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A Proposal for the Classification of Etiologies of Neurologic Deterioration after Acute Ischemic Stroke

James E. Siegler, MD[*], **Amelia K. Boehme, MSPH**[†,‡], **Karen C. Albright, DO, MPH**[†,‡,§,‖], **Alexander J. George, BS**[*], **Dominique J. Monlezun, BA**[*], **T. Mark Beasley, PhD**[¶], and **Sheryl Martin-Schild, MD, PhD**[*]

[*]Stroke Program, Department of Neurology, Tulane University Hospital, New Orleans, Louisiana

[†]Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama

[‡]Department of Neurology, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama

[§]Health Services and Outcomes Research Center for Outcome and Effectiveness Research and Education, University of Alabama at Birmingham, Birmingham, Alabama

[‖]Center of Excellence in Comparative Effectiveness Research for Eliminating Disparities, Minority Health and Health Disparities Research Center, University of Alabama at Birmingham, Birmingham, Alabama

[¶]Section on Statistical Genetics, Department of Biostatistics, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama

Abstract

Background—Neurologic deterioration (ND) occurs in one third of patients with ischemic stroke and contributes to morbidity and mortality in these patients. Etiologies of ND and clinical outcome according to ND etiology are incompletely understood.

Methods—We conducted a retrospective investigation of all patients with ischemic stroke admitted to our center (July 2008 to December 2010), who were known to be last seen normal less than 48 hours before arrival. First-time episodes of ND during hospitalization were collected in which a patient experienced a 2-point increase or more in National Institutes of Health Stroke Scale score within a 24-hour period. Proposed etiologies of reversible ND include infectious, metabolic, hemodynamic, focal cerebral edema, fluctuation, sedation, and seizure, whereas new stroke, progressive stroke, intracerebral hemorrhage, and cardiopulmonary arrest were nonreversible.

Results—Of 366 included patients (median age 65 years, 41.4% women, 68.3% black), 128 (34.9%) experienced ND (median age 69 years, 42.2% women, 68.7% black). Probable etiologies of ND were identified in 90.6% of all first-time ND events. The most common etiology of ND, progressive stroke, was highly associated with poor outcome but not death. Etiologies most

Address correspondence to Sheryl Martin-Schild, MD, PhD, Stroke Program at Tulane University Hospital, Department of Neurology, 1440 Canal St, TB-52, Suite 1000, New Orleans, LA 70112-2715. smartin2@tulane.edu.

associated with mortality included edema (47.8%), new stroke (50%), and intracerebral hemorrhage (42.1%).

Conclusions—In the present study, the authors identified probable etiologies of ND after ischemic stroke. Delineating the cause of ND could play an important role in the management of the patient and help set expectations for prognosis after ND has occurred. Prospective studies are needed to validate these proposed definitions of ND.

Keywords

Acute ischemic stroke; neurologic deterioration; reversible; etiology; progressive stroke

Introduction

Neurologic deterioration (ND) is common after ischemic stroke, occurring in up to one third of all patients. Nearly half of the patients who experience ND will do so within the first 48 hours of the index stroke,[1–3] and this significantly contributes to morbidity and mortality.[2,4,5]

The distinction between and definitions for etiologies of ND have not yet been described. Certain structural changes may contribute to potentially nonreversible worsening neurologic status after stroke (eg, focal cerebral edema and hemorrhagic transformation); however, other systemic issues may introduce secondary structural damage or may transiently disrupt neurologic function (eg, infection and metabolic abnormalities). Primary (cerebral) causes of ND may only be amenable to reperfusion and recanalization, but the permanence of secondary (systemic) damage–producing ND is not clearly elucidated. Secondary neurologic damage may be mitigated by early recognition and intervention, as is potentially the case for infection with fever and leukocytosis during episodes of ND.[6]

In the present study, we propose standard definitions for ND etiology and analyze the clinical outcomes associated with specific ND etiologies. We expect that this information will aid neurologists in identifying the cause of ND in acute stroke and provide the patient and their families with more accurate prognostic information and provide uniform definitions for classifying ND in subsequent investigations.

