Alcohol Intoxication as a Stroke Mimic and the Incidence of Acute Alcohol Intoxication in Stroke

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Background and Aim: Alcohol intoxication can be a posterior circulation stroke mimic as they share symptoms such as dysarthria, gait disturbances and nystagmus. We describe alcohol intoxication as a stroke mimic and the frequency of acute alcohol intoxication among stroke patients. *Methods:* Prospective observational single-center study (2014-2017, Haga Ziekenhuis, the Hague). In all patients older than 16 years presenting as possible acute stroke less than 6 hours of onset, blood ethanol was measured; greater than 0.1 blood alcohol concentration (BAC) was considered elevated. *Results:* In total 974 patients were included: 60 (6%) had elevated blood ethanol (mean: 1.3 BAC). In 180 of 974 patients (18%) a stroke mimic was diagnosed: 12 were due to alcohol intoxication (1% of total cohort, 7% of stroke mimic, mean ethanol level: 2.2 BAC). Half of these patients denied or downplayed their alcohol consumption. Stroke and concurrent alcohol intoxication occurred in 38 of 794 strokes (5%, mean ethanol level: 1.1 BAC). Compared to other stroke patients, these 38 patients presented more often after working hours (mean 6.38pm versus 2.23pm) and received alteplase and endovascular therapy less often (24% versus 43%, $P = .018$ and 3% versus 10%, $P = .241$, respectively). *Conclusions:* Of all patients presenting as possible acute stroke, 6% also drank alcohol. 18% of the whole cohort was diagnosed with a stroke mimic. Acute alcohol intoxication as sole diagnosis was diagnosed in 1% of the total cohort and 7% of stroke mimics, 50% denied or downplayed their alcohol consumption. 5% of all stroke patients also drank alcohol, they were significantly less likely to receive alteplase or endovascular treatment.

Key Words: Alcohol intoxication—stroke mimic—ischemic stroke—intracerebral hemorrhagic stroke—posterior circulation—thrombolytic therapy

Introduction

Stroke remains a big burden to national health.[1] Rapid evaluation and treatment of patients with possible acute ischemic stroke in the Emergency Department (ED) reduces morbidity, mortality, and disability.[2–4] However, the need for fast door-to-needle and door-to-groin times presses for diagnosis within a short window of time.

Previous studies have shown that both neurological (for example migraine or seizures) and non-neurological (for example conversion disorder) diseases can present like stroke.[5-10] These so-called stroke mimics (SM) are reported to represent 8% up to 43% of patients admitted to the ED.[5-9] Therefore, patients with SM sometimes receive intravenous thrombolysis (IVT) or are admitted to a hospital ward. Although research has shown that these patients have very low risk of IVT-related complications,[11-17] there are still unnecessary costs involved with therapy and admission,[1,18] which may be reduced by swiftly identifying patients with SM.

Acute alcohol intoxication typically is a posterior circulation SM as these diagnoses share symptoms such as slurred speech, diplopia, gait disturbances, nausea, and nystagmus. The risks of IVT in patients with acute alcohol intoxication may be greater than in patients with other SM, because ethanol impairs fibrinolysis and increases platelet activation.[19,20]

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Received August 27, 2019; accepted September 17, 2019.

Funding: None.

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1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104424

Only few studies describe acute alcohol intoxication as a SM, but none of these provide details on these patients.[5,6,11-13] Furthermore, studies have shown that chronic alcohol abuse is a risk factor for stroke, both ischemic and hemorrhagic.[21-23] A study by Lemarchand et al showed in a murine model that 6 week alcohol consumption worsens ischemic lesions and cancels the beneficial effects of IVT.[24] Acute alcohol intoxication and acute ischemic stroke may be concurrent and only little data has been published on outcome in these patients.[25,26]

The aim of this study is to describe the frequency and clinical characteristics of patients with acute alcohol intoxication as a SM. Furthermore, we aim to describe patients with stroke and concurrent alcohol intoxication.

