Clinically Confirmed Stroke With Negative Diffusion-Weighted Imaging Magnetic Resonance Imaging Longitudinal Study of Clinical Outcomes, Stroke Recurrence, and Systematic Review

Stephen D.J. Makin, MRCP; Fergus N. Doubal, BSc, PhD; Martin S. Dennis, MD; Joanna M. Wardlaw, MD

Background and Purpose—We sought to establish whether the presence (versus absence) of a lesion on magnetic resonance imaging (MRI) with diffusion weighting (DWI-MRI) at presentation with acute stroke is associated with worse clinical outcomes at 1 year.

Methods—We recruited consecutive patients with a nondisabling ischemic stroke and performed DWI-MRI. Patients were followed up at 1 year to establish stroke recurrence (clinical or on MRI), cognitive impairment (Addenbrooke Cognitive Assessment Revised, <88) and modified Rankin Scale.

Results—A median of 4 days post stroke, one third (76/264; 29%) of patients did not have a DWI lesion (95% confidence interval, 23%–35%). There was no statistically significant difference between those with and without a DWI lesion with respect to age or vascular risk factors. Patients without a lesion were more likely to be women or have previous stroke. At 1 year, 11 of 76 (14%) patients with a DWI-negative index stroke had a clinical diagnosis of recurrent stroke or transient ischemic attack, 33% had cognitive impairment (Addenbrooke Cognitive Assessment Revised <88), and 40% still had modified Rankin Scale >1, no different from DWI-positive patients; DWI-positive patients were more likely to have a new lesion on MRI (14%), symptomatic or asymptomatic, than DWI-negative patients (2%; P=0.02). Our data were consistent with 6 other studies (total n=976), pooled proportion of DWI-negative patients was 21% (95% confidence interval, 12%–32%).

Conclusions—Nearly one third of patients with nondisabling stroke do not have a relevant lesion on acute DWI-MRI. Patients with negative DWI-MRI had no better prognosis than patients with a lesion. DWI-negative stroke patients should receive secondary prevention. (Stroke. 2015;46:3142-3148. DOI: 10.1161/STROKEAHA.115.010665.)

Key Words: cognition ■ diffusion ■ ischemic attack, transient ■ magnetic resonance imaging ■ stroke

Magnetic resonance imaging (MRI) with diffusion weighting (DWI-MRI) detects more ischemic stroke lesions than computed tomography and is recommended to diagnose stroke in national stroke guidelines. There is an increasing reluctance to diagnose stroke in patients who have clinical features of stroke and a negative DWI. Previous studies found that DWI-MRI did not identify a relevant ischemic lesion in one third of patients with a nondisabling stroke, but there is little information on these patients’ long-term prognosis. If patients without a DWI-MRI lesion (DWI-negative) have not had a stroke, then we would expect that they would have a better prognosis with a lower risk of long-term dependency, recurrent stroke, and cognitive impairment than patients with a DWI-visible ischemic lesion (DWI-positive).

Objectives
We aimed to determine (1) the proportion of patients with nondisabling stroke without an acute ischemic lesion on DWI-MRI, (2) whether these patients are clinically different at presentation from those with a lesion, and (3) whether they have a reduced risk of recurrent stroke, ongoing significant symptoms, dependency, or cognitive impairment at 1 year. We also updated a systematic review and meta-analysis of all recent studies.

Methods
Study Population and Recruitment
We performed a prospective observational study, recruiting consecutive inpatients and outpatients with mild (ie, nondisabling) ischemic stroke who presented to the Lothian regional stroke service from May 2010 to May 2012. We defined a nondisabling ischemic stroke as focal onset of neurological symptoms lasting >24 hours, with no other explanation, which did not cause significant impairment in basic activities of daily living at presentation.

We excluded patients who did not have a diagnosis of stroke, those whose symptoms resolved within 24 hours, those who were unable to consent (eg, because of dementia or aphasia), those who had...
a contraindication to MRI, those with clearly disabling stroke, and those with another medical condition, which meant that they were unlikely to survive for a year.

All participants involved in the study gave written informed consent, and the study was approved by the Lothian Research Ethics committee (ref 09/S1101/54).