Methods

Patient Population

We conducted a single-center retrospective analysis of all consecutive patients who presented with acute ischemic stroke between July 2008 and December 2010 using a prospective registry.[7] Patients were excluded if they experienced an in-hospital stroke, presented more than 48 hours after last seen normal, or had an unknown time of last seen normal because ND is more likely to occur earlier after the cerebrovascular event and is the target for neuroprotection.[8] ND was defined as the first episode in which a patient experienced an increase in the National Institutes of Health Stroke Scale (NIHSS) score of 2 or more points within a 24-hour period during hospitalization, as previously described.[4] Episodes of ND subsequent to these first-time events were not examined. Stroke etiology

was defined according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST)[9] and validated online using https://ccs.mgh.harvard.edu/ccs_title.php.

Etiologies of ND

We organized and defined etiologies of ND (Table 1) according to the clinical experience of our center and defined these terms before abstraction of data from patient records. As described in Table 1, the differences in temporal detection of certain etiologies of ND (eg, "within the 24-hour period surrounding documentation of ND" versus "24 hours before documentation of ND") deserve additional clarification. Laboratory value derangements (during a metabolic cause of ND), for instance, are not monitored continuously, and therefore, ND because of these abnormalities may not be diagnosed via laboratory measurements until after the clinical documentation of ND. In contrast, patients on telemetry are continuously monitored for arrhythmias, and therefore, changes in hemodynamic stability must occur before the documentation of ND for physicians at our center to determine that the episode of ND was hemodynamic in etiology. Although autonomic instability may occur after certain severe strokes,[10] ND because of hemodynamic changes must mean that these hemodynamic parameters change before the episode of ND.

Some terms describing ND etiologies and/or mechanisms have been mentioned in previous reports,[4,8,11,12] and some etiologies have been targeted with certain treatment modalities (eg, low–molecular-weight heparin for progressive stroke).[13] We further classified etiologies of ND according to reversibility, with nonreversible causes being those that may produce or extend any areas of ischemic neurologic injury because of temporary or permanent impairment in cerebral perfusion. All etiologies were considered reversible except new stroke, progressive stroke, intracerebral hemorrhage, and cardiopulmonary arrest. When comparing reversible versus nonreversible etiologies of ND, any patient with multiple etiologies of ND who experienced at least 1 nonreversible cause of ND was categorized as having experienced nonreversible ND; all remaining patients were categorized as having experienced reversible ND. Only first-time episodes of ND were considered for this investigation. Patients may have had more than 1 etiology of ND documented for each first-time episode of ND if no single etiology could be determined as the driving cause of ND.

Etiology of ND was related to several outcome measures including persistent deterioration (discharge NIHSS > baseline NIHSS), discharge modified Rankin Scale (mRS)[14]—which serves as a marker of long-term functional disability[15]—poor functional outcome (discharge mRS score > 3), discharge NIHSS, length of stay, discharge disposition, and in-hospital mortality.

Statistics

Categorical data were presented as frequencies and compared using Pearson chi-square or Fisher exact test where appropriate. Continuous data were presented as mean (±standard deviation) or median (with range) and compared using independent-sample Student *t* test or Wilcoxon rank sum test where appropriate. Crude and adjusted logistic regression models were used to further assess associations. This study was approved by our center's Institutional Review Board.

Results

Of 596 patients screened, 366 met inclusion criteria (median age 65 years, 41.4% women, 68.3% black). One hundred twenty-eight (34.9%) experienced at least 1 episode of ND (median age 69 years, 42.2% women, 68.7% black). Demographic information comparing patients with and without ND are displayed in Table 2.

Stroke Etiology Is Related to ND Etiology

See Table 3 for breakdown of ND etiology according to stroke etiology. The percentage of ND was the highest in cardioembolic, large-vessel, and small-vessel infarctions. ND because of edema was more commonly observed among patients with cardioembolic (21.4%) and large-vessel (17.9%) strokes. ND because of infection was also most frequently observed in patients with cardioembolic disease (16.7%). A greater proportion of patients with a stroke of more than 1 etiology who experienced ND ultimately deteriorated because of nonreversible causes (76.9%) and in particular progressive stroke (46.2%). The remaining etiologies of ND were not as consistently related to stroke etiology.