Methods

Study Design and Setting

This was a prospective observational single-center study in our large urban teaching hospital. The study protocol was approved by the regional ethics committee (METC Zuid Holland). Due to the observational nature of our study, formal approval was waived. In all consecutive patients presented to the ED between January 2014 and December 2017, with a possible stroke who might be eligible for reperfusion therapy, the blood ethanol level was measured. According to our acute stroke protocol, these patients were evaluated by a stroke team, consisting of a neurologist, ED physician, ED nurse, and radiologist. All patients received a cranial computed tomography and blood examination. The neurologist, supported by the examination of imaging by the radiologist, determined whether the patient was eligible for IVT. Additional computed tomography-angiography was performed when ischemic stroke was diagnosed, to evaluate the possibility of endovascular treatment. Magnetic resonance imaging (MRI) was available, but was not part of the routine workup.

Patient Selection and Data

We included all patients that were 16 years or older and presented within 6 hours after symptom onset. Patients were excluded in case of missing data on final diagnosis, blood ethanol level or time of onset. The final diagnosis was established by the treating neurologist after the complete workup in the ED and in case of admission at discharge. Blood ethanol level was routinely measured as part of the standardized blood examination of patients suspected of acute stroke. Blood was drawn immediately after arrival to the ED. A ethanol level greater than .1 BAC (= 10 mg/dL) was considered to be elevated. Relevant clinical data was extracted from the medical records. Vertebrobasilary symptoms were defined as follows: one or more of following symptoms: dysarthria, diplopia, ataxia, gait disturbances, and/or nystagmus.

Outcome Measures

Primary endpoint was the incidence of acute alcohol intoxication as a SM. Secondary endpoints were the incidence of increased ethanol levels in all patients presented for possible reperfusion therapy and in patients with final diagnosis of stroke.

Statistical Analysis

Data are represented as frequency (percentage), mean (standard deviation), and median (interquartile range). We compared patients with and without increased ethanol values in the total cohort, in patients with final diagnosis of stroke and in SM. Furthermore, we describe characteristics of patients with final diagnosis of stroke versus patients with final diagnosis of SM, and of patients with a SM due to alcohol intoxication versus patients with stroke with concurrent alcohol intoxication and. intergroup comparisons were made with chi-square test or Fisher's exact test for discrete variables and with Mann Whitney test for continuous variables. All P values were two-sided and a value of less than .05 was considered to be statistically significant. Data were analyzed with SPSS (version 22, Armonk, NY: IBM Corp.).

Results

Between 2014 and 2017, 1181 patients with a suspected acute stroke were presented for possible reperfusion therapy. We excluded 207 patients: 47 because of missing data on blood ethanol level (mostly because they were referred from another hospital for endovascular recanalization at our institution) and 160 because of symptom onset greater than 6 hours, see Figure 1. Therefore, a total of 974 patients were eligible: 496 (51%) male with a mean age of 70 years (± 15 years).

As shown in Table 1, 60 of the 974 patients (6%) had an elevated ethanol level with a mean value of 1.3 BAC (range 0.2-3.8). These patients were more often male (61.7 versus 50.2%, P = .109), were significantly younger (66 versus 70 years, P = .010), had a lower systolic blood pressure (153 versus 164 mm Hg, P = .003) and presented to the ED later than patients without an elevated blood ethanol level (time 6.45 pm versus 2.24 pm, P < .001).

A total of 180 of 974 (18%) was diagnosed as a SM, they were more often female (58 versus 47%, P = .006), younger (62 versus 72 years, P < .001) and had a lower mean systolic blood pressure (152 versus 166, P < .001) compared to patients with a final diagnosis of stroke (see Table 2). Table 3 shows all different causes of SM. Somatoform disorder was diagnosed most often: 35 of 180 (19%), followed by peripheral vestibular disease (15%), seizure (12%), migraine (8%). Acute ethanol intoxication was found in 7%. Other diagnoses were much less frequent and are listed in Table 3. Of all SM 7.2% received IVT, no complications occurred.