**Collection of Clinical Data**

The clinical research fellow (S.D.J.M.) assessed all patients and recorded clinical features, baseline demographics, and risk factors (Table 1). We classified the stroke subtype using the Oxfordshire Community Stroke Project classification. We determined whether symptoms were likely to relate to anterior or posterior circulation and recorded whether the patient had previous stroke or transient ischemic attack (TIA), atrial fibrillation, hypertension (defined as blood pressure of ≥140/90 mm Hg on presentation or a previous diagnosis), hyperlipidemia (cholesterol >5 mmol/L on presentation or a previous diagnosis), previous diagnosis or current symptoms of peripheral vascular disease, diabetes mellitus (previous diagnosis or diagnosed on admission in accordance with the World Health Organization criteria), family history of stroke, and smoking status. We recorded the worst National Institutes of Health Stroke Scale score; if symptoms had improved before the assessment, we estimated the score at the worst point from the history and referral information.

**Imaging**

All patients underwent a brain MRI scan on the same 1.5 Tesla MRI scanner (Signa LX; General Electric, Milwaukee, WI) operating in research mode, and using a self-shielding gradient set with maximum strength of 33 mT/m, and an 8-channel phased-array head coil. The scanner was operated within a tight quality assurance program to maintain uniform performance. Sequences included axial DWI (30-direction axial diffusion tensor imaging, $b=1000$ s/mm$^2$ and $2\times b_0$ acquisitions, repetition time/echo time [TR/TE]=7700/82 ms, 24×24 cm field of view [FoV], 128×128 acquisition matrix, 28×5-mm slices), T2-weighted (TR/TE=6000/90 ms, 24×24 cm FoV, 384 (anterior-posterior)×224 acquisition matrix), 3D T1-weighted (TR/TE=800/15 ms, 20° flip angle, 24 (anterior-posterior)×18 cm FoV, 384×168 acquisition matrix, 2 averages, all with 28×5-mm slices and 1-mm slice gap), and sagittal 3D T1-weighted (TR/TE/inversion time=7/3/9.500 ms, 8° flip angle, 330 (superior-inferior)×214.5 cm FoV, 256×146 acquisition matrix, 100×1.8-mm slices). An ECG and routine blood tests (including serum glucose, lipids, erythrocyte sedimentation rate, and renal and liver function tests) were performed. Patients had carotid Doppler ultrasound imaging to identify carotid stenosis, defining symptomatic carotid stenosis as ≥50% stenosis on the relevant side measured by the North American Symptomatic Carotid Endarterectomy Trial criteria. Echocardiography and

| Table 1. Comparison of Patients With and Without a Lesion on Magnetic Resonance Imaging |
|-----------------------------------------------|
| **Patients With a Lesion at Index Stroke (n=188)** | **Patients Without a Lesion at Index Stroke (n=76)** | **P** | **OR on Multivariable Analysis** |
| Median age, y (IQR) | 67 (60–76) | 66 (57–75) | 0.38 | 1.00 (0.98–1.03) |
| Male sex | 117 (62%) | 37 (49%) | 0.053 | 2.09 (1.13–3.93)* |
| Diabetes mellitus | 22 (12%) | 8 (11%) | 1.00 | ... |
| Hypertension | 99 (53%) | 42 (54%) | 1.00 | ... |
| Hyperlipidemia | 114 (61%) | 47 (62%) | 0.89 | ... |
| Smoker in last 12 mo | 75 (40%) | 27 (36%) | 0.58 | ... |
| Atrial fibrillation | 21 (11%) | 4 (5%) | 0.16 | ... |
| Carotid stenosis (n=235) (either side) | 25/169 (15%) | 2/66 (3%) | 0.012 | ... |
| Stroke symptoms present at time of MRI | 148 (78%) | 49 (66%) | 0.06 | ... |
| Symptomatic carotid stenosis | 15 (9%) | 2 (3%) | 0.17 | ... |
| Potential embolic source (AF or symptomatic carotid stenosis) | 35 (20%) | 6 (9%) | 0.039 | 2.47 (0.98–7.24) |
| Ischemic heart disease | 31 (16%) | 22 (29%) | 0.027 | ... |
| Peripheral vascular disease | 12 (6%) | 3 (4%) | 0.57 | ... |
| Previous transient ischemic attack | 14 (7%) | 14 (18%) | 0.014 | ... |
| Previous stroke | 16 (9%) | 16 (21%) | 0.0068 | ... |
| Previous stroke or TIA | 0.23 (0.11–0.46) * |
| Previous large-vessel disease | 57 (30%) | 23 (30%) | 0.88 | ... |
| Median white matter lesions on index stroke Fazekas scale (IQR) | 3 (2–5) | 2 (2–4) | 0.015 | ... |
| Posterior circulation symptoms | 42 (22%) | 18 (24%) | 0.74 | ... |
| Median days from onset of symptoms: scan (IQR) | 4 (2–9) | 6 (3–11) | 0.026 | 1.00 (0.985–1.01) |
| Symptoms of lacunar stroke | 76 (41%) | 41 (54%) | 0.039 | ... |
| Median NIHSS (IQR) | 2 (1.25–4) | 2 (1–2) | 0.03 | ... |
| Stroke in follow-up | 16 (9%) | 8 (11%) | 0.64 | ... |
| TIA in follow-up | 3 (2%) | 3 (4%) | 0.34 | ... |
| Either stroke or TIA in follow-up | 19 (10%) | 11 (14%) | 0.39 | ... |
| modified Rankin Scale score ≥2 | 86 (46%) | 32 (42%) | 0.68 | ... |
| Cognitive impairment at 1 y (n=151) | 37 (33%) | 19 (48%) | 0.13 | ... |