Clinical Outcomes According to the Etiology of ND

Probable etiologies of ND were identified in 90.6% of all first-time ND events. Nonreversible causes of ND were identified in 52% of patients with ND. Among all cases of ND, the most commonly encountered etiology of ND was progressive stroke (28.7% of all first-time episodes of ND). It was the single most common cause of ND among patients regardless of TOAST classification and accounted for nearly half of all causes of ND among patients with small-vessel strokes and strokes of more than 1 cause (Table 3).

Among etiologies of ND, the etiologies most frequently associated with mortality included new stroke (50% expired), edema (47.8% expired), and intracerebral hemorrhage (42.1% expired) (Table 4). Among the 12 patients with ND because of cerebral edema who survived, all patients were discharged with poor functional outcome (discharge mRS score > 3, 100%). Furthermore, 78.3% of patients with ND because of edema never returned to their prior NIHSS during hospitalization.

ND because of fluctuation, progressive stroke, and sedation had the lowest percentages of fatality of the different types of ND (in-hospital mortality percentages of 14.3%, 14.3%, and 0%, respectively). However, progressive stroke was highly associated with poor functional outcome (73.5%). Patients with nonreversible etiologies of ND were not at significantly greater odds of persistent deterioration (odds ratio [OR] = 1.79, 95% confidence interval [CI]: .81–3.96, P = .1487), poor functional outcome (OR = 1.84, 95% CI: .77–4.42, P = .1717), or in-hospital mortality (OR = 1.02, 95% CI: .38–2.74, P = .9673) when compared with patients who deteriorated because of a reversible etiology. Length of stay was the longest for patients with reversible ND (median stay 11 days) and the shortest for patients with unknown causes of ND (7 days); however, these differences did not reach statistical significance (P =.0905).

Of the 29 patients with ND who expired, 10 (34.5%) were converted to “comfort measures only” before death. Four of these 10 patients experienced a nonreversible cause of ND

during a first-time ND event, 2 patients experienced a nonreversible cause of ND during subsequent ND events, and the last 4 patients only experienced reversible causes of ND (3 cases with edema and 1 with ND because of infection). Among these 10 patients who received comfort measures, 3 received comfort care before the first episode of ND (2 cases with intracranial hemorrhage and 1 with cardiopulmonary arrest), whereas the remaining 7 received comfort care after the initial ND event. When evaluating the differences in the length of stay between patients who received comfort care, the median stay was greatest for patients with reversible ND (8 days) and shortest for nonreversible ND (4 days) and remained nonsignificant (P =.2933).

Discussion

In the present study, we have identified likely causes of first-time ND following acute ischemic stroke in more than 90% of all cases. The most common etiology of ND was progressive stroke, occurring 38.3% of the time and among 13.4% of the total population of ischemic stroke patients studied. ND because of edema was the most frequently observed in cardioembolic strokes (40.9% of all cases of edema). However, there were no other clinically significant relationships between stroke etiology and etiology of ND.

Any worsening in the NIHSS is more highly associated with in-hospital mortality than a stable or improving NIHSS[4]; however, one third of patients with in-hospital death after ND in our sample ultimately received comfort care measures before expiration. Only 3 of the 29 patients who experienced ND and expired received comfort care prior the ND. Still, this leaves a large number of patients who ultimately expired during their stay despite receiving continuous standard of care measures. In our population, patients who deteriorate from extrinsic mechanisms have worse outcome than those who do not worsen, suggesting that at least early outcomes are compromised when this occurs.

