The Association between Substance Use Disorders and Long-Term Outcome of Stroke: Results from a Population-Based Study of Stroke among 450,229 Urban Citizens

Mohammad Sobhan Sheikh Andalibi^a Amir Rezaei Ardani^b Amin Amiri^c
Negar Morovatdar^d Amirhossein Talebi^{c, e} Mahmoud Reza Azarpazhooh^{f, g, h}
Naghmeh Mokhberⁱ

^aInternational UNESCO Center for Health-Related Basic Sciences and Human Nutrition, Mashhad University of Medical Sciences, Mashhad, Iran; ^bPsychiatry and Behavioural Sciences Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran; ^cDepartment of Neurology, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran; ^dClinical Research Development Unit, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; ^eDepartment of Neurology, Center of Expertise for Parkinson & Movement Disorders, Radboud University Medical Center, Nijmegen, The Netherlands; ^fDepartment of Clinical Neurological Sciences, Western University, London, ON, Canada; ^gDepartment of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada; ^hStroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, Western University, London, ON, Canada; ⁱDepartment of Psychiatry, St Joseph's Health Care London, Western University, London, ON, Canada

Keywords

Disability · Mortality · Population-based studies · Substance use disorder · Stroke outcome

Abstract

Introduction: Little is known regarding long-term stroke outcomes in patients with substance use disorder (SUD). Based on anecdotal data, some individuals use illicit drugs, particularly opioids, in an attempt to reduce stroke mortality, disability, or recurrence. This study is aimed to assess the effect of SUD on stroke outcomes. **Methods:** Patients were recruited from the Mashhad Stroke Incidence Study, a population-based study of stroke in Iran. For a period of 1 year, all patients with first-ever stroke (FES) were recruited and then

followed up for the next 5 years. Disability and functional dependency were defined using modified Rankin Scale (>2) and Barthel Index (<60), respectively. We compared the cumulative rates of mortality in follow-up points using the log-rank test. We used multivariable logistic, Cox regression and competing risk models to assess adjusted hazard ratio (aHR) with 95% confidence interval (CI) of stroke disability, functional dependency, mortality, and recurrence among those with a history of SUD. **Results:** 595 FES patients (mean age of 64.6 ± 14.8 years) were recruited in this study. Eighty-one (13.6%) were current substance users, including opium ($n = 68$), naswar ($n = 5$, 6.1%), hashish ($n = 1$), heroin ($n = 1$), and

M.S.S.A. and A.R.A. contributed equally.

($n = 7$) others. The frequency of vascular risk factors was similar between the SUD and non-SUD groups, except for a higher rate of cigarette smoking in the SUD group ($p < 0.001$). After adjusting for various sociodemographic variables, vascular risk factors, and the severity of stroke at admission, SUD increased the 3-month (aHR: 1.60, CI: 1.01–2.49), 1-year (aHR: 1.73, CI: 1.20–2.65), and 5-year (aHR: 1.72, CI: 1.23–2.35) post-stroke mortality risk. We did not observe a significant change in the risk of stroke recurrence, disability, and functional dependency in those with a history of SUD. **Conclusion:** SUD increased the hazard ratio of stroke mortality with no effect on the disability rate. The public should be advised about the potential harm of substance abuse.

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Introduction

Substance use disorders (SUD) may be a direct or indirect risk factor for stroke [1–7]. The relationship between illicit drugs and stroke incidence, especially in young adults, has been reported in several studies [1, 2, 8]. However, little is known regarding long-term stroke outcome in substance users. Such information is crucial in public health and substance use prevention programs. First, the overall rate of SUD is on the rise worldwide [9]; therefore, it is likely there are patients with clusters of noncommunicable disease, vascular risk factors, and SUD in all countries. In addition, in some Asian traditional medicine, such as Chinese, Indian, and Iranian, narcotics are considered as a remedy with possible therapeutic effects [10–13]. Many people in Middle Eastern countries have this misconception that opium consumption may have protective effects against vascular risk factors (e.g., hyperlipidemia and diabetes) [14] and cerebro- or cardiovascular diseases [15].