AF indicates atrial fibrillation; IQR, interquartile range; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; and TIA, transient ischemic attack.

*P<0.05.
Diagnosis

A panel of neurologists, stroke physicians, and neuroradiologists met weekly to discuss the clinical findings, MRI images, all other investigations and to reach a final consensus diagnosis. We included a patient if the final diagnosis was of ischemic stroke defined as a sudden onset of neurological symptoms, lasting >24 hours, with no other more likely causes identified.

An experienced neuroradiologist (J.M.W.) assessed all scans for acute ischemic lesions, according to well-defined criteria for identifying ischemic lesions on neuroimaging.7 We classed a lesion as relevant to the presenting symptoms if it was of the appropriate size and shape for an infarct, in the appropriate brain location, and appeared of the right age to have caused the stroke symptoms. We defined lacunar infarct as a lesion <20-mm axial diameter in the deep gray or white matter of the cerebral hemispheres or brain stem. We defined cortical infarct as a lesion involving cortex or a large subcortical infarct >20-mm axial diameter (striatocapsular). We rated white matter hyperin-
At 1 year post stroke, 4 patients with no index lesion had further events that had led to the original diagnosis of stroke being questioned: of these, 2 were thought to have epilepsy, 1 may have had functional symptoms, and 1 may have had dementia. One patient who had a DWI-MRI index lesion and clinical features of stroke contacted us at 3 years post stroke (ie, 2 years after the last follow-up) to inform us that that patient had since been diagnosed with multiple sclerosis.

Table 2. Clinical and Imaging Recurrence of Stroke in Patients With and Without a Lesion Who Attended for 1-Year Follow-Up MRI

| Events in the 1 y Follow-Up Period                                | Patients With an Index Stroke Lesion | Patients Without an Index Stroke Lesion | P Value |
|------------------------------------------------------------------|--------------------------------------|----------------------------------------|---------|
| Recurrent stroke or TIA                                         | n=188                                | n=76                                   | 0.39    |
| Sub-set of 198 patients who had an MRI at 1 y post stroke       | 19/188 (10%)                         | 11/76 (14%)                           |         |
| Any new lesion on MRI (with or without clinical features of stroke) patient had clinical features of stroke/TIA | n=147                                | n=50                                   | 0.018   |
| New symptomatic lesion                                          | 7 (5%)                               | 0 (0%)                                 | 0.19    |
| New silent lesion                                               | 13 (9%)                              | 1 (2%)                                 | 0.12    |
| Recurrent stroke or TIA, but no new lesion                      | 7 (5%)                               | 7 (14%)                                | 0.0496  |
| No new clinical features of stroke/TIA in follow-up and no lesion on 1 y MRI | 120 (62%)                            | 42 (84%)                               | 0.83    |

MRI indicates magnetic resonance imaging; and TIA, transient ischemic attack.
Systematic Review

Identification of Articles
We included 6 previous studies3,4,12–15 of 712 participants plus the present study, total sample of 976 participants (Table 3).

