Prognostic factors of brainstem infarction in a sample of Egyptian patients

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Background Ischemic brainstem stroke is estimated to constitute 10% of all first ischemic brain strokes. Because the brainstem is involved in almost all of the important functions of the central nervous system, brainstem infarction (BSI) is relatively dangerous with a high mortality. Early prediction of the severity and degree of disability and identification of high-risk patients are critical for the treatment of patients with BSI.

Objective This study aimed to evaluate patients with BSI in terms of clinical, laboratory, and radiological factors to study the outcomes of these patients.

Patients and methods Patients were admitted at the Stroke Unit and Internal Neurology Department of Al-Azhar University Hospitals (Al-Hussein and Sayed Galal Hospitals), over a period of 6 months, from 1 December 2016 to 30 May 2017, with a diagnosis of acute BSI, confirmed by computed tomography brain and MRI brain with diffusion. The study included 31 patients and were subjected to clinical, laboratory, radiologic assessment (by computed tomography brain and MRI brain with diffusion), and assessment of severity by the National Institute of Health Stroke Scale (NIHSS) score at the time of admission and discharge. The modified Rankin Scale (mRS) score at discharge was used to divide patients into three groups: patients with mRS less than or equal to 2 were considered to have achieved a good outcome, those with mRS greater than 2–5 were considered to have achieved a poor outcome, and those who died had mRS equal to 6.

Results Overall, 14 (45.2%) patients had a good prognosis, 13 (41.9%) patients had a poor prognosis, and four (12.9%) patients died. Dysphagia, vomiting, cranial neuropathy, and high NIHSS score on admission were associated with a poor outcome. There was no relationship between the outcomes of the studied patients in relation to age, sex, hypertension, atrial fibrillation, diabetes mellitus, ischemic heart disease, high lipid profile, smoking, previous cerebrovascular stroke, obesity.

Conclusion Dysphagia, vomiting, cranial neuropathy, and high NIHSS score were associated with a poor prognosis.
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Introduction

Stroke is a clinical syndrome with rapidly developing symptoms and signs of focal or global loss of cerebral function with no apparent cause other than of vascular origin, lasting more than 24 h, or may lead to death [1].

Stroke is the main cause of neurologic morbidity and mortality worldwide. Ischemic brainstem strokes constitute 10% of all ischemic strokes [2].

Brainstem infarctions (BSIs), even if the extent is very small, may cause significant neurological deficits. Strokes located within the posterior circulation are considered by some as a condition with high morbidity and mortality [3] as the relatively tight packaging of numerous ascending and descending tracts as well as nuclei within the brainstem enables even small lesions to produce very significant neurological deficits [4]. Although the symptoms and signs related to hemispheric involvement are well recognized and are part of the National Institute of Health Stroke Scale (NIHSS) score [5], less attention is paid to brainstem signs.

The aim of the present work was to evaluate patients with BSI in terms of clinical, laboratory, and radiological factors to study the outcome of these patients.

Patients and methods

This study was carried out on 31 patients with a diagnosis of BSI by clinical examination and imaging to confirm the diagnosis. The study was approved by the Ethics Committe of, Al–Azhar University, Faculty of Medicine, Cairo, Egypt. Patients were admitted in the Stroke Unit and Internal Neurology Department of Al-Hussein and Sayed Galal Hospitals.

Inclusion criteria

(1) Patients older than 18 years of age.
(2) Clinical presentation of BSI on admission and at discharge.
(3) Detection of acute BSI by computed tomography (CT) and MRI with diffusion.
(4) Patients with other infarctions concomitant with BSIs were included (old, acute infratentorial, and supratentorial infarctions).

Exclusion criteria

(1) Patients with presentation of anterior circulation strokes confirmed by CT or MRI brain.
(2) Patients with tumors or a history of multiple sclerosis.
(3) Patients with hemorrhagic infraction.

All patients were subjected to the following:

(1) Clinical assessment:
    (a) Full clinical assessment with a special focus on stroke risk factors and neurological examination including level of consciousness and neurological deficit on admission.
    (b) Neurovascular examination.
    (c) Assessment of stroke severity using the NIHSS score at admission and discharge.
    (d) Modified Rankin scale at discharge according to the categorization of patients into three groups.
(2) Laboratory assessment:
    Routine laboratory investigations were performed (complete blood count, liver and renal function tests, erythrocyte sedimentation rate and lipid profile, serum uric acid, prothrombin time, partial thromboplastin time, and international normalized ratio).
    Specific laboratory investigations were performed such as protein C, S, and antiphospholipid antibodies when needed.
(3) Radiological assessment:
    (a) Brain CT was performed as the initial step to exclude intracerebral hemorrhage.
    (b) Brain MRI: diffusion-weighted imaging was performed to detect the site, size, and areas of acute infarction.

