New-Onset Constipation at Acute Stage After First Stroke: Incidence, Risk Factors, and Impact on the Stroke Outcome

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Background and Purpose—The prevalence of constipation after stroke varies from 30% to 60%. The incidence of new-onset constipation during the early stage of stroke remains uncertain. The present study was designed to investigate the prevalence of new-onset constipation, its risk factors, and its impact on stroke outcome in patients with their first stroke at acute stage.

Methods—This is a prospective cohort study of 154 patients admitted with their first stroke. New-onset constipation during the first 4 weeks of stroke was recorded, using the Rome II criteria for constipation. Demographics, characteristics of the stroke, laboratory parameters, and use of medications were evaluated as risk factors for constipation. Death, recurrent stroke, and handicap at 12 weeks were regarded as poor outcome. The impact of constipation on poor outcome was also studied.

Results—The cumulative incidence of new-onset constipation was 55.2% at 4 weeks poststroke. The occurrence of constipation was associated with dependence ($P<0.01$) and use of bedpan for defecation ($P<0.05$). Among patients with moderate stroke severity (NIHSS 4 to 11) at baseline, constipation at 4 weeks was associated with a poor outcome at 12 weeks.

Conclusions—New-onset constipation is a common complication of acute stroke. Its occurrence is associated with dependence and use of bedpan for defecation. Its development may predict a poor outcome at 12 weeks in patients with moderately severe stroke.

Key Words: stroke • constipation • incidence • risk factors • outcome

Constipation occurs frequently in the elderly with a prevalence as high as 28%.1–2 Its prevalence among stroke patients is even higher, ranging from 30% to 60%.3–5 Such large difference in the results can be attributed to the adoption of different time points,3,4,6,7 use of different diagnostic criteria for constipation,4,7 and the enrollment of patients with different characteristics.4,5 Most studies included preexisting constipation before stroke and so the incidence of new-onset constipation at an acute stage of stroke remains uncertain. In the present study, we adopted the symptom-based Rome II criteria8 to exclude preexisting constipation before stroke and diagnose new-onset constipation at acute stage after stroke because this is widely used in research and clinical practice, retrospectively and prospectively.9–13

Constipation among stroke patients is related to multiple factors. A prospective study by Robain and colleagues4 reported that constipation of stroke patients in rehabilitation center was strongly related to Barthel Index (BI) with a lower rate of constipation among those with a higher BI score. Other possible risk factors for constipation among stroke patients include old age, use of a number of different drugs, dehydration, and physical inactivity.7 On the other hand, constipation has a negative impact on the patient’s quality of life and would restrict their social activities.14,15 However, the risk factors for new-onset constipation and its impacts on outcome in acute stroke patients remain unclear.

The purpose of the present study was to determine the incidence of new-onset constipation among patients at 4 weeks after their first strokes, its risk factors, and association with the stroke outcome at 12 weeks after stroke.

Materials and Methods
The study protocol was approved by the local ethical committee for clinical research and all procedures involving the participant were conducted according to institutional guidelines in compliance with

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the regulations. Both oral and written informed consents were obtained from all participants.

This prospective observational study was designed to follow up stroke patients at the department of neurology and stroke center in a university hospital. A sample size of 150 would provide a power of 80% to detect a prevalence of 40% with a precision of 0.08. \( \chi^2 \) was used to test for the prevalence of new-onset constipation. Nonparametric variables were expressed as median and quartile range and analyzed using the Mann–Whitney U test. Discrete and nonparametric variables were analyzed with the \( \chi^2 \) test, or Fisher exact test. Univariate analysis was performed to identify the predictors for the new-onset constipation after stroke by odds-ratio (OR) calculation and 95% confidence intervals (95% CI). Survival analysis and life-table were used to determine the incidence of new-onset constipation and the timing of the occurrence, respectively. Cox proportional hazards analysis was performed to calculate the net risk of new-onset constipation after adjusting for selected risk factors using backward selection method. A probability value under 0.05 was considered statistically significant.

### Subjects

On admission, stroke patients were screened for eligibility over a 12-month period between November 1, 2003 and October 31, 2004. The inclusion criteria were (1) age 18 years old; (2) first attack of stroke; and (3) admission within 7 days of stroke onset. Stroke was defined according to the World Health Organization criteria and confirmed by CT scan or MR image. Subarachnoid hemorrhage was excluded. Other exclusion criteria were (1) a previous history of stroke; (2) admission beyond 7 days of stroke onset; (3) death within 7 days of stroke onset; (4) history of severe liver or kidney diseases, and malignant tumor; (5) history of structural diseases in the rectum or colon; (6) a prior history of constipation; and (7) disturbance of consciousness or other deficits affecting the investigation.