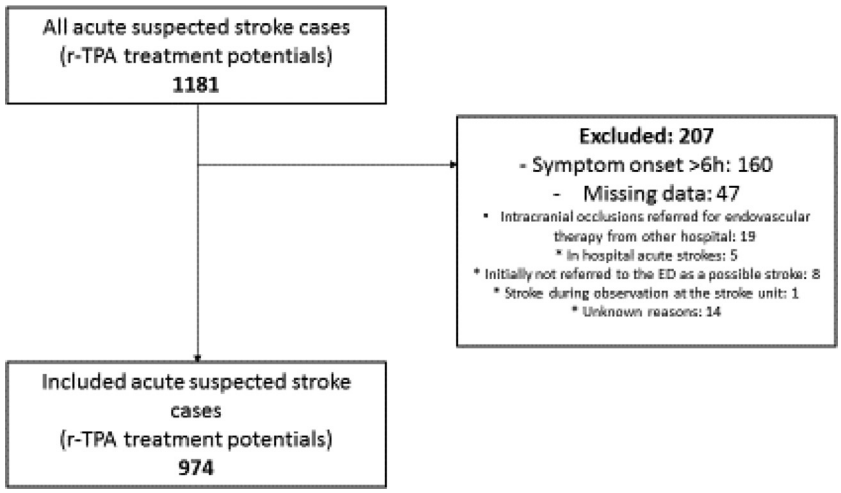

Figure 1. *Exclusions of patients.*

As shown in Table 4, 12 patients had a final diagnosis of only alcohol intoxication, comprising 1% of the total cohort, 5% of patients with vertebrobasilary symptoms and 7% of SM. Compared to the 38 patients with stroke and concurrent alcohol intoxication, patients with only alcohol intoxication had a higher mean blood ethanol level: 2.2 BAC versus 1.1 BAC ($P = .001$). They more often had a nystagmus (64% versus 13%, $P = 0.003$) and other vertebrobasilary symptoms (92% versus 26%, $P < .001$): 9 of 12 patients had dysarthria, 10 of 12 had gait disturbances and 4 of 12 had either a difficulty finding words or incoherent speech. Only one patient did not experience vertebrobasilary symptoms: he was found by his neighbor in a state of confusion and had the inability to repeat a sentence or perform simple tasks. Of the patients that were diagnosed with a SM due to alcohol intoxication, 50% denied or downplayed their alcohol intake versus 29% of the stroke patients with concurrent alcohol intoxication ($P = .017$). They were no differences in the time of presentation ($P = .928$). None of the patients diagnosed with only alcohol intoxication received IVT.

Stroke (either ischemic or hemorrhagic) was diagnosed in 794 of 974 (82%) patients. As shown in Table 1, 38 of 794 (5%) patients had a concurrent alcohol intoxication with a mean ethanol value of 1.1 BAC (range .2-3.7). The mean level of ethanol in SM due to alcohol intoxication was double compared to stroke patient with concurrent alcohol intoxication. 30 of 38 patients were diagnosed with a stroke in the anterior circulation and only 1 of these 30 patients experienced vertebrobasilary symptoms. Next to a paresis of the right arm and leg, neurologic examination showed a bidirectional nystagmus with a mean ethanol level of 2.0 BAC. Seven patients had a final diagnosis of ischemic stroke in the posterior circulation with comorbid alcohol intoxication; all these patients experienced vertebrobasilary symptoms. One of these 38 patients had a small hypertensive hemorrhage in the brainstem with mild hemiparesis on the left and vomiting. On average, patients with stroke and concurrent alcohol intoxication were 7 years younger than patients with a stroke without alcohol intoxication ($P = .007$). Their systolic and diastolic blood pressure were lower, 156 mm Hg versus 167 mm Hg, $P = .049$ and 86 mm Hg versus 88 mm Hg, $P = .963$, respectively. They were presented to the ED more often after working hours (79% versus 46%, $P < .001$) with a median time of presentation of 6.38 pm versus 2.23 pm ($P = .024$). Fewer patients with ischemic stroke and concurrent alcohol intoxication received IVT and endovascular recanalization: 9 of 38 (24%) versus 327 of 756 (43%) ($P = .018$) and 1 of 38 (3%) versus 67 of 756 (9%) ($P = .145$), respectively (see Table 1). No complications of these procedures occurred in stroke patients with concurrent alcohol intoxication.