Study Characteristics
The studies used different definitions of nondisabling stroke: Schulz et al14 (n=164) included patients not requiring hospital admission; Winbeck et al13 (n=37) and Urra et al14 (n=208) included patients with National Institutes of Health Stroke Scale score of ≤5; Marx et al13 (n=19) only included patients with brain stem ischemia whose symptoms resolved completely within 1 week; Kastrup et al12 (n=37) only included patients referred for a carotid endarterectomy; and Doubal et al11 (n=253) (also performed in Edinburgh) used the same definition as the present study.

Meta-Analysis
Including the present study, the pooled estimate of the proportion of patients with DWI-negative nondisabling stroke was 21% (95% confidence interval, 12%–32%; Figure 2), with significant heterogeneity (I²; 93.3%). Excluding our study, the pooled proportion was 27% (95% confidence interval, 24%–30%), indicating that our findings are consistent with the other studies.

Discussion
We found that nearly one third of patients with a nondisabling stroke have no visible acute ischemic lesion on DWI-MRI. One year later, they were just as likely to have recurrent stroke, cognitive impairment (Addenbrooke Cognitive Assessment Revised <88), or stroke-related disability (modified Rankin Scale score ≥5; NIHSS <5, premorbid modified Rankin Scale score =2, no contraindication to tPA) as the patients with an acute index lesion. The only difference was that DWI-positive index stroke patients were more likely to have a new lesion on MRI at 1 year (symptomatic or asymptomatic) than the DWI-negative index stroke patients.

Table 3. Characteristics of Studies Included in Systematic Review

| Setting and Population | Definition of Nondisabling Stroke | Median NIHSS | Median Time Onset-Scan (Range or IQR) | n | Number DWI Negative | Ant/Post |
|------------------------|----------------------------------|-------------|--------------------------------------|---|---------------------|---------|
| Urra et al14            | Consecutive patients with nondisabling stroke admitted to a stroke unit in Barcelona, Spain | NIHSS<5, premorbid modified Rankin Scale score <2, no contraindication to tPA | Thrombolyzed (n=119) 3 (IQR, 2–4) | 203 | 62 (31%) | Included |
| Winbeck et al12         | Stroke Unit, at Department of Neurology, Germany | NIHSS <5 | 3.3 (mean) (0–5) | 37 | 0 | Anterior |
| Marx et al13            | Neurology Department, Germany | Lasted no >1 wk and resolved completely | Not reported | 19 | 10 (53%) | Brain stem only. |
| Kastrup et al12         | Patients admitted to hospital for an carotid endarterectomy; all had a carotid stenosis ≥70% | Fit for carotid endarterectomy | Not reported | 36 | 0 | Anterior |
| Schulz et al11          | Referred to an outpatient TIA and nondisabling stroke clinic >3 d after the event | Well enough to remain at home and not need inpatient admission. | 1 (0–9) 17 (IQR, 10–22) | 164 | 50 (30%) | Both |
| Doubal et al10          | Inpatients and outpatients: Lothian | Lacunar stroke, and partial anterior circulation stroke. Inpatient and outpatient | 2 (0–8) 12 (IQR, 4–27) | 253 | 81 (32%) | Anterior |

DWI indicates diffusion-weighted imaging; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; and tPA, tissue-type plasminogen activator.

Of the studies identified in our review, ours is the largest, and the only one to follow-up all patients at 1 year with repeat MRI for those able to attend. The patients’ diagnoses were all assessed by a panel of stroke experts with access to all clinical information and investigations, and we only included patients for whom the panel was unable to find a more likely explanation for the symptoms and signs than stroke. We followed up all patients at 1 year and carefully sought alternative diagnoses. It remains possible that some of the participants without an acute index lesion may have had a stroke mimic, such as migraine. But one might expect patients presenting with a stroke mimic to experience further events that would clarify the diagnosis, but in 95% of the DWI-negative patients, no other diagnosis has been made and several represented with recurrent stroke (including one who was given thrombolytic treatment).

Although it was the largest study on this topic to date, the sample is limited for a common disease like stroke. We scanned patients on the day of presentation to stroke specialists, but for some this may have been too late; our findings may not be applicable to a population where all are assessed immediately at symptom onset. However, our cohort represents a typical population of patients presenting with stroke and is consistent with other studies. Repeated scanning might identify some additional lesions, but this would be impractical and not representative of routine clinical practice. Although no patients were lost to follow-up, 25% were not able to have repeat MRI scanning at 1 year.