### Diagnosis of New-Onset Constipation After First Stroke

To assess the preexisting constipation, the items of Rome II criteria: (1) Straining in >1/4 defecations; (2) Lumpy or hard stools in >1/4 defecations; (3) Sensation of incomplete evacuation in >1/4 defecations; (4) Sensation of anorectal obstruction/blockade in >1/4 defecations; (5) Manual maneuvers to facilitate >1/4 defecations (eg, digital evacuation, support of the pelvic floor); and (6) <3 defecations/wk were used. Loose stools are absent, and a diagnosis of irritable bowel syndrome cannot be established. In the present study, patients were considered as having a positive history of constipation if she/he fulfilled 2 or more of the diagnostic criteria during a 2-month period before the stroke. Using the Rome II criteria, every consecutive 7-day stool diary for the patients without a positive history of constipation was assessed from stroke onset for 4 weeks. If the patient fulfilled 2 or more of the diagnostic criteria, new-onset constipation was diagnosed.

### Risk Factors Definition

The following information was extracted through chart review: age (<65 years, ≥65 years), sex, information on defecation (eg, using bedpan instead of going to toilet), and types of stroke (ie, ischemic or hemorrhagic stroke).

Stroke severity, in terms of neurological deficits, was assessed by the National Institutes of Health Stroke Scale (NIHSS). This scale was administered on admission and at 1, 2, and 4 weeks after stroke.

Disability was evaluated using the Barthel index (BI). The assessment was conducted via interview and observation on admission and at 1, 2, and 4 weeks after stroke.

Laboratory parameters including electrolyte, osmotic pressure (OP), peripheral white blood cells (WBC), erythrocyte sedimentation rate (ESR), and hypersensitive C reactive protein (hs-CRP) at first week after stroke were collected.

Use of medications, which may affect gastrointestinal functions, during the first 2 weeks of stroke were recorded. Such medications include analgesic, osmotic diuretic (eg, mannitol), diuretic (eg, frusemide), antidepressant, anticoagulant, antihistamine, and antacid.

Complications including new-onset poststroke depression and dysphagia were assessed after stroke. Depression was diagnosed at 1st and 2nd weeks after stroke with the diagnostic and statistical manual of mental disorders (DSM-IV) and dysphagia was diagnosed at admission with the clinical swallow assessment designed by Leslie et al. A nasogastric tube was set up for feeding in the patient with dysphagia.

Habitual use of substances was assessed via personal interview. Tobacco use (Yes or No) was classified into current or previous smoking for more than five cigarettes a day. Consumption of spicy food (Yes or No) was checked against the habit of eating hot pepper on a daily basis.

### Stroke Outcome

Poor stroke outcomes included vascular death and handicap.

Death, which occurred within 12 weeks after stroke and were related to the index stroke, myocardial infarction, other cardiac diseases, or sudden death, were regarded as vascular death. Handicap was assessed by the modified Rankin scale (mRS). This observational scale provides a clinical handicap score reflecting interference with lifestyle and with independent living. It is a frequently used outcome measure in stroke research and should be viewed as a global functional health index with a strong emphasis on physical disability. In this study, we dichotomized the mRS scores into functionally independent (0, 1, or 2) and dependent (3, 4, or 5) scores. Patients classified as dependent were considered as handicapped at 12 weeks.

Stroke recurrence was defined as for the index stroke with an additional criterion: either a new neurological deficit or worsening of the previous deficit not attributable to cerebral edema, hemorrhagic transformation, or an intercurrent illness. Only recurrences 7 days after the index stroke or, if earlier, clearly in another part of the brain were included.

### Statistical Analysis

Data were analyzed using SPSS 13.0 (Abacus Concepts Inc.). Nonparametric variables were expressed as median and quartile range and analyzed using the Mann–Whitney U test. Discrete variables were analyzed with the \( \chi^2 \) test, or Fisher exact test. Univariate analysis was performed to identify the predictors for the new-onset constipation after stroke by odds-ratio (OR) calculation and 95% confidence intervals (95% CI). Survival analysis and life-table were used to determine the incidence of new-onset constipation and the timing of the occurrence, respectively. Cox proportional hazards analysis was performed to calculate the net risk of new-onset constipation after adjusting for selected risk factors using backward selection method. A probability value under 0.05 was considered statistically significant.