Discussion

To our knowledge, we are the first study to measure blood ethanol consistently in every patient presented to the ED for possible reperfusion therapy. Kostulas et al reported 8% of their stroke mimics to be alcohol intoxication which is in line with our result.[13] Others report lower percentages of alcohol intoxication: 1-4% of all SM.[5,6,11-13] As we also found that 34% of patients (and up to 50% of the patients with only alcohol intoxication) with an elevated ethanol level denied or downplayed their alcohol intake, it is possible that earlier studies that did not routinely measure ethanol level or ask about alcohol intake, have underdiagnosed alcohol intoxication as a SM. McClelland et al reported in their systematic review that 22% of all patients presented to the ER with a possible acute stroke are diagnosed with a SM which is comparable to our result.[9] Also consistent with previous studies is the younger age,[7-9,11-13,27] higher percentage of females,[8-12] and lower systolic blood pressure we report in patients with SM.[7,10,11-13]

Of all patients with a final diagnosis of stroke, 5% was also intoxicated with alcohol. Thirty of these 38 intoxicated patients with concurrent stroke were diagnosed

Table 1. *Characteristics of the Study Population (with Subgroups of All Strokes and All Stroke Mimics), Subdivided into without and with Elevated Ethanol Level*

	Total Cohort N = 974	Ethanol < .10 BAC N = 914 (94%)	Ethanol >.10 BAC N = 60 (6%)	*P* Value	All Strokes N = 794 (82%)	Ethanol < .10 BAC N = 756 (95%)	Ethanol > .10 BAC N = 38 (5%)	*P* Value	All Stroke Mimics N = 180 (18%)	Ethanol < .10 BAC N = 158 (88%)	Ethanol > 0.10 BAC N = 22 (12%)	*P* Value
Male sex, n (%)	496 (50.9%)	459 (50.2%)	37 (61.7%)	.109	421 (53.0%)	394 (52.1%)	27 (71.1%)	.029	75 (41.7%)	65 (41.1%)	10 (45.5%)	.818
Age in years, mean (SD)	70 (±15)	70 (±15)	66 (±14)	.010	72 (±14)	72 (±14)	65 (±15)	.007	62 (±17)	61 (±17)	66 (±14)	.350
Ethanol in BAC, mean (min-max)	-	-	1.3 (.2-3.8)		-	-	1.1 (.2-3.7)		-	-	1.6 (.2-3.8)	
Systolic BP in mm Hg, mean (SD)	164 (±31)	164 (±31)	153 (±32)	.003	166 (±31)	167 (±31)	156 (±31)	.049	152 (±31)	154 (±31)	142 (±26)	.169
Diastolic BP in mm Hg, mean (SD)	87 (±18)	87 (±18)	82 (±19)	.375	88 (±18)	88 (±18)	86 (±19)	.963	83 (±19)	85 (±18)	76 (±21)	.230
Time of presentation, median	2.33 pm	2.24 pm	6.45pm	.001	2.28 pm	2.23 pm	6.38 pm	.024	3.19 pm	2.45 pm	7.41 pm	.027
Presented to ED at working hours, n (%)	502 (51.5%)	491 (53.7%)	11 (18.3%)	.000	418 (52.6%)	410 (54.2%)	8 (21.2%)	<.001	84 (46.7%)	81 (51.3%)	3 (13.6%)	.001
IVT†, n (%)	349 (35.8%)	339 (37.1%)	10 (16.7%)	.001	336 (42.3%)	327 (43.3%)	9 (23.7%)	.018	13 (7.2%)	12 (7.6%)	1 (4.5%)	1.000
EVT*, n (%)	68 (7.0%)	67 (7.3%)	1 (1.7%)	.116	68 (8.6%)	67 (8.9%)	1 (2.6%)	.145	-	-	-	-
Vertebrobasilary symptoms,n (%)	235 (24.1%)	213 (23.3%)	22 (36.7%)	.028	175 (22.0%)	167 (22.1%)	8 (21.1%)	1.000	60 (33.3%)	46 (29.1%)	14 (63.6%)	.003

