

NIHSS and acute complications after anterior and posterior circulation strokes

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Background: The purpose of this study was to determine whether the National Institutes of Health Stroke Scale (NIHSS) score was associated with in-hospital neurological and medical complications (NMC) in patients with posterior circulation infarction.

Methods: This retrospective study included all patients admitted to our stroke unit during a one-year period (n = 289). NMC included neurological deterioration (ie, worsening by 4 points or more of the NIHSS score during the hospital stay) and all other medical complications based on what was recorded in the patients' charts.

Results: Seventy-nine patients (27%) experienced NMC. In posterior circulation infarction patients (n = 90), patients with NMC had a higher baseline NIHSS score (10.9 versus 2.2, $P = 0.004$) and a baseline NIHSS score >2 (78% versus 36%, $P = 0.003$). In stepwise logistic regression, an NIHSS score >2 (odds ratio: 8.2; 95% confidence interval: 1.64–41.0; $P = 0.01$) was associated with NMC. Similar results were observed for anterior circulation infarction patients but with a higher cutoff value for NIHSS score.

Conclusion: In ischemic stroke patients, an increased baseline NIHSS score was associated with an increased risk of NMC. This association applied to anterior-circulation as well as posterior circulation stroke, although zero on the NIHSS for posterior circulation stroke does not mean the absence of NMC during hospitalization. The clinical significance of these findings requires further evaluation in larger prospective studies.

Keywords: acute, stroke, rating scales, complications

Introduction

During the acute phase of ischemic stroke, patients frequently experience neurological and medical complications (NMC). Post-stroke neurological event, so-called early neurological deterioration, is common, occurring in up to 40% of patients and is associated with a worse clinical outcome.^{1–3} Early neurological deterioration is caused by several pathophysiological mechanisms, including extension of infarction, hemorrhage, brain swelling (edema), seizure, and hydrocephalus. In addition, stroke patients can experience other medical events, such as urinary and chest infections, congestive heart failure, falls, pressure ulcer, gastrointestinal bleeding, deep venous thrombosis, and pulmonary embolism.^{2,4–6} These complications are a major cause of death during the acute and subacute phases of stroke.² Despite scarce data to guide the management of these complications, it remains essential to predict these complications early in the course of ischemic stroke.

The National Institutes of Health Stroke Scale (NIHSS) is widely used as a standard instrument to evaluate the severity of a patient's neurological deficit, both in the

emergency department and in the stroke unit.⁷ The NIHSS is a stroke-specific quantitative scale that examines the level of consciousness, language function, neglect, visual field, eye movements, facial palsy, motor strength, sensory function, and coordination. The examination can be performed quickly, and the NIHSS score can be assessed by neurologists as well as non-neurologists after appropriate training.^{8,9} This scale shows excellent reliability and validity and has been used in most stroke trials in order to evaluate neurological outcome.^{10,11} Furthermore, evidence exists to show that the NIHSS is associated with final outcome after a stroke in terms of length of stay,¹² survival, and discharge destination.¹³ However, this scale is mainly weighted toward signs caused by anterior-circulation infarction.¹⁴ To date, it is still unclear whether baseline NIHSS score can also predict NMC in patients with posterior circulation infarction. The aim of this study was thus to determine whether baseline NIHSS score is associated with NMC, whatever the stroke localization.

Materials and methods

Study population

This retrospective study was carried out in the stroke unit at Amiens University Hospital and included all patients referred for an acute ischemic stroke during a one-year period. Patients with a transient ischemic attack ($n = 42$) or absence of a corresponding ischemic lesion ($n = 12$), poor initial prognosis (comatose or intubated patients; pulmonary infection at admission, $n = 26$), patients with onset of cerebral ischemic event more than 6 hours earlier ($n = 30$), and patients with multiple infarcts affecting both anterior and posterior circulations ($n = 5$) were excluded. The remaining 289 patients were included. Cranial computed tomography and/or magnetic resonance imaging, 12-lead electrocardiography, cervical Doppler ultrasonography, transthoracic echocardiography, and standard laboratory tests were performed in all patients on admission. Transesophageal echocardiography, specialized laboratory tests, and Holter electrocardiographic monitoring were performed in selected patients.