Certain causes of ND were more highly associated with poor functional outcome and in-hospital mortality. For instance, ND because of hemorrhage or edema was highly related to poor functional outcome and mortality as compared with the remaining etiologies of ND. All patients with documented cerebral edema on brain imaging with a worsening in the NIHSS of 2 or more points were discharged with significant disability. As demonstrated in prior investigations,[16,17] ischemic strokes producing focal cerebral edema often involve the greatest volume and produce more severe neurologic deficits than cortical strokes involving a smaller cerebral distribution. Therefore, it was expected that ND because of cerebral edema would be strongly associated with poor outcome and death after stroke. Hemodynamic causes of ND (eg, fluctuating blood pressure or alterations in cardiac output) were associated with significant disability. Although we cannot prove this because of the limitations of our methods, this finding may reflect autonomic nervous system dysfunction secondary to severe stroke[10,18] that may persist up to 6 months after the cerebrovascular insult[19] and is associated with worse functional outcome.[20] ND because of infection resulted in more than 80% of these patients having a discharge mRS score more than 3, with a substantial risk of in-hospital mortality compared with other etiologies, as in prior studies.[21] As we have described previously,[6] regardless of the presence of infection, inflammatory

processes producing leukocytosis during ND significantly affect the severity of deterioration.

All outcomes were worse among patients with ND, regardless of the etiology being reversible (no impairment in cerebral perfusion) or nonreversible (temporary or permanent impairment in cerebral perfusion). Because we found no difference in outcomes based on the reversibility of the cause of ND among patients with ND, there are important adverse consequences of experiencing reversible causes, and these causes can be prevented.

Several ND etiologies including fluctuation, sedation, and progressive stroke were not as frequently associated with poor outcomes in contrast with other etiologies of ND. Although progressive stroke was identified as the most common etiology of ND, it was associated with a lower percentage of in-hospital mortality compared with other etiologies (14.3% for ND because of progressive stroke versus 22.8% for all causes of ND). The lower percentage of mortality because of progressive stroke may be due to the less severe nature of the disease (compared with other etiologies like infection that may result in multiorgan dysfunction) or may indicate that it is a more treatable cause of deterioration. As our study is retrospective, we are unable to determine if more aggressive or expeditious management of progressive stroke may offset mortality.

Our study was limited by its small size and the experience at a single center. The small size was especially prohibitive from comparing singular etiologies of ND with respect to clinical outcome measures, which should be investigated in larger trials. Our smaller-than-expected proportion of patients with cryptogenic stroke (20% according to a recent study),[22] despite using a validated online tool for stroke etiology determination (https://ccs.mgh.harvard.edu/ccs_title.php), may be related to our comprehensive strategy for evaluation. Although definitions of ND etiologies were created before the data abstraction process (to reduce the potential for abstractor bias), some etiologies of ND were not experienced during first-time ND episodes. For instance, a small proportion of patients in our population ultimately experienced cardiopulmonary arrest; however, the arrest occurred after the documentation of the first episode of ND. This would preclude these patients from being categorized as having experienced cardiopulmonary arrest (and therefore nonreversible ND) for this particular analysis of first-time ND episodes. Additionally, we did not separate or exclude extrinsic (non-neurological) from intrinsic (primary neurological) pathophysiologic etiologies for ND in our analysis. We included all extrinsic and intrinsic mechanisms together in this proposal because regardless of the mechanism, each still produced a clinical worsening in neurologic symptoms (be it temporary or permanent). Furthermore, we aimed to describe how frequent each mechanism, intrinsic or extrinsic, was observed in our cohort to establish expectations for frequency of each of these mechanisms.

When dichotomizing ND etiologies by reversibility, we found no relationship between any stroke etiology and reversible or nonreversible ND. Among specific etiologies of ND, our results support an earlier observation[23] that clinical deterioration in small-vessel occlusions are because of the extension of the initial infarction (which we have termed, “progressive stroke”). Nearly half of our patients with small-vessel occlusions who deteriorated were found to have progressive stroke on the workup of ND.