*EVT = endovascular therapy.
†IVT = intravenous therapy.

with a stroke in the anterior circulation; only 1 of these 30 patients with a stroke in the anterior circulation experienced vertebrobasilary symptoms; a bidirectional nystagmus next to paresis of the right arm and leg. Seven patients had a final diagnosis of ischemic stroke in the posterior circulation with comorbid alcohol intoxication; all these patients experienced vertebrobasilary symptoms. Considering this last subgroup of patients, the diagnostic dilemma becomes greater, because their symptoms could be attributable to both stroke and intoxication. We could not find literature to confirm these findings. A blood ethanol level and/or a cranial MRI might, in these cases, help the clinicians in making an accurate diagnosis.

We showed that patients with a SM due to alcohol intoxication compared to patients with stroke and concurrent alcohol intoxication had a higher mean ethanol levels and a 5 fold higher incidence of nystagmus. This is of particular importance, as our results show that significantly fewer patients with ischemic stroke and concurrent alcohol intoxication receive IVT and endovascular recanalization in comparison to patients with an ischemic stroke without alcohol intoxication. Little has been published on this specific group of patients, but Gattringer et al also found that patients with ischemic stroke and chronic or acute alcohol consumption have a decreased likelihood of receiving IVT.[25] A recent published article by Arokszallasi et al, describes 3 case reports that show that alcohol intoxication can even delay stroke diagnosis and therefor treatment.[26] Dubiety about the right diagnosis (only alcohol intoxication or comorbid ischemia in the posterior circulation) might be the explanation why in some cases reperfusion therapy is abandoned. Subsequently, clinicians might feel the concern of an increased risk of hemorrhage, even though the use of alcohol or acute alcohol intoxication is not a formal contraindication. Of all patients in our cohort with ischemic stroke and comorbid alcohol intoxication 10 received IVT and 1 endovascular recanalization. No complications occurred, which is in line with the conclusion drawn by Gattringer et al that IVT in patients with ischemic stroke with comorbid chronic or acute alcohol intoxication does not result in an increased risk for symptomatic intracranial hemorrhage.[25] However, a conclusive answer about safety of reperfusion therapy in patients with acute alcohol intoxication remains to be elucidated in larger studies. Even if IVT is safe in these patients, there are still unnecessary costs involved if acute alcohol intoxication as a SM is treated with IVT and submitted to a stroke ward.[18] Dawson et al estimate that stroke unit bed occupancy by SM could be reduced from 9.2% to 3.2% if MRI is performed upon suspicion and several studies have shown the feasibility of diffusion weighted imaging - only MR protocols in patients with SM in the ED.[6,28] However, cost effectiveness of this approach has not been tested. Moreover, MRI can be false-negative, especially in acute ischemic stroke of the posterior circulation.[29–31] In these patients, measurements of ethanol levels may be helpful in differentiating between a stroke and a SM.