For each patient, clinical data were prospectively collected according to a standardized protocol,¹⁵ ie, age, gender, cause of ischemic stroke according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria¹⁶ (to which we added two well-known etiologies, ie, intracranial atherosclerotic disease and aortic atherosclerotic disease) and stroke risk factors that had been previously identified or discovered during hospitalization, including hypertension (antihypertensive treatment or systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg prior to hospitalization),

diabetes (insulin or oral antidiabetic therapy or fasting blood glucose >7 mmol/L on two occasions during hospitalization), hypercholesterolemia (lipid lowering treatment or low-density lipoprotein >1 g/L), coronary artery disease (defined as a known history of myocardial infarction or angina), current smoking, regular alcohol consumption (more than two alcoholic drinks daily), peripheral artery disease, and body mass index (kg/m^2). Glomerular filtration rate was estimated using the four-component Modification of Diet in Renal Disease equation, which is based on age, gender, race, and serum creatinine concentration determined on admission. The presence of chronic kidney disease was defined as glomerular filtration rate <60 mL/minute/1.73 m^2 , in accordance with the National Kidney Foundation criteria.¹⁷ Furthermore, treatment before hospitalization was also recorded. Severity of stroke was assessed using the NIHSS at hospital admission and then every 6 hours during the first 72 hours and once a day after the third day. All clinical physicians who recorded the NIHSS score were certified in administration of the scale, to improve intrareliability and inter-reliability. The present study received institutional review board approval (from the Commission d'Evaluation Ethique des Recherches Non Interventionnelles, Amiens University Hospital).

Definition of stroke localization

Diagnosis of stroke was based on clinical and radiological evaluation by a stroke fellow (MB) and a stroke attending physician (JMB) regardless of symptom duration. Anterior circulation infarction was defined as an acute focal neurological deficit with at least two of the following three features: hemiparesis or hemisensory loss, and/or aphasia or other cortical dysfunction, and/or homonymous hemianopia, with a corresponding ischemic lesion on brain imaging. A diagnosis of posterior circulation infarction was based on hemiparesis or hemisensory loss and/or brainstem or cerebellar signs or isolated homonymous hemianopia, with corresponding ischemic lesion on brain imaging.¹⁸ Patients with lacunar syndromes, including pure motor stroke, pure sensory stroke, sensorimotor stroke, and ataxic hemiparesis, were diagnosed as anterior circulation infarction or posterior circulation infarction according to vascular imaging.¹⁹

Definition of NMC

During hospitalization, detailed data on NMC (including neurological and other medical events) were prospectively recorded using a standardized form for each patient. A neurological event was defined as worsening by 4 points

or more of the NIHSS score during the hospital stay. This clinical deterioration was systematically documented by instrumental examination (brain computed tomography scan and/or magnetic resonance imaging to determine the mechanism of this complication). For other medical events, the occurrence of infectious complications was recorded prospectively. The presence of other complications was based on what was recorded in the patients' charts and according to clinical signs and diagnostic tests. Whenever needed, a specialist consultation was used to confirm a diagnosis.

Statistical analysis

Clinical variables in patients with anterior circulation infarction and posterior-circulation infarction were first compared using Student's *t*-tests for continuous variables and χ^2 tests for categorical variables. NIHSS score was analyzed both as a continuous variable and as a categorical variable. The best cutoff value was selected by building a receiver-operating characteristic curve using the Youden index. To compare patients with and without NMC, we then divided our population into two groups, ie, anterior circulation infarction and posterior circulation infarction. In each group, the same baseline variables were analyzed. Pertinent variables selected by univariate analysis with $P < 0.1$ were tested in a backward logistic regression analysis, and adjusted odd ratios (OR) and 95% confidence intervals (CI) were generated. P values < 0.05 were considered to be statistically significant. All statistical analyses were performed using SPSS statistical software (SPSS Inc, Chicago, IL).