MRI was performed within 48h of admission using a 1.5 T MRI unit. The results were evaluated by consultants of radiology and clinical pathology.

Statistical analysis

Statistical presentation and analysis of the present study were carried out using the mean, SD, one-way analysis of variance, and χ^2 using the statistical program of social science. A *P*-value less than 0.05 was considered to indicate significance. All statistical analyses were carried out using SPSS (Statistical Package for the Social Sciences) 11.0, J version.

Results

This study was carried out on 31 patients with a diagnosis of BSI. Patients were divided in three groups: patients with a good outcome, 14 (45.2%), patients with a poor outcome, 13 (41.9%), and patients who died, four (12.9%). There were 18 men and 13 women. Their ages ranged between 20 and 78 years.

There was no statistically significant difference between the outcomes of the studied patients in relation to hypertension, atrial fibrillation, diabetes mellitus, ischemic heart disease, high lipid profile, smoking, previous cerebrovascular stroke, and obesity ($P>0.05$).

There was no significant difference between the outcomes of the patients studied in relation to the site of infarction ($P>0.05$). There was a highly significant difference between the outcomes of the studied patients in relation to the NIHSS score at admission and discharge ($P=0.000$).

There was no statistically significant difference between the outcomes of the studied patients in relation to vertigo, ataxia, motor weakness, headache, and visual symptoms ($P>0.05$). There was a significant difference between the outcomes of the group studied in relation to cranial neuropathy ($P<0.05$). There was a highly significant difference between the outcomes of the patients studied in relation to vomiting and dysphagia ($P=0.000$) (Tables 1–3 and Figs 1–5).

Discussion

A wide variety of factors influence stroke prognosis and mortality, including age, stroke severity, stroke mechanism, infarct location, comorbid conditions, clinical findings, and related complications. In addition, interventions such as thrombolysis, stroke unit care, and rehabilitation can play a major role in the outcome of ischemic stroke [6].

BSIs, even of a small extent, may cause significant neurological deficits [7].

In the present study, the prognosis of BSIs was studied in correlation with other risk factors.

Table 1 Comparison between the outcomes of the patients studied in relation to risk factors

	Good [*n* (%)]	Poor [*n* (%)]	Died [*n* (%)]	χ^2	*P*-value
HTN					
No	9 (64.3)	3 (23.1)	1 (25.0)	5.242	0.073
Yes	5 (35.7)	10 (76.9)	3 (75.0)		
AF					
No	14 (100.0)	13 (100.0)	4 (100.0)	–	–
Yes	0 (0.0)	0 (0.0)	0 (0.0)		
DM					
No	8 (57.1)	5 (38.5)	1 (25.0)	1.704	0.427
Yes	6 (42.9)	8 (61.5)	3 (75.0)		
IHD					
No	12 (85.7)	9 (69.2)	4 (100.0)	2.276	0.321
Yes	2 (14.3)	4 (30.8)	0 (0.0)		
Lipid profile					
High	9 (64.3)	10 (76.9)	2 (50.0)	1.154	0.562
Normal	5 (35.7)	3 (23.1)	2 (50.0)		
Smoking					
No	6 (42.9)	11 (84.6)	2 (50.0)	5.201	0.074
Yes	8 (57.1)	2 (15.4)	2 (50.0)		
Previous CVS					
No	10 (71.4)	9 (69.2)	2 (50.0)	0.676	0.713
Yes	4 (28.6)	4 (30.8)	2 (50.0)		
BMI (obesity)					
No	7 (50.0)	5 (38.5)	2 (50.0)	0.406	0.816
Yes	7 (50.0)	8 (61.5)	2 (50.0)		

AF, atrial fibrillation; CVS, cerebrovascular stroke; DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease.