In our investigation, we have suggested that ND may originate from a single underlying etiology (eg, infectious process, hemodynamic alterations, metabolic abnormalities), whereas other investigators argue that ND is likely a multifactorial process involving a sophisticated interplay of hemodynamic, metabolic, and cellular pathophysiologic mechanisms which may be the case for ND due to progressive stroke.[24] Furthermore, we have observed a relationship between certain etiologies of ND and specific stroke subtypes (eg, cerebral edema after cardioembolic occlusions or progressive stroke after small-vessel occlusions). Foresight into which mechanisms of ND are more related to certain stroke etiologies may aid clinicians in predicting the most likely culprits of clinical worsening. This may also assist in determining the most cost-effective workup of a stroke patient who deteriorates. For example, because focal cerebral edema and intracerebral hemorrhage comprise more than half of all causes of ND in patients with a stroke caused by more than 1 etiology according to the TOAST classification system, brain imaging may be the most appropriate initial method to evaluate these patients during an episode of deterioration. Future investigations are needed to validate the aforementioned definitions of ND etiologies to standardize definitions for use in multicenter trials and ultimately optimize a workup for patients with stroke who clinically deteriorate.

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Table 1

Proposed definitions of ND etiologies

Etiology of ND	Definition
Reversible	
Infectious	When in the presence of a diagnosed infection (eg, of the urinary or respiratory tracts, cerebral ventricles or meninges, skin or soft tissue, blood vessels or heart valves)* with identified pathogen on microbiology or consolidation on chest imaging with clinical symptoms, in the case of pneumonia
Metabolic	When in the presence of a new clinically relevant derangement in laboratory value based on our laboratory standards (eg, uremia, hyper/hypocalcemia, hyper/hypoglycemia, hyper/hyponatremia, or hyperammonemia) during the 24-h window surrounding the documentation of ND
Hemodynamic	When in the presence of a significant rise or drop in blood pressure during the 24 h before documentation of ND as determined clinically, new-onset arrhythmia as determined via electrocardiography or telemetry, or cardiovascular event (including myocardial infarction) as determined via electrocardiographic, telemetric, and/or laboratory methods (for instance, elevated serum troponin I level†) that may have impaired cerebral perfusion but did not cause a new imaging-confirmed stroke
Edema	When focal cerebral or cerebellar mass effect was identified on follow-up computed tomographic or magnetic resonance imaging in the 24-h window surrounding the date of ND
Fluctuation	When the patient returned to prior (day before ND) NIHSS score on the day after the episode of ND in the absence of other identified causes of ND
Sedation	When the patient was given any medication with sedative effects, as determined by the attending physician's clinical experience, in the 24 h before documentation of ND and when no other cause of ND was identified
Seizure	When in the presence of electroencephalogram-confirmed epileptiform activity or periodic rhythm or clinical observation of seizure-like activity during the 24-h window surrounding the documentation of ND
Nonreversible	
New stroke	New ischemic findings on CT or MRI (detected within the 24-h window surrounding the documentation of ND) outside the distribution of the initial vessel occlusion after new deficits on physical examination
Progressive stroke	When extension of ischemic findings were detected on computed tomographic or magnetic resonance imaging by the attending physician or staff radiologist within the distribution of the initial vessel occlusion (during the 24-h window surrounding the documentation of ND)
Intracerebral hemorrhage	When new or progressive hemorrhage of PH1 or PH2 grade was identified on 24-h follow-up imaging study
Cardiopulmonary arrest	When documented by progress notes as having occurred within the 24-h window surrounding the documentation of ND
Unknown etiology	When no etiology of ND was determined by the attending physician, and none of the above findings were documented in the progress notes

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; ND, neurologic deterioration; NIHSS, National Institutes of Health Stroke Scale.

*Bacteremia was defined as the growth of a bacterium on a culture from a venous blood sample (excluding common contaminants). Urinary tract infection was defined as > 10,000 colony-forming units per millimeter of urine in a clean-catch specimen (excluding contaminants) or suggestive findings on urinalysis. Pneumonia was defined as an infiltrate on chest radiography with appropriate clinical correlates. Other infection types (eg, cellulitis, pseudomembranous colitis, meningitis, ventriculitis) were diagnosed clinically or via laboratory/imaging findings. Clinical symptoms producing ND may have occurred hours or days before the diagnosis of ND because of infection, depending on the manner in which the infection was diagnosed. For example, pneumonia diagnosed via chest radiography in the presence of clinical symptoms may only take 1 h for the imaging order to be processed, performed, and interpreted, whereas confirmation of bacterial specimen in blood culture may have taken up to 5 days according to our laboratory standards.