Results

Baseline variables

Amongst the 289 included patients, 199 (69%) had anterior circulation infarction and 90 had posterior circulation infarction. Demographic data and vascular risk factors did not differ between anterior circulation infarction and posterior circulation infarction patients, but baseline NIHSS scores did and were higher in anterior circulation infarction than in posterior circulation infarction (Table 1).

ME during hospitalization

Seventy-nine patients (27%) experienced 108 NMC (Table 2). Amongst the NMC, ischemic stroke recurrence was the most frequent neurological event, and pneumonia and urinary tract infection was the most frequent medical complication. A tendency for higher frequency of NMC in patients with anterior circulation infarction than in patients with posterior circulation infarction (31% versus 20%, $P = 0.065$)

Table 1 Baseline variables by stroke localization (n = 289)

	ACI (n = 199)	PCI (n = 90)	P value
Age (years)	68.0 ± 15.4	67.6 ± 14.7	0.83
Men	102 (51)	57 (63)	0.07
Previous main risk factors			
Hypertension	118 (59)	63 (70)	0.09
Diabetes mellitus	52 (26)	23 (26)	1.00
Dyslipidemia	65 (33)	30 (33)	1.00
Active smoking	40 (20)	18 (20)	1.00
Coronary artery disease	27 (14)	13 (14)	0.86
Atrial fibrillation	39 (20)	10 (11)	0.09
PAD	21 (11)	12 (13)	0.55
Stroke	36 (18)	23 (26)	0.16
BMI ≥ 25 kg/m ²	103 (52)	44 (49)	0.70
Alcohol consumption	30 (15)	12 (13)	0.86
Chronic kidney disease	52 (26)	26 (29)	0.67
Baseline NIHSS			
NIHSS score	7.3 ± 7.1	4.0 ± 6.3	<0.001
Causes of ischemic stroke			
Large vessel atherosclerosis	29 (15)	11 (12)	0.71
Cardioembolic	76 (38)	24 (27)	0.06
Lacunar	19 (10)	10 (11)	0.68
Undetermined	63 (32)	34 (38)	0.35
Other	14 (7)	7 (8)	0.81

Notes: Results are presented either as means ± standard deviation (age and NIHSS score) or as n (%).

Abbreviations: ACI, anterior circulation infarction; PCI, posterior circulation infarction; CAD, coronary artery disease; PAD, peripheral artery disease; BMI, body mass index; NIHSS, National Institutes of Health Stroke Scale.

was observed. Using the receiver-operating characteristic curve analysis (Figure 1), the cutoff value of baseline NIHSS score predicting NMC was 5 for anterior circulation infarction (area under the curve = 0.797; 95% CI: 0.73–0.86; $P < 0.001$) and 2 for posterior circulation infarction (area under the curve = 0.799; 95% CI: 0.66–0.93; $P < 0.001$).

Patients with anterior circulation infarction

In 199 patients with anterior circulation infarction, smoking status (10% versus 25%, $P = 0.02$), hypercholesterolemia (18% versus 39%, $P = 0.003$), and body mass index ≥ 25 (41% versus 56%, $P = 0.047$) were less frequent in patients with NMC, whereas a tendency was observed for higher frequency of chronic kidney disease in patients with NMC (34% versus 22%, $P = 0.08$). Patients with NMC had a higher NIHSS score (12.6 ± 8.3 versus 4.9 ± 5.0 ; $P < 0.001$) and baseline NIHSS score > 5 (75% versus 22%, $P < 0.001$). Stepwise logistic regression selected the following independent factors for NMC: NIHSS score > 5 (OR: 6.3, 95% CI: 2.80–14.14; $P < 0.001$), smoking status (OR: 0.30, 95% CI: 0.10–0.85; $P = 0.024$), hypercholesterolemia (OR: 0.24, 95% CI: 0.09–0.61; $P = 0.003$), and chronic kidney disease (OR: 3.4, 95% CI: 1.45–7.94; $P = 0.005$).