Table 2. *Characteristics of the Study Population, Subdivided into Stroke and Stroke Mimic*

	Total Cohort N = 974	Stroke N = 794 (82%)	Stroke Mimic N = 180 (18%)	*P* Value
Male sex, n (%)	497 (51%)	421 (53.0%)	75 (41.7%)	.006
Age in years, mean (SD)	70 (±15)	72 (±14)	62 (±17)	<.001
Systolic BP in mmHg, mean (SD)	164 (±31)	166 (±31)	152 (+-31)	<.001
Diastolic BP in mmHg, mean (SD)	87 (±18)	88 (±18)	83 (±19)	.094
Vertebrobasilary symptoms, n (%)	235 (24.1%)	175 (22.0%)	60 (33.3%)	.002
Time of presentation, median	2.33 pm	2.28 pm	3.19 pm	.195

Table 3. *Total and Frequency of All Final Diagnosis*

Diagnosis	Total Patients, n	% of Stroke or Stroke Mimics	% of Total Cohort
Stroke	794	-	82%
Ischemic stroke in posterior circulation	180	23%	18%
Ischemic stroke in anterior circulation	555	70%	57%
Haemorrhage in posterior circulation	9	1%	1%
Haemorrhage in anterior circulation	50	6%	5%
Stroke mimic	180	-	18%
Somatoform	35	19%	3.6%
Peripheral vestibular disorder	27	15%	2.8%
Seizure	22	12%	2.3%
Other*	18	10%	1.8%
Migraine	15	8.3%	1.5%
Cardiac/collaps/orthostasis/syncope	15	8.3%	1.5%
Acute alcohol intoxication	12	6.7%	1.2%
Infection (in the brain or elsewhere)	9	5%	0.9%
No final diagnosis given	9	5%	0.9%
Intoxication, other**	6	3.3%	0.6%
Malignancy	6	3.3%	0.6%
Hyperventilation	6	3.3%	0.6%

*Other: transient global amnesia (n = 3), subdural hematoma (n = 1), local thrombosis in the arm (n = 1), delirium (n = 1), hypoperfusion (n = 2), hypertensive encephalopathy (n = 1), hyperglycaemia (n = 1), tiredness (n = 3), amyloid spells (n = 1), dementia (n = 1), retention of the bladder (n = 2), atrial flutter (n = 1).
**Other intoxication included: cannabis oil (n = 2), smoking cannabis (n = 2), sedative-use (n = 2).

Table 4. *Alcohol Intoxication Only Compared to Stroke with Concurrent Alcohol Intoxication*

	Alcohol Intoxication Only N = 12	Stroke + Alcohol Intoxication N = 38	*P* Value
Male sex, n (%)	6 (50.0%)	27 (71.1%)	.294
Age in years, median (SD)	70 (±12)	65 (±15)	.363
Ethanol in BAC, mean (min-max)	2.2 (1.0-3.8)	1.1 (.2-3.7)	.001
Systolic BP in mm Hg, mean (SD)	143 (±33)	156 (±31)	.289
Diastolic BP in mm Hg, mean (SD)	67 (±24)	86 (±19)	.034
Time of presentation, mean	6.42 pm	6.38 pm	.928
Working hours, n (%)	1 (8.3%)	8 (21.1%)	.425
IVT†, n (%)	-	9 (23.7%)	
EVT*, n (%)	-	1 (2.6%)	
Vertebrobasilary symptoms, n (%)	11 (91.7%)	8 (21.1%)	0.000
History of alcoholabuse, n (%)	4 (33.3%)	18 (47.4%)	0.512
Denial or downplay alcohol consumption, n (%)	6 (50.0%)	11 (28.9%)	0.017
Nystagmus, n (%)	7 (63.6%)	5 (13.2%)	0.003

Abbreviations: am, before noon; BAC, blood alcohol level; BP, blood pressure; EVT, endovascular therapy; h, hours; IVT, intravenous therapy; mm Hg, millimetres of mercury; pm, after noon; r-TPA, recombinant tissue plasminogen activator; SD, standard deviation.
*EVT = endovascular therapy.
†IVT = intravenous therapy.