In a large prospective population-based study of stroke, the Mashhad Stroke Incidence Study (MSIS), we reported an excessive stroke incidence in Iran compared with most Western countries, with stroke occurring at younger ages [16]. Unfortunately, a substantial number of our patients died [17, 18], remained disabled [19], or had stroke recurrences [20] during 5-year follow-up. A higher rate of stroke with poor outcomes in our study may be explained by differences in the rate of vascular risk factors [16] and etiology of stroke in our population [21, 22]. In addition, socioeconomic disadvantage [23], unhealthy lifestyle [24], and different socioeconomic variables [25], including high-risk behaviors (e.g., SUD), may be associated with stroke incidence and outcomes. The current study was designed to assess the association be-

tween SUD and long-term outcomes of stroke, including mortality, stroke recurrence, disability, and functional dependency.

Materials and Methods

Study Population

Patients were recruited from the MSIS. The methods of the MSIS have been previously described elsewhere in detail [16]. In summary, during a 12-month period (2006–2007), we prospectively ascertained all potential cases with stroke in 3 health districts of Mashhad ($N = 450,229$), an urban area of Iran. We delineated the study area by the main boulevards in Mashhad. About 1,000 volunteers helped us to find stroke patients not admitted to the hospital. A group of stroke experts reviewed all potential cases before inclusion in the study. To identify mortality [17], stroke recurrence [20], poststroke disability, and functional dependency [19], we followed all cases at 5 points, including 1 week, 1 month, 3 months, 1 year, and 5 years after their index stroke. The MSIS is the first population-based cohort study of stroke in the Middle East. Our database includes a wide range of variables, including sociodemographic information, vascular risk factors, and type and etiology of stroke.

The study was conducted according to the Declaration of Helsinki guidelines and approved by the Ethics Committee of Mashhad University of Medical Sciences (No. 910678). Informed consent was obtained from each participant or the next of kin before any interview or neurologic examination.

Definitions

We defined stroke according to the World Health Organization [26]. The severity of stroke was defined based on the National Institutes of Health Stroke Scale (NIHSS) at admission and each follow-up session. Poststroke disability was assessed using modified Rankin Scale (mRS). The mRS measures the degree of poststroke disability in 6 different levels, ranging from 0 (lack of symptoms) to 5 (severe disability) and 6 indicating death. We used Barthel Index (BI) to measure functional dependency. The BI is an ordinal score, including 10 important questions regarding performance in activities of daily living. We defined disability as an mRS of > 2 and functional dependency as a BI of < 60 [19]. According to the patients' neighborhood, patients were categorized into 3 subgroups: less privileged area, middle privileged area, and high privileged area [23]. As a part of our clinical assessments, trained nurses and medical students at the residency level had a face-to-face interview regarding SUD, including opioids (burned and the sap), hashish, or similar compounds, heroin, amphetamine-type stimulants, hallucinogens, naswar (a mixture of tobacco and slaked lime, usually with some flavors such as indigo and juniper ash), and inhalants. We divided the patients into 2 groups: current substance users, including former users who had not reached sustained remission (SUD group), and lifelong nonsubstance users or former users who had reached sustained remission (non-SUD group). We used the Diagnostic and Statistical Manual of Mental Disorders 4th edition, text revision (DSM IV-TR) criteria to define the sustained remission in drug users. According to the DSM IV-TR criteria, one should continue complete abstinence for at least 1 year (12 consecutive months) to reach sustained remission [27].

Table 1. Demographic and socioeconomic characteristics of 595 cases with first-ever stroke with and without history of current SUD

Parameters	SUD group (<i>n</i> = 82)	Non-SUD group (<i>n</i> = 513)	<i>p</i> value
Age, yr [†]	63.5±16.0	64.5±14.8	0.57
Sex (male), <i>n</i> (%)	58 (70.7)	250 (48.7)	<0.001
Married, <i>n</i> (%)	62 (76.5)	386 (75.7)	0.87
Low education (<12 yr), <i>n</i> (%)	64 (79.0)	410 (80.7)	0.72
Low income, <i>n</i> (%)	50 (61.0)	266 (51.9)	0.24
Children number [‡]	5.0 (3.0–8.0)	5.0 (3.0–6.0)	0.40
Living on less privileged area, <i>n</i> (%)	45 (54.9)	209 (40.8)	0.04
Body mass index, kg/m ^{2†}	24.6±5.9	25.6±5.5	0.17
Waist circumference, cm [‡]	94.5 (86.2–100.0)	96.0 (87.0–105.0)	0.12
Atrial fibrillation, <i>n</i> (%)	4 (5.1)	46 (9.2)	0.22
Transient ischemic attack, <i>n</i> (%)	3 (3.7)	40 (7.8)	0.18
Hypertension, <i>n</i> (%)	43 (52.4)	309 (60.6)	0.16
Diabetes mellitus, <i>n</i> (%)	20 (24.4)	156 (30.5)	0.26
Hyperlipidemia, <i>n</i> (%)	20 (24.4)	122 (24.1)	0.95
Alcohol consumption, <i>n</i> (%)	5 (6.5)	13 (2.5%)	0.06
Current cigarette smokers, <i>n</i> (%)	24 (29.3)	73 (14.2)	<0.001
Former cigarette smokers, <i>n</i> (%)	18 (22.0)	73 (14.2)	
Lifelong nonsmokers, <i>n</i> (%)	40 (48.8)	367 (71.5)	
NIHSS at the time of admission [‡]	6.5 (3.0–22.0)	6.0 (3.0–17.7)	0.65
Intracerebral hemorrhage, <i>n</i> (%)	12 (14.6)	60 (11.7)	0.26
Ischemic stroke, <i>n</i> (%)	63 (76.8)	431 (84.0)	
Subarachnoid hemorrhage, <i>n</i> (%)	4 (4.9)	10 (1.9)	
Undefined stroke, <i>n</i> (%)	3 (3.7)	12 (2.3)	