### Results

During the study period, 648 stroke patients were admitted to the department of neurology and stroke center of the hospital. Of all stroke patients, 160 met the inclusion criteria on admission. Six patients were excluded because of death within 7 days (2 cases) or lost to follow-up (4 cases). We studied 154 stroke patients with median for admission times was 2 (1, 4) days and the median length of stay was 22 (15, 29) days including the stay in department of neurology and department of rehabilitation; their mean age was 65.61±14.53 (range: 17 to 94 years). The majority of them were males (60.4%). There were 122 (79.2%) ischemic strokes and 32 intracerebral hemorrhages (20.8%). The demographic variables and medical information are presented in Table 1.

### Incidence and Risk Factors of New-Onset Constipation

Eighty-five patients (55.2%) developed new-onset constipation within 4 weeks after first stroke (Figure 1). The first 3 cases developed constipation on the third poststroke day. The cumulative incidence increased steeply from the 4th day to
the 9th day. Development of new-onset constipation became uncommon after the 10th day, and no case was observed after the 20th day. The length of stay was longer for constipated patients (24 [18.5, 32.5] days) than for nonconstipated ones (17 [13.0, 27.0] days; \(z = 3.374, P = 0.001\)). The patients stayed longer than 2 weeks had higher rate of constipation than those stayed less than 2 weeks (63.0% versus 28.6%, \(z = 12.98, P < 0.001\)).

Figure 2 shows the hazard of new-onset constipation after first stroke. The highest hazard (13.8%) was observed at the 6th day. The hazard began to decline after the 7th day. On the 14th day, the hazard decreased to 1.4%, and it was 0 on or after 21st day.

Table 1 shows the demographic and clinical factors in patients with and without constipation during the study period. The prevalence of new-onset constipation was significantly higher in the patients with a low BI (\(P < 0.001\)) and a high NIHSS score (\(P < 0.001\)) in the first week. The rates of paralysis (\(P < 0.01\)), use of Analgesic (\(P < 0.05\)), osmotic diuretics (\(P < 0.01\)), other diuretics (\(P < 0.01\)), dysphagia

table: Table 1. Univariate Analysis on the Association Between New-Onset Constipation and Demographics, Information on Stroke, or Other Clinical Parameters