Our results should be interpreted in the context of its strengths and limitations. To our knowledge, we are the first to explore patients (> 16 years) presenting with a possible acute stroke and concurrent alcohol intoxication systematically. Our results give an accurate account of alcohol intake in patients presenting to the ED for possible reperfusion therapy, as we measured ethanol levels in all consecutive patients and not only in patients clinically suspected of alcohol intoxication thereby limiting possible selection bias. In addition, our study was conducted in a large urban teaching hospital that services a large heterogeneous population comparable to many worldwide. Several limitations need warranting. First, although we are the first to report alcohol intake in consecutive patients with acute neurological symptoms over a 3-year period, the small number of patients with elevated ethanol levels restrict us from drawing strong conclusions on their distinguishing characteristics and since this is a single center study, the external validity may be limited. Second, future studies are needed to assess the risk of IVT in patients with concurrent alcohol intoxication and the long-term outcome. Last, final diagnoses are based on clinical expertise and are not routinely confirmed with cranial MRI. Therefore, it is possible that some patients were misdiagnosed. However, acute alcohol intoxication becomes very unlikely in case of symptoms, lasting for several days.

Summary and Conclusions

In conclusion, this is the first cohort study to describe ethanol blood level in all patients presenting with possible acute stroke. Alcohol intoxication occurred in 6% of all patients presenting for possible reperfusion therapy. In our cohort, 18% was diagnosed with a SM and 1% is diagnosed with only alcohol intoxication. If only patients with vertebrobasilary symptoms are taken into account, this number rises to 5%. An interesting observation is that patients presenting to the ED with a possible acute stroke and elevated ethanol levels have a 2-fold increased risk of any SM. 5% of all patients with final diagnosis of stroke also drank alcohol. Patients with elevated ethanol levels in general and patients with only alcohol intoxication in particular most often present after working hours. They are not always forthcoming and truthful about their alcohol intake. Therefore, clinicians should consider measuring blood ethanol levels in the acute setting in patients with a possible stroke of the posterior circulation presenting after working hours. But, since knowledge so far does not show an increased risk of symptomatic intracranial hemorrhage, these patients should not be withheld from IVT or EVT.