According to the patients' neighborhood, patients were categorized into 3 subgroups: less privileged area, middle privileged area, and high privileged area. NIHSS, National Institutes of Health Stroke Scale; SUD, substance use disorders; SUD group, patients with current use or history of SUD; non-SUD group, patients without any history of SUD. All variables were shown as number (percentage) except the following: [†] Mean ± SD. [‡] Median (Q1–Q3).

Statistical Analysis

Data were expressed as means ± SD or median (interquartile range) according to the pattern of data distribution. We used the χ^2 test to analyze categorical variables. Group comparisons were performed using the sample *t* test (for normally distributed data) or Mann-Whitney test (for nonnormally distributed data). Using binary univariable and multivariable logistic regression models (backward stepwise method), we analyzed the odds ratios of post-stroke severity, disability, and functional dependency, stroke among substance users compared to the non-SUD group. The cumulative rates of mortality were compared using the log-rank test. Using multivariable Cox regression models, we calculated the adjusted hazard ratio (aHR) of SUD on poststroke mortality at 7 days, 1 month, 3 months, 1 year, and 5 years after stroke. Variables with a significant or borderline *p* value (*p* < 0.1) in univariable analyses were entered into a multivariable regression model [28]. We used competing risk analysis to adjust the possible effect of death on the recurrence rate and estimated subdistribution hazard ratio of recurrence. A two-sided *p* < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows TM, version 25, software package (SPSS Inc., Chicago, IL, USA) and Stata (version 13).

Results

Data regarding stroke and SUD were available for 595 patients with FES (mean age of 63.5 ± 16.0 years). Eighty-six (14.5%) patients had a hemorrhagic stroke, 494 (83.0%) had an ischemic stroke, and 15 (2.5%) had a stroke with undefined etiology. Table 1 summarizes demographic and socioeconomic differences between these SUD versus non-SUD groups. Eighty-two (13.8%) patients were current substance users including opium (*n* = 68, 82.9%), naswar (*n* = 5, 6.1%), hashish (*n* = 1, 1.2%), and heroin (*n* = 1, 1.2%). Seven (8.5%) patients used other types of substances or a combination of them. SUD was more frequent in men than women (M/F: 2.42, *p* < 0.001). The rate of vascular risk factors was similar between the SUD and non-SUD groups, except for a higher rate of cigarette smoking in the SUD group (*p* < 0.001).

Table 2. Hazard ratio of poststroke mortality among current substance user versus non-substance user groups within 5-year follow-up: results of univariable and multivariable Cox proportional regression analyses