†Elevated serum troponin I is defined as troponin I level > .015 mg/dL, according to our laboratory standards.

Table 2

Demographic and outcome data for all included patients

	No ND (N = 238)	ND (N = 128)	*P* value
Gender, female, n (%)	100 (42.0)	54 (42.2)	.9748
Age, y, median (range)	62 (19–97)	69 (28–96)	<.0001
Race, n (%)			.4478
Black	151 (63.9)	88 (68.7)	
White	73 (30.9)	38 (29.7)	
Medical history, n (%)			
Stroke	92 (38.7)	55 (42.9)	.4221
CAD	39 (16.4)	33 (25.9)	.0282
Dyslipidemia	107 (45.5)	51 (40.8)	.3891
Hypertension	179 (75.5)	99 (79.2)	.4313
Diabetes	74 (31.2)	46 (36.5)	.3083
Atrial fibrillation	22 (9.4)	16 (12.8)	.3121
Systolic heart failure	19 (8.1)	14 (11.1)	.3352
Home medications, n (%)			
Antiplatelet agent	89 (37.9)	63 (49.2)	.0363
Lipid-lowering agent	94 (39.8)	54 (43.5)	.4957
Antihypertensive agent	40 (16.9)	49 (38.6)	<.0001
Oral diabetes medication	49 (20.7)	28 (22.6)	.6747
Active smoker, n (%)	74 (31.5)	29 (23.6)	.1163
SBP, mm Hg, median (range)	158 (82–280)	163 (89–260)	.1308
DBP, mm Hg, median (range)	92 (46–180)	93 (52–179)	.3614
Admission NIHSS, median (range)	5 (0–34)	12 (0–29)	<.0001
Admission glucose, mg/dL, median (range)	114 (72–569)	126 (76–663)	.0036
Treatment, n (%)			
IV tPA	78 (32.8)	49 (38.3)	.2911
IAT	6 (2.5)	8 (6.2)	.0761
HDL, mg/dL, median (range)	42 (19–100)	45 (11–100)	.1876
LDL, mg/dL, median (range)	105 (17–540)	103 (29–540)	.3318
HbA1c, %, median (range)	5.8 (4.5–13.7)	6.1 (4.6–12.7)	.0104
24-h NIHSS, median (range)	2 (0–32)	12 (0–42)	<.0001
TOAST, n (%)			.1038
Cardioembolic	61 (25.6)	42 (32.8)	
Large vessel	55 (23.1)	37 (28.9)	
Small vessel	48 (20.2)	27 (21.1)	
Cryptogenic (no cause)	7 (2.9)	2 (10.6)	
Cryptogenic (>1 cause)	57 (23.9)	13 (10.2)	
Other	10 (4.2)	7 (5.5)	
Any HT, n (%)	21 (13.3)	39 (35.8)	<.0001
sICH, n (%)	0	10 (8.7)	<.0001

	No ND (N = 238)	ND (N = 128)	*P* value
Discharge NIHSS, median (range)	1 (0–42)	11 (0–42)	<.0001
Length of stay, d, median (range)	4 (1–43)	9 (1–52)	<.0001
Discharge mRS, median (range)	2 (0–6)	4 (0–6)	<.0001
Discharge disposition, n (%)			<.0001
Home	147 (62.5)	23 (18.1)	
Inpatient rehabilitation	66 (28.1)	52 (40.9)	
Skilled nursing facility	9 (3.8)	13 (10.2)	
Long-term acute care facility	4 (1.7)	4 (3.1)	
Hospice	6 (2.5)	6 (4.7)	
Expired	0	30 (23.4)	
Other	2 (.9)	0	

Abbreviations: CAD, coronary artery disease; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; HT, hemorrhagic transformation; IAT, intra-arterial thrombolysis; IV tPA, intravenous tissue plasminogen activator; LDL, low-density lipoprotein; mRS, modified Rankin Scale; ND, neurologic deterioration; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; sICH, symptomatic intracranial hemorrhage (parenchymal hematoma grade 2 with accompanying increase in NIHSS score of 4 or more points within 36 h or death); TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Table 3