Our findings are consistent with the 6 other studies identified in our systematic review (n=718, n=978 including our study). Our finding that 11% of subjects without an index MRI lesion had a recurrent stroke in the first year is similar to the findings by Fujimoto et al16 who found that 7.8% of 102 subjects without a DWI lesion had a recurrent stroke in the first 3 months (only published in abstract at present so not in our review). A retrospective study of a stroke unit population with more severe stroke17 found a much smaller proportion...
of stroke patients without a lesion on DWI-MRI (16/701) although retrospective studies are prone to bias.

Why did some patients not have a DWI-MRI lesion? Perhaps the diagnosis was wrong; however, no DWI-negative patients were proven to have a nonvascular cause of their symptoms on either a subsequent scan or autopsy. DWI-MRI may also have false positives because DWI is not specific for ischemia.18 Four patients had some evidence that their index event could possibly have been a stroke mimic because they had further events that led to the original diagnosis being questioned although no alternative was proven. However, in general, patients with mimics such as migraine or seizures should not be disabled or cognitively impaired at 1 year, and 42% of DWI-negative patients had a modified Rankin Scale score ≥2 at 1 year, similar to those with a DWI-positive index lesion. The excess of previous vascular disease in patients without an index acute lesion on MRI suggests that these patients may be more aware of the need to seek medical attention for any new neurological symptoms.

DWI is sensitive to acute ischemia. The increased signal that makes the ischemic tissue visible is because of restricted water diffusion in the extracellular space as water shifts from the extra- to the intracellular space (intracellular edema) in early ischemia. However, consideration of the pathophysiological changes that lead to cellular edema shows that the reduction in cerebral blood flow required to initiate cell swelling is more severe than that required to produce acute neurological symptoms (Figure 3).19 Additionally, the chance of seeing an acute ischemic lesion on DWI-MRI increases as the severity of the stroke increases and with the duration of ischemia.20 Data from highly standardized experimental large artery stroke models demonstrate variability in infarct extent on DWI and a close relationship between depth and duration of the perfusion reduction and DWI visibility,21 but there are no data (to our knowledge) on DWI appearances in experimental minor stroke. Therefore, it is possible that some small (nondisabling) strokes reflect a reduction in blood flow severe enough to cause symptoms, but not severe enough to cause a DWI lesion, or that the DWI lesion was transient, was missed by scanning, and did not show up on structural MR sequences either (these are known to be less sensitive to small infarcts).22

It is intriguing that there were more recurrent infarcts, including silent infarcts, visible on the 1-year follow-up MRI in the patients with a visible index DWI-MRI lesion than in those without. This might suggest some differential vulnerability to developing infarction, which might be consistent with there being more WMH in the patients with DWI-positive index lesions than in those with DWI-negative lesions; WMH are associated with more infarct growth after hyperacute stroke,23 which has been interpreted as greater susceptibility to ischemia. Alternatively, the excess of previous vascular disease in patients without an index acute lesion on MRI suggests that these patients may be more aware of the need to seek medical attention for any new neurological symptoms.

Additional studies should include long-term follow-up to determine why some patients with no other explanation for their neurological symptoms apart from stroke do not to
develop a visible lesion on DWI yet have similar cognitive and physical outcomes to those with a DWI lesion. Similar patients must have been included in secondary prevention studies, many of which were performed before widespread DWI availability or did not use DWI positivity as an entry requirement. Meantime patients with a clinical diagnosis of stroke who are DWI-negative have the same high risk of recurrent stroke and disability as DWI-positive patients and should receive secondary stroke prevention until further evidence on their specific management is available.

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Dr Makin recruited and assessed the patients, performed statistical analysis, drafted and edited the article. Dr Wardlaw conceived and supervised the original project, provided input and direction, edited the articles, and prepared the final version. Dr Doubal provided guidance and edited the manuscript. Dr Dennis identified patients, participated in expert panel, read and critically appraised the article.