Variable/follow-up time	7 days		1 month		3 months		1 year		5 years	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
<i>Univariable regression</i>										
Male	1.07 (0.68–1.69)	0.77	1.03 (0.72–1.46)	0.89	1.10 (0.80–1.51)	0.57	1.10 (0.83–1.46)	0.50	1.15 (0.92–1.44)	0.21
Age, years	1.02 (1.00–1.04)	0.03	1.03 (1.02–1.05)	<0.001	1.03 (1.02–1.05)	<0.001	1.04 (1.02–1.05)	<0.001	1.04 (1.03–1.05)	<0.001
Education (<12 years)	1.63 (0.81–3.29)	0.17	1.71 (1.00–2.95)	0.05	1.96 (1.18–3.25)	0.01	2.20 (1.38–3.50)	0.001	2.32 (1.63–3.32)	<0.001
Living on less privileged area	3.94 (1.22–12.79)	0.02	2.10 (1.04–4.25)	0.04	2.36 (1.22–4.57)	0.01	2.64 (1.44–4.81)	0.002	2.16 (1.43–3.26)	<0.001
SUD	1.23 (0.66–2.28)	0.51	1.33 (0.83–2.13)	0.23	1.40 (0.92–2.12)	0.11	1.49 (1.03–2.15)	0.03	1.55 (1.15–2.07)	0.004
Current smoker	0.66 (0.33–1.34)	0.25	0.54 (0.30–0.97)	0.04	0.61 (0.37–1.01)	0.06	0.68 (0.44–1.05)	0.08	0.77 (0.56–1.06)	0.12
Exsmoker	0.62 (0.30–1.31)	0.21	0.58 (0.32–1.03)	0.07	0.66 (0.40–1.08)	0.10	0.89 (0.60–1.33)	0.56	1.04 (0.76–1.41)	0.82
Alcohol consumption	1.13 (0.28–4.62)	0.86	1.25 (0.40–3.94)	0.70	1.59 (0.51–5.00)	0.42	2.08 (0.67–6.52)	0.21	0.51 (0.23–1.14)	0.10
NIHSS at admission	1.12 (1.10–1.15)	<0.001	1.12 (1.10–1.14)	<0.001	1.12 (1.10–1.13)	<0.001	1.12 (1.10–1.13)	<0.001	1.10 (1.09–1.11)	<0.001
Atrial fibrillation	2.01 (1.06–3.83)	0.03	2.67 (1.63–4.22)	<0.001	2.45 (1.58–3.79)	<0.001	2.49 (1.68–3.71)	<0.001	2.30 (1.64–3.23)	<0.001
Hypertension	1.49 (0.91–2.45)	0.11	1.47 (1.01–2.16)	0.047	1.39 (0.99–1.95)	0.06	1.38 (1.02–1.86)	0.04	1.34 (1.06–1.69)	0.01
Diabetes mellitus	0.71 (0.41–1.21)	0.21	0.62 (0.40–0.96)	0.03	1.45 (1.00–2.12)	0.05	0.83 (0.61–1.15)	0.27	0.95 (0.74–1.21)	0.67
Hyperlipidemia	0.74 (0.41–1.32)	0.31	0.72 (0.46–1.13)	0.16	1.42 (0.94–2.14)	0.10	0.81 (0.57–1.15)	0.25	0.95 (0.73–1.24)	0.72
<i>Multivariable regression*</i>										
SUD	1.36 (0.70–2.65)	0.37	1.51 (0.91–2.51)	0.11	1.58 (1.01–2.49)	0.048	1.78 (1.20–2.65)	0.004	1.75 (1.28–2.40)	0.001
Age	–	–	1.03 (1.01–1.04)	<0.001	1.03 (1.02–1.04)	<0.001	1.03 (1.02–1.05)	<0.001	1.04 (1.03–1.05)	<0.001
NIHSS at admission	1.12 (1.10–1.15)	<0.001	1.12 (1.10–1.14)	<0.001	1.11 (1.10–1.13)	<0.001	1.12 (1.10–1.13)	<0.001	1.10 (1.09–1.12)	<0.001
Atrial fibrillation	–	–	–	–	–	–	1.59 (1.03–2.44)	0.03	1.77 (1.23–2.54)	0.002

CI, confidence interval; HR, hazard ratio; NIHSS, National Institutes of Health Stroke Scale; SUD, substance use disorders. * These models were adjusted for age, sex, NIHSS at the time of admission, cigarette smoking status, educational level (<12 years), living on the less privileged area, atrial fibrillation, diabetes, hypertension, and hyperlipidemia.

Fig. 1. Adjusted cumulative mortality rate among current substance user versus non-substance user groups within 5-year follow-up: at 1 month (a), 3 months (b), 1 year (c), and 5 years (d) after stroke index. SUD, substance use disorder.