Table 2 NMC observed in stroke patients (108 NMC were observed in 79 patients)

	Cases (n)
Neurological event	48
Ischemic stroke recurrence	15
Symptomatic intracranial hemorrhage	14
Seizure	14
Malignant cerebral infarction	5
Medical event	60
Post-stroke infections	44
Nosocomial pneumonia	30
Urinary tract infection	12
Acute cholecystitis	1
Septic shock	1
Other causes	12
Acute renal failure	5
Severe hematuria	1
Peripheral arterial embolism	1
Aortic dissection	1
Mesenteric ischemia	1
Symptomatic bradycardia	1
Gastrointestinal bleeding	1
Acute pulmonary edema	1

Abbreviation: NMC, neurological and medical complications.

Patients with posterior circulation infarction

In the 90 patients with posterior circulation infarction, demographic data, and vascular risk factors were not statistically different according to the presence of NMC (Table 3). Patients with NMC had a higher baseline NIHSS score and more frequently baseline NIHSS score >2, large vessel atherosclerosis,

and less frequently stroke with undetermined etiology. Stepwise logistic regression selected the following independent factors for NMC: NIHSS score >2 (OR: 8.2, 95% CI: 1.64–41.0; $P = 0.01$), large vessel atherosclerosis (OR: 18.3, 95% CI: 2.70–124.71; $P = 0.003$) and stroke of undetermined etiology (OR: 0.11, 95% CI: 0.01–0.97; $P = 0.047$).

When considering only patients who experienced neurological events ($n = 10$), similar results were observed: these patients had a higher baseline NIHSS score >2 (100% versus 37%, $P < 0.001$), more frequently large vessel atherosclerosis (50% versus 7%, $P = 0.002$), and less frequently stroke with undetermined etiology (0% versus 42%, $P = 0.012$). When considering only patients who experienced medical events ($n = 13$), they had more frequently large vessel atherosclerosis (31% versus 9%, $P = 0.05$) and less frequently stroke with undetermined etiology (8% versus 43%, $P = 0.015$), whereas there was a tendency for higher baseline NIHSS score >2 (69% versus 40%, $P = 0.071$).

Patients with baseline NIHSS score of 0

The 40 patients with posterior circulation infarction more frequently had a baseline NIHSS score of 0 than did patients with anterior circulation infarction (20% versus 11%, $P = 0.001$); two posterior circulation infarction patients experienced NMC, whereas no NMC occurred in anterior circulation infarction patients in this population.

Discussion

The present study showed that an increased baseline NIHSS score in ischemic stroke patients was associated with an increased risk of NMC. This association applied to anterior circulation as well as posterior circulation stroke, although the cutoff value for the baseline NIHSS score predicting NMC was different between anterior circulation infarction and posterior circulation infarction patients. Indeed, despite a higher baseline NIHSS score in anterior circulation infarction patients than in posterior circulation infarction patients, the NIHSS score on admission can predict NMC, both in anterior circulation infarction and posterior circulation infarction patients, with a 6–8-fold increase in risk. Our findings suggest that NIHSS assessment may be a useful approach to predict all NMC, even in patients with posterior circulation infarction, because it can alert the physician to the anticipated risk of NMC in an individual patient and can thus affect early decisions about further surveillance and diagnostics.