<table>
<thead>
<tr>
<th>Variable Category</th>
<th>Constipation Present in 85 Patients, n (%) or Median and Quartile Range</th>
<th>Constipation Absent in 69 Patients, n (%) or Median and Quartile Range</th>
<th>Odds Ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Demographics</td>
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<tr>
<td>Age, y</td>
<td>&lt;65 35 (41.2) 33 (47.8) 0.76 (0.40–1.45)</td>
<td>≥65 50 (58.8) 36 (52.2)</td>
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<td>Gender</td>
<td>Female 28 (32.9) 33 (47.8) 0.54 (0.28–1.03)</td>
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<td>Information on stroke</td>
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<tr>
<td>Stroke type</td>
<td>Ischemic stroke 63 (74.1) 59 (85.5) 0.49 (0.21–1.11)</td>
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<tr>
<td>Stroke severity</td>
<td>NIHSS (1 week) 9 (3.5, 14)** 4 (2, 6)</td>
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<td>BI (1 week) 40 (20, 55)** 65 (55,80)</td>
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<td>Risk factors</td>
<td>Hypertension 62 (72.9) 47 (68.1) 1.26 (0.63–2.53)</td>
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<td>Diabetes mellitus 15 (17.6) 14 (20.3) 0.84 (0.38–1.89)</td>
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<td>Atrial fibrillation 4 (4.7) 4 (5.8) 0.80 (0.19–3.33)</td>
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<td></td>
<td>Preceding TIA 1 (1.2) 2 (2.9) 0.40 (0.04–4.49)</td>
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<td></td>
<td>Smoking 33 (38.8) 23 (33.3) 1.27 (0.65–2.47)</td>
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<td>Alcohol abuse 19 (22.4) 14 (20.3) 1.13 (0.52–2.46)</td>
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<td>Medications</td>
<td>Analgesic 40 (47.1)* 21 (30.4) 2.03 (1.04–3.96)</td>
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<td>Antidepressant 13 (15.3) 7 (10.1) 1.60 (0.60–4.26)</td>
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<td>Anticonvulsants 39 (45.9) 31 (44.9) 1.04 (0.55–1.97)</td>
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<td>Antihistaminic 9 (10.6) 6 (8.7) 1.24 (0.42–3.68)</td>
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<td>Osmotic diuretics 34 (40.0)** 14 (20.3) 2.62 (1.26–5.43)</td>
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<td>Other diuretics 36 (42.4)** 9 (13.0) 4.90 (2.15–11.15)</td>
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<td>Antacid 26 (30.6) 17 (24.6) 1.35 (0.66–2.76)</td>
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<td>Anticholinergics 3 (3.5) 2 (2.9) 1.23 (0.20–7.55)</td>
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<td>Stroke complications</td>
<td>Poststroke depression (2 weeks) 15 (17.6) 8 (11.6) 1.67 (0.65–4.12)</td>
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<td>Dysphagia 18 (21.2)* 6 (8.7) 2.82 (1.05–7.56)</td>
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<td>Paralysis 58 (68.2)** 23 (33.3) 4.30 (2.18–8.46)</td>
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<td>Time changed for defecation 83 (97.6) 63 (91.3) 3.95 (0.77–20.24)</td>
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<td>Posture changed for defecation 71 (83.5) 50 (72.5) 1.93 (0.88–4.20)</td>
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<td>Bedpan usage for defecation 64 (75.3)** 21 (30.4) 6.97 (3.42–14.19)</td>
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<td>Laboratory data</td>
<td>Electrolyte disturbance At admission 33 (38.8) 28 (40.6) 0.93 (0.49–1.78)</td>
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<td>Within 2 weeks 38 (44.7) 32 (46.4) 0.94 (0.49–1.77)</td>
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<td>Elevated OP 43 (50.6) 41 (59.4) 0.70 (0.37–1.33)</td>
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<td>Infection parameters Elevated WBC 17 (20.2) 12 (17.4) 1.19 (0.52–2.69)</td>
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<td>Elevated ESR 26 (30.6) 15 (21.7) 1.59 (0.76–3.31)</td>
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<td>Elevated hs-CRP 9 (10.6) 2 (2.9) 3.97 (0.83–19.01)</td>
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Compared to patients without constipation; *\(P < 0.05\), **\(P < 0.01\).

NIHSS indicates National Institutes of Health Stroke Scale; BI, Barthel Index; OP, osmotic pressure; WBC, peripheral white blood cells; ESR, erythrocyte sedimentation rate; hs-CRP, hypersensitive C reactive protein; n, No. of patients.
The highest hazard is at 6th day and then it begins to descend after 7th day. After 21 days the hazard is 0.

Figure 2. Hazard function of new-onset constipation after first stroke. The highest hazard is at 6th day and then it begins to descend after 7th day. After 21 days the hazard is 0. X-axis, follow-up days; Y-axis, hazard rate.

Table 2 shows the association between new-onset constipation and poor stroke outcome at 12th weeks with patients stratified according to the stroke severity using the NIHSS score at 1 week: mild (0 to 3), moderate (4 to 11), and severe (12 to 29). Among patients with moderate severity (NIHSS 4 to 11), new-onset constipation is associated with poor stroke outcome at 12 weeks ($P<0.05$).

Recurrent stroke occurred in 3 patients with new-onset constipation and only 1 patient without new-onset constipation. Risk of recurrent stroke was not associated with new-onset constipation ($P=0.628$).

Discussion

It is important to have a clear and reliable definition of constipation. Using different criteria for constipation, previous studies have reported a large variation in the incidence or prevalence of constipation after stroke. In the study by Robain and colleagues, constipation was defined as fewer than 3 stools per week or use of laxatives; of 152 patients in a stroke rehabilitation center, constipation was found in 60% of patients. In contrast, the cross-sectional study by Scivoletto et al. reported a 30% incidence rate of constipation in stroke patients. Rome II criteria, a symptom-based diagnostic criteria used for chronic functional constipation, has been widely used in research and clinical practice retrospectively and prospectively. In this study, we also used Rome II criteria to diagnose the new-onset constipation after stroke and exclude preexisting constipation before stroke. In addition, the observation period was confined to the first 4 weeks after stroke so that we could derive the incidence of the new-onset constipation. The present results essentially confirm that new-onset constipation is a common complication seen in 55% of patients within 4 weeks after first stroke.