Clinical Outcomes

During the study period, the cumulative rates of mortality among current substance users versus the non-SUD group were significantly different at 1-year (0.43 vs. 0.31; $p = 0.03$) and 5-year follow-ups (0.72 vs. 0.55; $p = 0.003$). After adjustment for covariates including age, sex, sociodemographic data (educational level <12 years and living in the less privileged area), vascular risk factors (cigarette smoking, alcohol consumption, atrial fibrillation, diabetes, hypertension, and hyperlipidemia), and NIHSS at admission, current substance users had a higher hazard ratio of death at 3-month (aHR: 1.58, CI: 1.01–2.49), 1-year (aHR: 1.78, CI: 1.20–2.65), and 5-year (aHR: 1.75, CI: 1.28–2.40) follow-ups as compared to the non-SUD group (Table 2; Fig. 1a–d). In multivariable binary logis-

tic regression analysis, there was no significant difference in the odds ratio of stroke severity, poststroke disability, functional dependency, and recurrence among the SUD group versus non-SUD group. In addition, in competing risk analysis, we did not observe any significant difference in the risk of stroke recurrence between the SUD group versus non-SUD group (Table 3).

Discussion

In a population-based study of stroke among 595 cases with the first-ever stroke, we examined the association of substance use and long-term stroke outcomes, including mortality, recurrence, poststroke disability, and func-

Table 3. Odds ratio of poststroke disability, functional dependency, and recurrence and severity of stroke among current substance user versus non-substance user groups within 5-year follow-up: results of the multivariable logistic regression model

Stroke outcomes	3 months		1 year		5 years	
	odds ratios (95% CI) [†]	p value	odds ratios (95% CI) [†]	p value	odds ratios (95% CI) [†]	p value
Severe stroke [‡]	1.34 (0.51–3.56)	0.55	1.08 (0.23–5.06)	0.93	–	–
Disability**	0.63 (0.23–1.67)	0.35	1.19 (0.42–3.37)	0.74	0.54 (0.09–3.22)	0.50
Functional dependency**	0.90 (0.30–2.64)	0.84	1.49 (0.48–4.59)	0.49	0.75 (0.08–7.07)	0.80
	Subdistribution hazard ratio [†]	p value	Subdistribution hazard ratio (95% CI) [†]	p value	Subdistribution hazard ratio (95% CI) [†]	p value
Recurrence [‡]	0.80 (0.24–2.62)	0.71	0.78 (0.23–2.58)	0.69	1.05 (0.51–2.15)	0.88

[†] Odds ratios for the substance use disorder group. [‡] Severe stroke was defined as National Institutes of Health Stroke Scale (NIHSS) ≥ 8 ; this model was adjusted for age, sex, atrial fibrillation, hypertension, diabetes mellitus and hyperlipidemia, cigarette smoking status, alcohol consumption, education level (<12 years), and living in the less privileged area. ** Disability and functional dependency were defined as mRS >2 and Barthel Index <60 ; models were adjusted for age, sex, NIHSS at the time of admission, cigarette smoking status, alcohol consumption, education level (<12 years), living on the less privileged area, diabetes, hypertension, and hyperlipidemia. [‡] Adjusted for age, sex, atrial fibrillation, hypertension, diabetes mellitus, hyperlipidemia, NIHSS at the time of admission, cigarette smoking status, alcohol consumption, education level (<12 years), and living on the less privileged area. Subdistribution hazard ratio for the substance use disorder group.

tional dependency. After adjustment for a wide range of socioeconomic and vascular risk factors, current SUD significantly increased the hazard ratio of stroke mortality. There was no significant difference in odds of having a poststroke disability, functional dependency, severity of the stroke, and stroke recurrence between those with a history of current SUD versus their counterparts.

A large body of evidence suggests an association between different substances, including stimulants, opioids, hallucinogens, and cannabis, with stroke [1–7]. However, little is known regarding the long-term outcome of stroke among substance users. In the current study, 13.8% of patients with stroke were current substance users at the time of the index stroke. Opium was the most frequent substance of abuse (82.9%). These findings are in line with the Iranian household Mental Health Survey (Iran-MHS), showing opium use disorder as the most common SUD in Iran [29]. Likewise, the rate of opium addiction among cases with stroke in Iran varied from 11.5% [2] to 30.8% [4] and 39.9% [30]. Despite the differences in the age of population between the MSIS and IranMHS (relatively younger population than MSIS), a higher rate of SUD in cases with stroke is worrisome, requiring the urgent attention of health authorities.