Table 2 Comparison between the outcomes of the group studied in relation to the National Institute of Health Stroke Scale score and site of infarction

	Good (*N*=14)	Poor (*N*=13)	Died (*N*=4)	Test	*P*-value
NIHSS at admission					
Median (IQR)	6.5 (5–8)	9 (7–11)	34.5 (21–35.5)	Kruskal–Wallis test=14.289	0.001
Range	4–9	6–13	8–36		
Site					
Medulla	0 (0.0)	2 (15.4)	0 (0.0)	χ^2=17.655	0.127
Midbrain	0 (0.0)	2 (15.4)	0 (0.0)		
Pontine	13 (92.9)	7 (53.8)	3 (75.0)		
Pontine, cerebellar, occipital	0 (0.0)	1 (7.7)	0 (0.0)		
Pontine, cerebellar, middle cerebellar peduncle	0 (0.0)	1 (7.7)	0 (0.0)		
Pontine, frontal, parietal	0 (0.0)	0 (0.0)	1 (25.0)		
Pontine, thalamic	1 (7.1)	0 (0.0)	0 (0.0)		
NIHSS at discharge					
Mean±SD	4.21±1.05	7.3±1.60	–	*t*=–5.978	0.000
Range	2–6	4–9	–		

IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale.

There was no significant difference between the three outcome results in terms of age (*P*=0.388); this is in agreement with Li *et al.* [8], who found no difference in outcomes among different age groups, and also in contrast to Zhang *et al.* [9], who found a significant difference between the two outcome groups: the group with poor outcomes were older age than the patients with a good outcome (on the basis of the modified Rankin scale score).

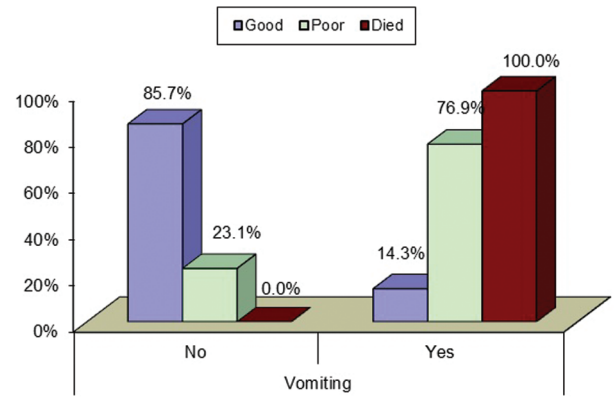
In the present study, vertigo was the most common clinical presentation, in 29 (93.5%) patients, which is in agreement with a previous study of Mehndiratta *et al.* [10].

Vertigo in posterior circulation stroke is because of the involvement of the vestibular nucleus or its connections. Vertigo is a predominant feature of lateral medullary syndrome and cerebellar stroke especially because of posterior inferior cerebellar artery and anterior inferior cerebellar artery territory involvement. Because of the high density of nuclei and tracts in the

Table 3 Comparison between the outcomes of the studied patients in relation to the clinical presentation of the studied group

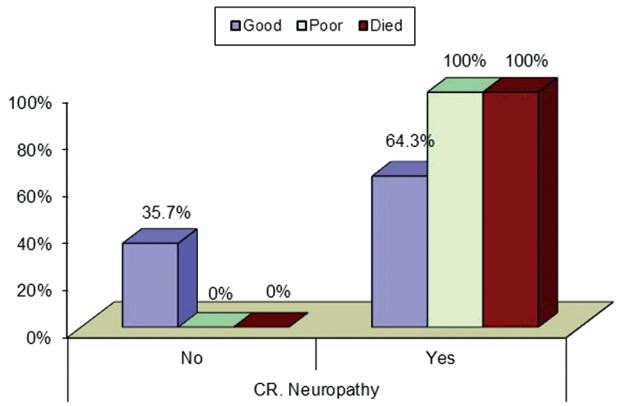
	Good [*n* (%)]	Poor [*n* (%)]	Died [*n* (%)]	χ^2	*P*-value
Vertigo					
No	1 (7.1)	0 (0.0)	1 (25.0)	3.188	0.203
Yes	13 (92.9)	13 (100.0)	3 (75.0)		
Ataxia					
No	2 (14.3)	1 (7.7)	2 (50.0)	4.111	0.128
Yes	12 (85.7)	12 (92.3)	2 (50.0)		
Motor weakness					
No	2 (14.3)	1 (7.7)	0 (0.0)	0.827	0.661
Yes	12 (85.7)	12 (92.3)	4 (100.0)		
Vomiting					
No	12 (85.7)	3 (23.1)	0 (0.0)	14.895	0.001
Yes	2 (14.3)	10 (76.9)	4 (100.0)		
Headache					
No	4 (28.6)	1 (7.7)	2 (50.0)	3.656	0.161
Yes	10 (71.4)	12 (92.3)	2 (50.0)		
Cranial neuropathy					
No	5 (35.7)	0 (0.0)	0 (0.0)	7.239	0.027
Yes	9 (64.3)	13 (100.0)	4 (100.0)		
Dysphagia					
No	12 (85.7)	5 (38.5)	0 (0.0)	11.654	0.003
Yes	2 (14.3)	8 (61.5)	4 (100.0)		
Visual symptoms					
No	10 (71.4)	7 (53.8)	2 (50.0)	1.125	0.570
Yes	4 (28.6)	6 (46.2)	2 (50.0)		