We used survival analysis to obtain the incidence of new-onset constipation because it allows precise evaluation of both completed and uncompleted follow-up and determines the time of onset of constipation. Our results indicate
that the highest risk of new-onset constipation of almost 14% occurs on day 6 after stroke. As the decline in risk is rapid after day 7, we did not observe any new case beyond the first 3 weeks. This is in contrast to our general belief that prolonged bed-bound status is a major cause of poststroke constipation. More importantly, our results suggest that early intervention for or prevention of new-onset constipation should commence within the first 2 weeks after stroke may prevent the development of new-onset constipation.

There has been few studies on the risk factors of poststroke constipation. In the general population, constipation is more common in the females and the elderly. We did not find any association between constipation and age or gender, and this is in agreement with a prospective study conducted in a stroke rehabilitation ward. Instead, we found that BI score and use of bedpan were associated with new-onset constipation after first stroke. BI is a standard measurement of disability. Patients with a low BI score are more dependent but physically less active, and so they may be more susceptible to constipation. Similarly, our data suggest that bedpan used is a risk factor for constipation, although requesting a bedpan is a common desire of constipated patients. We think that our data are solid because assessment of bedpan use started right after the onset of stroke which is prior to occurrence of constipation. However, we believe that the association of bedpan usage with constipation is attributable to decrease of daily living activity and unfavorable environment for defecation. In our center, a patient usually requests a bedpan when his/her daily living activity is decreased. There are usually 2 to 4 stroke patients in a ward and the privacy is very poor, which in turn negatively affects environment for defecation. Consequently, unfavorable environment further leads to constipation. Factors such as changes in the environment and alteration in the way of defecation may adversely affect bowel movements.

Dehydration is a risk factor for constipation in chronic stroke patients. This is probably attributable to increased water absorption in the colon. In the present study, use of osmotic diuretics such as mannitol or diuretics such as frusemide was associated with new-onset constipation. We also found that patients with dysphagia had higher incidence of new-onset constipation than those without dysphagia. The higher constipation rate and lower BI in patients with dysphagia suggest that lower BI may at least partially be responsible for the constipation in dysphagia cases. However, use of nasogastric tube may also have some roles in constipation in dysphagia cases because our current data are not sufficient to rule out the possibility that use of nasogastric tube might cause constipation. Alternatively, dysphagia may lead to reduced intake of dietary fiber, and constipation is one of the complications for intragastric enteral nutrition.

In the observation, we found that 23 of 154 (14.9%) patients had depression in the first 2 weeks. The prevalence of poststroke depression in different studies shows a very wide range, because of the different definition, the scales of evaluation used, the time of first evaluation, and the selection criteria of the patients. It is estimated that up to 27% of the stroke patients present with symptoms of depression. Constipation is recognized as one of the possible symptoms of depression, and antidepressant-induced constipation is a well-known phenomenon. However, neither poststroke depression nor the use of antidepressants was correlated with constipation in our study, suggesting that depression and antidepressants may not affect the occurrence of constipation at early stage after stroke. Indeed, majority (86%) of the new-onset constipation occurred within 9 days whereas all of the depression was diagnosed and antidepressants started at 8.5 days in median after stroke.

Constipation has been found to be associated with poor stroke outcome in rehabilitation unit. In our study, the patients with new-onset constipation stayed longer in the hospital than those without constipation. New-onset constipation was associated with poor stroke outcome among patients with strokes of moderate severity at baseline (NIHSS 4 to 11). Nevertheless, such an association cannot be shown in patients with mild or severe strokes. We speculate that patients with mild strokes tend to have a good outcome and that most patients with severe strokes will develop constipation and have a poor outcome. Further studies with a larger stroke population and a longer observation period are needed to address the underlying mechanisms.

In summary, new-onset constipation after first stroke is a frequent complication during the first 4 weeks after stroke. Patients with greater disability or bedpan usage for defecation are apt to develop constipation. New-onset constipation after first stroke is associated with a poor stroke outcome among patients with strokes of moderate severity. Early exercise for daily living activity and offering a favorable environment for defecation should be recommended for stroke patients to prevent new-onset constipation. However, the limitation
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Disclosures
None.

References
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