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臨床的に確認された拡散強調画像 (DWI) 病変のない脳卒中
臨床転帰、脳卒中再発の継続的研究と統計的レビュー

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表 1 1年後の追跡調査で MRI を施行した DWI 病変のある患者ない患者における臨床的および画像上の脳卒中再発

| 1年の追跡期間中のイベント | 虚血性脳卒中病変のある患者 | 虚血性脳卒中病変のない患者 | P 値 |
|-------------------------|---------------------------|---------------------------|-----|
| 脳卒中または TIA の再発 | 19/188 (10%) | 11/76 (14%) | 0.39 |
| 脳卒中から 1年後に MRI を施行した 198 例のサブセット | n = 147 | n = 50 |
| 新規の MRI 病変（脳卒中の臨床的特徴の有無にかかわらず）を有する患者 | 20 (14%) | 1 (2%) | 0.018 |
| 新規の急性性病変 | 7 (5%) | 0 (0%) | 0.19 |
| 新規の無急性性病変 | 13 (9%) | 1 (2%) | 0.12 |
| 脳卒中または TIA の再発あり、新規の病変なし | 7 (5%) | 7 (14%) | 0.0496 |
| 追跡期間中、新規の脳卒中/TIA の臨床的特徴なし、および 1年後の MRI 病変なし | 120 (82%) | 42 (84%) | 0.83 |

MRI: 磁気共鳴画像法；TIA: 一過性脳虚血発作。

注: 本論文においては、身体障害を伴わない虚血性脳卒中は「神経学的局所症状で突然発症し、24 時間以上持続し、他の疾患として説明できず、受診時に基本的な日常生活に明らかに支障をきたしていないイベント」と定義されている。出血性脳卒中は CT あるいは本研究の MRI で除外されていると推察される。
확산강조 MR 영상에서 병변이 없으나 임상적으로 확인된 뇌졸중
임상적 예후 및 뇌졸중 재발에 대한 장기적 연구 및 체계적 종설

Clinically Confirmed Stroke With Negative Diffusion-Weighted Imaging Magnetic Resonance Imaging
Longitudinal Study of Clinical Outcomes, Stroke Recurrence, and Systematic Review

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Key Words: cognition □ diffusion □ ischemic attack, transient □ magnetic resonance imaging □ stroke

배경과 목적
저자들은 급성뇌졸증으로 내원한 환자에서 확산강조영상(DWI-MRI)를 포함한 자기공명영상(MRI)의 병변 유무 여부가 1년 시점의 나쁜 임상적 예후와 연관이 있는지를 조사하고자 하였다.

방법
저자들은 DWI-MRI를 시행한 비장애성허혈뇌졸중 환자들을 연속적으로 모집하였다. 중증 발생 1년 시점에서 환자들을 추적관찰하였으며, 이 때 뇌졸중 재발(임상적 혹은 MRI로 확인), 인지저하(Addenbrooke Cognitive Assessment Revised, <88) 및 mRS를 수집하였다.

결과
뇌졸중 증상 발생 이후 증상이 4일이 지난 시점에서, 환자들 중 1/3에서 DWI로 확인되는 뇌졸중 병변이 없었다(95% CI, 23-35%). DWI 병변 유무로 분류할 때, 연령 및 혈관성 위험인자의 분포는 유의한 차이를 보이지 않았다. 병변이 없는 환자들에서 이상 및 이전 뇌졸중 병력의 빈도가 높았다. 1년 시점에서 DWI 병변이 없었던 76명 중 11명(14%)의 환자에서 임상적으로 뇌졸중의 재발 혹은 TIA가 있었으며, 33%에서 인지기능저하(Addenbrooke Cognitive Assessment Revised<88) 및 40%에서 mRS>1점이 확인되었으며, 이러한 양상은 DWI-양성 환자와 차이를 보이지 않았다. DWI 양성 환자들은 MRI에서 증상성 혹은 무증상의 새로운 병변이 발생하는 빈도가 높았다(14% vs. 2%, P=0.02). 본 연구 결과는 다른 6개의 연구와 일치하며(전체 연구 대상자 수, 976명), 전체적으로 DWI 병변이 없었던 환자는 21% (95% CI, 12-32%)였다.