We showed that stroke patients experienced neurological and medical events in similar proportion. Our rate of complications is low compared with previous studies. Indeed, the

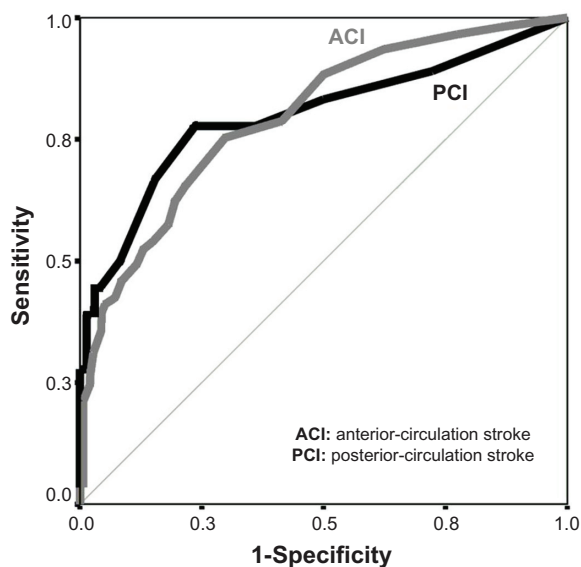


Figure 1 Receiver-operating characteristic curve analysis of National Institutes of Health Stroke Scale scores in patients with neurological and medical complications according to the type of ischemic stroke.

Table 3 Demographic and clinical characteristics of patients with posterior circulation infarction (n = 90) according to the presence or absence of NMC

	All patients (n = 90)	NMC (n = 18)	No NMC (n = 72)	P value
Age (years)	67.6 ± 14.7	72.0 ± 9.8	66.6 ± 15.9	0.16
Men	57 (63)	10 (56)	47 (65)	0.58
Previous main risk factors				
Hypertension	63 (70)	12 (67)	51 (71)	0.78
Diabetes mellitus	23 (26)	7 (39)	16 (22)	0.22
Dyslipidemia	30 (33)	7 (39)	23 (32)	0.59
Active smoking	18 (20)	3 (17)	15 (21)	1.00
CAD	13 (14)	1 (6)	12 (17)	0.45
PAD	12 (13)	2 (11)	10 (14)	1.00
Stroke	23 (26)	7 (39)	16 (22)	0.22
BMI > 25 kg/m ²	44 (49)	8 (44)	36 (50)	0.79
Alcohol consumption	12 (13)	2 (11)	10 (14)	1.00
Chronic kidney disease	26 (29)	4 (22)	22 (31)	0.57
Baseline NIHSS				
NIHSS score	4.0 ± 6.3	10.9 ± 11.0	2.2 ± 2.4	0.004
NIHSS score >2	40 (44)	14 (78)	26 (36)	0.003
Causes of ischemic stroke				
Large vessel atherosclerosis	11 (12)	7 (39)	4 (6)	0.001
Cardioembolic	24 (27)	6 (33)	18 (25)	0.55
Lacunar	10 (11)	2 (11)	8 (11)	1.00
Undetermined	34 (38)	1 (6)	33 (46)	0.001
Other	7 (8)	2 (11)	5 (7)	0.6
Therapeutics before hospitalization				
Antihypertensive therapy	60 (67)	12 (67)	46 (64)	1.00
Antiplatelet agents	35 (39)	6 (33)	29 (40)	0.79
Anticoagulants	4 (4)	2 (11)	2 (3)	0.18
Statins	24 (27)	3 (17)	21 (29)	0.38

Note: Results are presented either as the mean ± standard deviation (age and NIHSS score) or as n (%).

