher risk of 30-day mortality than nonsmokers.

Several pathophysiological mechanisms have been proposed to explain the link between smoking and spontaneous ICH. Nicotine, one of the predominant ingredients of cigarette smoke, has been shown to transiently increase blood pressure through the activation of the sympathetic nervous system, which in turn activates nicotinic acetylcholine receptors. The transient increase in blood pressure while smoking may potentially increase not only the risk of ICH but the volume of bleeding.[21] Denser fibrin clots observed in smokers may also impair fibrinolysis hematoma resolution, which results in greater tissue damage.[22] The risk of intracerebral aneurysms, which are one of the frequent causes of ICH, has also been reported to be higher in the smoking population.[23] Another mechanism that may explain the link between smoking and ICH is the impairment in the permeability of the blood–brain barrier observed among smokers.[24] This impairment may be associated with an increased risk of ICH. Moreover, the weakening of the blood–brain barrier could facilitate the development of higher-volume hematomas following ICH. With this in mind, we speculate that tobacco use is associated with a higher risk of 30-day mortality following spontaneous ICH owing to the transient increase in blood pressure, impairment in the permeability of the blood–brain barrier, increase in relative oxygen species production, and activated proinflammatory pathways.

This study has some limitations. The retrospective design and relatively small sample size are the main drawbacks of this study. The lack of serial CT imaging to assess hematoma expansion with the greater temporal resolution is another limitation. Nevertheless, our findings provide valuable insights for clinicians dealing with spontaneous ICH.

Conclusion

This study clearly shows that smokers have a significantly higher 30-day mortality rate following spontaneous ICH compared to nonsmokers. Multiple logistic regression revealed that smokers had a 2.069-fold risk of 30-day mortality rate following spontaneous ICH than nonsmokers. Given the high risk of morbidity and mortality after spontaneous ICH, smoking should be accepted as a critical negative prognostic marker.

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