The substance may increase the risk of stroke directly via vascular damage or indirectly because of drug-associated organ lesions (i.e., heart and liver) [31]. A wide range of drug-associated mechanisms can contribute to both

ischemic and hemorrhagic strokes. Acute hypertension, rupture of aneurysms, and vasculitis can lead to hemorrhagic strokes [31, 32]. Arrhythmias, hypoxia, hypotension, vasospasm, atherosclerosis, thrombus formation, and embolism may cause ischemic strokes [31, 32]. The risk, etiology, and type of stroke vary according to the type and route of drug administration [31, 33], therapeutic usage [34, 35], and the purity of drugs [36–38]. For example, opioids may cause ischemic stroke due to cardiac dysrhythmia [39], endocarditis [31], and atherosclerosis [40]. Soroosh et al. [41] reported the association between prolongation of QTc interval, as one of the risk factors for stroke incidence [42], and opium overdose. Opioids are also associated with hemorrhagic stroke due to pyogenic arteritis, aneurysmal rupture, and eosinophilia [31]. Recent studies have suggested that impurities of illicit drugs may contribute to the long-term side effects of substances [36]. Unlike prescription opioids [34], illicit opium often contains adulterants and may transmit heavy metals (i.e., lead) [37] or microbial contaminations into the body [4, 35, 37]. Likewise, cannabis may also be associated with both types of stroke via different mechanisms [31, 32].

SUD is a major risk factor for premature mortality, reducing the average life span by 22.5 years [30]. While psychostimulants may increase poststroke mortality [8], there is not enough evidence for such associations with other substances [6]. In the current study, SUD signifi-

cantly increased the hazard ratio of mortality at 3-month, 1-year, and 5-year follow-ups. Therefore, we showed an increase in the mortality rate of stroke among current substance users. We are not able to comment on the exact reasons for increased mortality based on the current study. However, a higher rate of death among cases with stroke and SUD, including opioid use disorders, may be due to an acceleration of the atherosclerosis process [15, 40, 43, 44] through multiple mechanisms, including increased oxidative stress, hyperlipidemia, hyperhomocysteinemia, insulin resistance, hypercoagulable state, and decreased plasma adiponectin [15, 45–47]. The other probable reasons for the higher rate of mortality in patients with stroke and SUD are high-risk behaviors (e.g., drug intoxication, suicide, and intravenous injections) [45, 48, 49], nonadherence to medications [50], baseline comorbidities such as respiratory diseases [49], and infections (hepatitis and HIV) [49, 50]. We also observed no significant association of 7-day and 1-month poststroke mortality with SUD. This is in agreement with recent reports indicating the nonsignificant association between opioid use and in-hospital mortality from CVD [39].

In our study, an increased hazard ratio of mortality was independent of the traditional vascular risk factors and sociodemographic variables, indicating the importance of SUD as a determinant of stroke outcome. We did not find any association between SUD and stroke recurrence and disability. This finding goes against some alleged beliefs regarding the benefit of SUD and, in particular, opium on alleviating the risk factors of vascular events [14]. The public should be aware that illicit drugs, including opium, have no benefit whatsoever in improving stroke disability and may increase the chance of death.

Our study has some limitations. Collecting data regarding substance use by interviewing patients – or their next of kin – is a subject of self-report response bias or underreporting SUD. We are not able to comment regarding the amount, duration of usage before admission, and abstinence rates after discharge. We considered participants with a history of substance use as a non-SUD group if they had continued their abstinence for at least 1 year; however, there is no evidence that 1 year of abstinence is enough to eliminate all possible vascular effects of substances. This study could not reveal the underlying pathophysiological mechanisms of the observed association between stroke, poststroke mortality, and SUD due to many confounders, such as the possible effects of adulterants of illicit drugs. The major strength of our study is that its population-based design makes our sample a good representative of stroke patients in the Middle East. In

addition, the rich database in the MSIS provides an opportunity to adjust our data for a wide range of traditional vascular risk factors and sociodemographic variables.

Conclusion

In summary, SUD is a strong determinant of mortality among stroke survivors. SUD, including opium, does not reduce stroke disability or functional dependency. The public should be aware of the risk of all substances and avoid them.

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Statement of Ethics

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the ethics committee of the Mashhad University of Medical Sciences, Mashhad, Iran (No. 910678). Informed consent was obtained from the participants or the next of kin before any interview or neurologic examination.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Mohammad Sobhan Sheikh Andalibi: reporting of the work described in the article, manuscript revision, data analysis, and submitting the manuscript. Amir Rezaei Ardani, Mahmoud Reza Azarpazhooh, and Naghme Makhber: planned and supervised the study, reporting of the work described in the article, and revised the manuscript. Amin Amiri: conducted the study and reporting of the work described in the article. Negar Morovatdar: reporting of the work described in the article and data analysis. Amirhossein Talebi: reporting of the work described in the article. All authors reviewed, edited, and approved the final version of the article.

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