Abbreviations: CAD, coronary artery disease; PAD, peripheral artery disease; BMI, body mass index; NIHSS, National Institutes of Health Stroke Scale; NMC, neurological and medical complications.

first studies which focused on NMC after stroke reported frequencies up to 90%.^{6,20–22} More recently, the complication rate decreased, and it was estimated to be around 25%.^{2,23,24} One explanation could be the better care of patients in stroke units,²⁵ because improvement in outcome has been largely attributed to more effective prevention and treatment of NMC arising during stroke recovery. On the other hand, the heterogeneity of these results may be partly explained by the differences in study designs, criteria used for identifying complications, and also variations in identification and recording of complications. Chest infection is known to be one of the most frequent medical complications of stroke.^{4,21} Several investigations have studied demographic

data and conventional risk factors associated with the risk of pneumonia in patients with stroke, and reported age older than 65 years, impaired consciousness, speech impairment, dysphagia, cognitive impairment, and brainstem strokes to be associated with development of chest infections.^{26–28} Urinary tract infections are also a frequent occurrence in patients with acute stroke.^{21,23} Similarly, increased age and stroke severity are independent predictors of urinary tract infections.^{29,30} The association of pneumonia with baseline NIHSS has been reported previously,^{30,31} but no cutoff value was determined. Recently, Chumbler et al found that NIHSS score at admission, associated with several other clinical variables, can identify stroke patients at higher risk of pneumonia.³²

The NIHSS is increasingly being used as a measure of stroke severity among patients with ischemic stroke. However, previous studies have mainly included patients with anterior circulation infarction, with volumes of infarct lesions correlating well with NIHSS,³³ whereas lesion volumes do not correlate with NIHSS score in patients with posterior circulation infarction.³⁴ We found that NIHSS score was significantly associated with NMC in patients with posterior circulation infarction, albeit with a lower cutoff point than anterior circulation infarction. Despite posterior circulation infarction representing a heterogeneous group of strokes with various clinical presentations which cannot be captured as deficits on the NIHSS, our findings underscore the importance of using the NIHSS not only as a measure of stroke severity, but also as part of the assessment of risk of NMC. This may have some practical clinical implications to redirect preventive strategies in patients at risk because it can alert the physician to the anticipated risk of NMC in an individual patient. However, we also showed that patients with posterior circulation infarction (but not those with anterior circulation infarction) who had a baseline NIHSS score of 0 could experience NMC. Similar results have been reported by Sato et al to determine the cutoff baseline NIHSS score that predicts long-term outcome in anterior circulation versus posterior circulation ischemic strokes.³⁵ This finding indicates that NIHSS score alone cannot be used to rule out the risk of NMC in posterior circulation infarction patients and that the NIHSS does not substitute for further surveillance and diagnostics.

We also found that medical events were significantly more frequent in patients with large vessel atherosclerosis and significantly less frequent in patients with stroke of “undetermined” etiology. It is well known that stroke patients suffering from large vessel atherosclerosis have a higher risk of morbidity from other clinical manifestations

of atherosclerotic disease, such as myocardial infarction, angina, peripheral artery disease, and vascular death.^{36,37} Furthermore, the presence of large vessel atherosclerosis reflects inflammation, and there is evidence to suggest that systemic inflammation is predictive of poor outcome after stroke. For example, Whiteley et al showed that the C-reactive protein level was associated with both vascular and nonvascular deaths after stroke, independently of initial stroke severity.³⁸

This study has several potential limitations. First, baseline NIHSS scoring was not performed in the emergency department but in our stroke unit. This may have biased our results, because patients could deteriorate during transfer from the emergency department to the stroke unit, although patients with a history of an acute ischemic cerebral event more than 6 hours earlier were excluded from the study. Furthermore, our data were obtained from a single academic hospital setting and therefore may not be generalizable to other settings. Our results are also obtained from a retrospective analysis in a small sample size, and therefore prospective validation is required before NIHSS score can be considered as a predictor of NMC.

In conclusion, despite some methodological limitations, the present study shows that, in ischemic stroke patients, baseline NIHSS score is associated with an increased risk of NMC during hospitalization. This association between baseline NIHSS and NMC applies to anterior circulation as well as posterior circulation strokes, although NIHSS appears to have limitations in the latter, because zero on the NIHSS does not equal the absence of NMC. The clinical significance of these findings requires further evaluation in larger prospective studies.

Disclosure

The authors report no conflicts of interest in this work.

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