Figure 1



Relationship between vomiting and outcome accorging to mRS score.

Figure 2



Relationship between cranial neuropathy and outcome accorging to mRS score.

brainstem, vertigo is usually accompanied by the involvement of other cranial nerves and or long tracts [11]. It has been reported that isolated episodes of vertigo continuing for more than 3 weeks are almost never caused by vertebrobasilar disease [12].

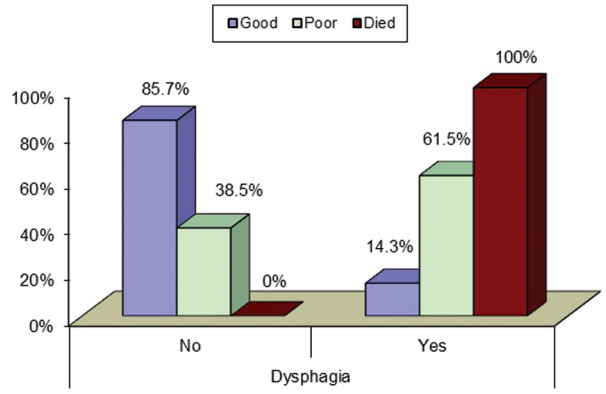
In the current study, motor weakness was the second most common clinical presentation in 28 (90.3%) patients, which is in agreement with the study of Shi *et al.* [13] that reported a relatively higher percentage of patients with motor weakness (81.9%), but not in agreement with another study of Mehndiratta *et al.* [10].

In our study, ataxia was the third most common clinical presentation in 26 (83.9%) patients, which is not in agreement with another previous study of Mehndiratta *et al.* [10] that considered ataxia as the second most common clinical presentation.

Visual symptoms were present in 12 (38.7%) patients, which is not in agreement with Yasumasa *et al.* [14], who reported visual field loss in 84% of patients with posterior cerebral artery infarct.

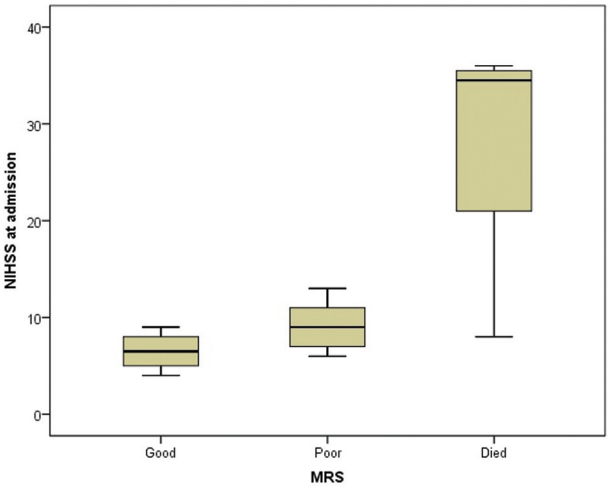
In the present study, we found no significant difference between the outcome groups in terms of differences in

Figure 3



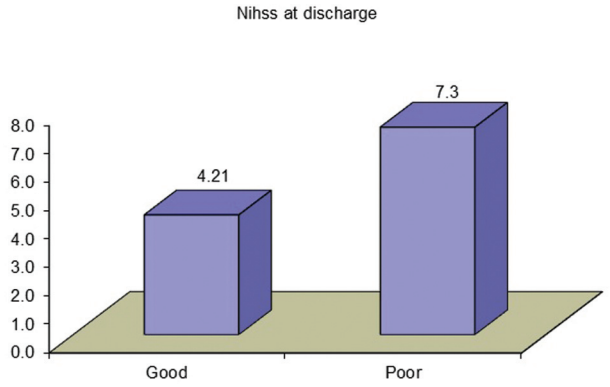
Relationship between dysphagia and outcome accorging to mRS score.