References

1. Feigin VL, Mensah GA, Norrving B, et al. Atlas of the Global Burden of Stroke (1990-2013): the GBD 2013 study. Neuroepidemiology 2015;45:230-236.
2. Musuka TD, Wilton SB, Traboulsi M, et al. Diagnosis and management of acute ischemic stroke: speed is critical. CMAJ 2015;187:887-893.
3. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008;359:1317-1329.
4. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11-20.
5. Okano Y, Ishimatsu K, Kato, et al. Clinical features of stroke mimics in the emergency department. Acute Med Surg 2018;5:241-248.
6. Dawson A, Cloud GC, Pereira AC, et al. Stroke mimic diagnoses presenting to a hyperacute stroke unit. Clin Med (Lond) 2016;16:423-426.
7. Neves Briard J, Zewude RT, Kate MP, et al. Stroke mimics transported by emergency medical services to a comprehensive stroke center: the magnitude of the problem. Stroke Cerebrovasc Dis 2018;27:2738-2745.
8. Merino JG, Luby M, Benson RT, et al. Predictors of acute stroke mimics in 8187 patients referred to a stroke service. J Stroke Cerebrovasc Dis 2013;22:397-403.
9. McClelland G, Rodgers H, Flynn D, et al. The frequency, characteristics and aetiology of stroke mimic presentations: a narrative review. Eur J Emerg Med 2019;26:2-8.
10. Hand PJ, Kwan J, Lindley RI, et al. Distinguishing between stroke and mimic at the bedside: the brain attack study. Stroke 2006;37:769-775.
11. Tsivgoulis G, Alexandrov AV, Chang J, et al. Safety and outcomes of intravenous thrombolysis in stroke mimics: a 6-year, single-care center study and a pooled analysis of reported series. Stroke 2011;42:1771-1774.
12. Zinkstok SM, Engelter ST, Gensicke H, et al. Safety of thrombolysis in stroke mimics: results from a multicenter cohort study. Stroke 2013;44:1080-1084.
13. Kostulas N, Larsson M, Kall TB, et al. Safety of thrombolysis in stroke mimics: an observational cohort study from an urban teaching hospital in Sweden. BMJ Open 2017;7.
14. Sivakumaran P, Gill D, Mahir G, et al. A retrospective cohort study on the use of intravenous thrombolysis in stroke mimics. J Stroke Cerebrovasc Dis 2016;25:1057-1061.
15. Nguyen PL, Chang JJ. Stroke mimics and acute stroke evaluation: clinical differentiation and complications after intravenous tissue plasminogen activator. J Emerg Med 2015;49:244-252.
16. Giraldo EA, Khalid A, Zand R. Safety of intravenous thrombolysis within 4.5 h of symptom onset in patients with negative post-treatment stroke imaging for cerebral infarction. Neurocrit Care 2011;15:76-79.
17. Winkler DT, Fluri F, Fuhr P, et al. Thrombolysis in stroke mimics: frequency, clinical characteristics, and outcome. Stroke 2009;40:1522-1525.
18. Goyal N, Male S, Al Wafai A, et al. Cost burden of stroke mimics and transient ischemic attack after intravenous tissue plasminogen activator treatment. J Stroke Cerebrovasc Dis 2015;24:828-833.
19. Engström M, Schött U, Reinstrup P. Ethanol impairs coagulation and fibrinolysis in whole blood: a study performed with rotational thromboelastometry. Blood Coagul Fibrinolysis 2006;17:661-665.
20. Mostofsky E, Burger MR, Schlaug G, et al. Alcohol and acute ischemic stroke onset: the stroke onset study. Stroke 2010;41:1845-1849.
21. Zhang C, Qin YY, Chen Q, et al. Alcohol intake and risk of stroke: a dose-respone meta-analysis of prospective study. Int J Cardiol 2014;174:669-677.

22. Wood AM, Kaptoge S, Butterworth AS, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. Lancet 2018;391:1513-1523.
23. Ariesen MJ, Claus SP, Rinkel GJ, et al. Risk factors for intracerebral hemorrhage in the general population, a systematic review. Stroke 2003;34:2060-2065.
24. Lemarchand E, Gauberti M, Martinez de Lizarrondo S, et al. Impact of alcohol consumption on the outcome of ischemic stroke and thrombolysis: role of the hepatic clearance of tissue-type plasminogen activator. Stroke 2015;46:1641-1650.
25. Gattringer T, Enzinger C, Fischer R, et al. IV thrombolysis in patients with ischemic stroke and alcohol abuse. Neurology 2015;85:1592-1597.
26. Arokszallasi T, Balogh E, Csiba L, et al. Acute alcohol intoxication may cause delay in stroke treatment - case reports. BMC Neurol 2019;19:14.
27. Chang J, Teleb M, Yang JP, et al. A model to prevent fibrinolysis in patients with stroke mimics. J Stroke Cerebrovasc Dis 2012;21:839-843.
28. Eichel R, Hur TB, Gomori JM, et al. Use of DWI-only MR protocol for screening stroke mimics. J Neurol Sci 2013;328:37-40.
29. Oppenheim C, Stanescu R, Dormont D, et al. False-negative diffusion-weighted MR findings in acute ischemic stroke. Am J Neuroradiol 2000;21:1434-1440.
30. Lövblad KO, Laubach HJ, Baird AE, et al. Clinical experience with diffusion-weighted MR in patients with acute stroke. AJNR Am J Neuroradiol 1998;19:1061-1066.
31. Zuo L, Zhang Y, Xu X, et al. A retrospective analysis of negative diffusion-weighted image results in patients with acute cerebral infarction. Sci Rep 2015;5:8910.