Etiology of ND with respect to stroke etiology

	Cardioembolic (N = 42)	Large vessel (N = 39)	Small vessel (N = 24)	Cryptogenic (no cause) (N = 2)	Cryptogenic (>1 cause) (N = 13)	Other (N = 8)
Patients with any ND (%)*	42/103 (40.8)	39/94 (41.5)	24/73 (32.9)	2/9 (22.2)	13/70 (18.6)	8/18 (44.4)
Reversible ND	16	15	7	1	2	4
Infectious	7	4	2	0	2	1
Metabolic	1	0	1	0	0	0
Hemodynamic	5	0	4	1	0	0
Edema	9	7	0	0	4	3
Fluctuation	3	5	3	0	1	2
Sedation	2	2	1	0	0	0
Seizure	0	1	0	0	0	0
Nonreversible ND	20	19	14	1	10	3
New stroke	1	1	0	0	0	0
Progressive stroke	14	15	13	0	6	1
Intracerebral hemorrhage	6	5	1	1	4	2
Cardiopulmonary arrest	0	0	0	0	0	0
Unknown etiology	6	5	3	0	1	1

Abbreviation: ND, neurologic deterioration.

Several patients deteriorated by >1 etiology. Patients with >1 etiology of ND who experienced a nonreversible cause of ND were classified as having nonreversible ND and not categorized as having a reversible ND in the analysis comparing reversible versus nonreversible ND.

*Percentages described are reported as the number of patients having a certain stroke etiology who experienced ND divided by the total number of patients with the respectful stroke etiology.

Table 4

Outcomes according to etiology of ND

Etiology of ND	N*	Length of stay, d, median (range)	No. of patients with persistent deterioration† (%)	No. of patients with poor functional outcome‡ (%)	No. of patients who expired during stay (%)
Reversible	45	11 (2–44)	21 (50.0)	31 (68.9)	11 (24.4)
Infectious	16	12 (4–44)	7 (46.7)	13 (81.2)	5 (31.3)
Metabolic	2	14 (11–16)	0	2 (100.0)	0
Hemodynamic	10	13 (2–21)	3 (33.3)	5 (50.0)	2 (20.0)
Edema	23	10 (2–45)	18 (78.3)	23 (100.0)	11 (47.8)
Fluctuation	14	8 (3–28)	5 (35.7)	6 (42.9)	2 (14.3)
Sedation	5	14 (7–28)	1 (25.0)	3 (60.0)	0
Seizure	1	39	1 (100.0)	1 (100.0)	0
Nonreversible	67	9 (1–52)	42 (63.6)	53 (79.1)	15 (22.4)
New stroke	2	37 (21–52)	2 (100.0)	2 (100.0)	1 (50.0)
Progressive stroke	49	9 (2–45)	30 (61.2)	46 (73.5)	7 (14.3)
Intracerebral hemorrhage	19	10 (2–31)	11 (61.1)	17 (89.5)	8 (42.1)
Cardiopulmonary arrest	0	n/a	n/a	n/a	n/a
Unknown etiology	16	7 (1–33)	8 (50.0)	10 (62.5)	3 (18.7)
P value§		.0905	.3095	.2149	.8940

Abbreviations: n/a, not applicable; ND, neurologic deterioration; NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile range.

Several patients deteriorated by >1 etiology.

*N represents the total number of patients who experienced each respective etiology of ND. However, when comparing patient groups in this table (patients with reversible ND against patients with nonreversible ND), patients were dichotomized as stated in the "Methods" section. Patients with both a reversible and nonreversible ND etiology were categorized only as having nonreversible ND. Therefore, several patients with reversible ND were not categorized as having reversible ND for these comparisons.

†Persistent deterioration was defined as discharge NIHSS score > admission NIHSS score.

‡Poor functional outcome was defined as discharge modified Rankin Scale score > 3 points.

§Compares reversible versus nonreversible etiologies of ND. Patients were dichotomized for this comparison as described in the "Methods" section.