Figure 4



Relationship between outcome accorging to mRS score and NIHSS score at admission.

Figure 5



Relationship between outcome accorging to mRS score and NIHSS score at discharge.

sex (*P*=0.388); this is in agreement with Li and colleagues and Zhang and colleagues, who found the same results.

Also, we found no significant difference in the BMI (*P*=0.892), which is in agreement with Li and colleagues and Zhang and colleagues.

Also, in terms of the presence of diabetes in relation to the outcome of patients, we found no significant difference between the outcome groups in terms of the history of diabetes; this is in agreement with Zhang and colleagues, who found the same results in terms of a history of diabetes, but was not in agreement with Li and colleagues, who found significant differences between groups with good and poor outcomes in terms of the number of diabetic patients in each group.

Also, there was no significant difference between the outcome groups in the number of smokers in each group, which is in agreement with Li and colleagues, who found no significant difference in outcomes between smokers and nonsmokers; this is not in agreement with Zhang and colleagues, who found a significant difference in the number of smokers in each of the outcome groups.

We also found no significant difference in the outcome groups in the presence of hypertension and this is in agreement with Zhang and colleagues, who found similar results, but in contrast to Li and colleagues, who found a significant difference in the number of hypertensive patients in terms of both good and poor outcomes. We also found that there was a highly significant difference between the outcomes of the group studied in relation to the NIHSS score at admission and discharge, which is in agreement with the study of Inoa *et al.* [15] that showed that the NIHSS score, which identifies patients at risk for poor outcomes, is lower in patients with posterior circulation stroke.

The scale is highly weighted toward anterior circulation deficits, including cortical signs and motor function, whereas posterior circulation deficits, including cranial nerve signs and ataxia, receive fewer points, Libman *et al.* [16], Kasner [17] ataxia is frequently excluded from scoring because of the coexistence of motor deficits. Thus, NIHSS may not appropriately evaluate the spectrum of posterior circulation-related signs.

We found that there was a highly significant difference between the outcomes of the studied group in relation to dysphagia, which is in agreement with the study of Okubo *et al.* [18] that showed that there was a positive relationship between dysphagia and the NIHSS score in stroke.

This was also in agreement with the study of Seo *et al.* [19], who found that dysphagia was associated with a 5.77-fold increased risk of moderate-to-severe stroke.

Dysphagia associated with brainstem lesions may be caused by two mechanisms: pseudobulbar paralysis because of damage to the corticobulbar tract and bulbar paralysis because of damage to the swallowing center. The nucleus ambiguus and the nucleus tractus solitarius, which are known as the swallowing center, are located in the medulla oblongata [20].

Current clinical guidelines recommend that all patients with high risk for aspiration and/or dysphagia, including those with brainstem stroke, be tested by video fluoroscopic modified barium swallow [21]. A brainstem stroke is believed to have a direct effect on the swallowing centers and, hence, the lower motor neurons [22]. In addition, Kruger *et al.* [23] noted that the structure of the brainstem contains dense packaging of cranial nuclei, sensory fibers, neurons, and reticular interneurons that are vital to swallowing. As a consequence, dysphagia following a brainstem stroke is often more severe and the chances for spontaneous recovery are lower compared with dysphagia following a hemispheric stroke [24]. The higher incidence and greater severity of dysphagia highlight the importance of timely screening and appropriate management.

We found that there was a highly significant difference between the outcomes of the studied patients in relation to vomiting, which is in agreement with the study of Shigematsu *et al.* [25], who reported that vomiting at stroke onset could be a prompt predictor of early death after stroke.

In our study, we found that there was a significant difference between the outcomes of the studied patients in relation to cranial neuropathy. Classically, cranial nerve palsies because of brainstem lesions have been described in association with long tract signs such as contralateral hemiparesis, hemihypothesia, ipsilateral ataxia, or contralateral ataxia [26].

Limitations

There are some limitations in this study. There were only 31 patients in this study and there was no long-term follow up after discharge.

Conclusion

The present study found unfavorable outcomes of BSI in patients had vomiting, dysphagia, a high NIHSS score, and cranial neuropathy. We found that vertigo and ataxia were the most common manifestations in BSI.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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