Table 2. Clinical and Imaging Recurrence of Stroke in Patients With and Without a Lesion Who Attended for 1-Year Follow-Up MRI

| Events in the 1 y Follow-Up Period | Patients With an Index Stroke Lesion | Patients Without an Index Stroke Lesion | P Value |
|-----------------------------------|--------------------------------------|----------------------------------------|---------|
| Recurrent stroke or TIA           | n=188                                | n=76                                   | 0.39    |
| Sub-set of 198 patients who had an MRI at 1 y post stroke | n=147                               | n=50                                   |         |
| Any new lesion on MRI (with or without clinical features of stroke) patient had clinical features of stroke/TIA | 20 (14%)                            | 1 (2%)                                 | 0.018   |
| New symptomatic lesion            | 7 (5%)                               | 0 (0%)                                 | 0.19    |
| New silent lesion                 | 13 (9%)                              | 1 (2%)                                 | 0.12    |
| Recurrent stroke or TIA, but no new lesion | 7 (5%)                              | 7 (14%)                                | 0.0496  |
| No new clinical features of stroke/TIA in follow-up and no lesion on 1 y MRI | 120 (82%)                           | 42 (84%)                               | 0.83    |

MRS indicates magnetic resonance imaging; and TIA, transient ischemic attack.
뇌졸중 발생 3개월 이내에 재발한 뇌졸중에 대한 정맥내혈전용해치료

Intravenous Thrombolysis for Stroke Recurring Within 3 Months From the Previous Event

Michal Karlinski, MD, PhD; Adam Kobayashi, MD, PhD; Anna Czlonkowska, MD, PhD; Robert Mikulik, MD, PhD; Daniel Vaclavik, MD, PhD; Miroslav Brozman, MD, PhD; Zuzana Gdovinova, MD, PhD; Janica Körv, MD, PhD; Vida Demarin, MD, PhD; Vanja Bašic-Kes, MD; Aleksandras Vilionskis, MD; Dalius Jatuzis, MD, PhD; Yakup Krespi, MD; Nikolay Shamalov, MD, PhD; Miroslav Brozman, MD, PhD; Zuzana Gdovinova, MD, PhD; Viktor Švigelj, MD; Laszlo Csiba, MD, PhD; Klara Fekete, MD; Laszlo Csiba, MD, PhD; Klara Fekete, MD; Janika Kõrv, MD, PhD; Janika Kõrv, MD, PhD; Janika Kõrv, MD, PhD.

Abstract 6

뇌졸중 발생 3개월 이내에 재발한 뇌졸중에 대한 정맥내혈전용해치료

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Key Words: acute stroke ■ alteplase ■ off-label use ■ recurrence ■ thrombolysis ■ treatment outcome

배경과 목적

유럽의 허가 기준에 의하면, alteplase는 최근 3개월 이내에 뇌졸중이 있었던 환자에게만 투여되야 한다. 그러나 뇌졸중의 과거력이 치료 효과에 미치는 영향에 대해서는 알려져 있지 않다. 저자들의 연구결과에서 최근 3개월 이내에 뇌졸중이 있었던 환자에게 정맥내혈전용해치료를 투여한 경우, 뇌졸중이 처음 있었던 환자에게 투여한 경우에 비해 그 안전성과 기능적 예후에 차이가 있는지 검토하고자 하였다.

방법

저자들은 12개 국가에서 수집된 SITS-Eastern Europe 연구 데이터를 기반으로 하여, 2003년 10월부터 2014년 7월의 기간 동안 alteplase 치료를 받은 일련의 환자를 분석하였다. 대응비는 로지스틱회귀분석을 통하여 계산하였다.

결과

총 13007명의 환자 가운데, 11221명(86%)은 뇌졸중 병력이 없었으며 249명(2%)은 내원 3개월 이내의 뇌졸중 병력이 있었다. 3개월 이내에 뇌졸중 병력이 있던 환자들은 고혈압 및 고지혈증의 비율이 높았다. 양 군에서 ECASS 기준에 의한 중상성뇌내출혈(미보정 독립비, 1.27; 95% CI 0.74–2.15) 및 3개월 시점의 생존 및 독립적 기능 유지(독립비 0.81, 95% CI 0.61–1.09) 등의 결과에서도 유의한 차이가 없었다.

결론

3개월 이내의 뇌졸중이 있었지만 alteplase 치료를 받은 환자들에 친 뇌졸중으로 치료받은 환자들에 비해 예후가 나빠지지 않은 것으로 보인다. 주의 깊게 환자를 선정하는 것은 매우 중요하지만, 저자들의 연구 결과는 이러한 집단의 환자들도 혈전용해치료로 안전하게 효과를 볼 수 있고 일관적으로 배제되어서는 안 된다는 점을 제시한다. 이전 뇌졸중이 이후 어느 정도 시간이 경과해야 혈전용해치료가 안전한 것인지에 대한 추가 연구가 필요하다.