Short report

Characteristics of patients with minor ischaemic strokes and negative MRI: a cross-sectional study

Fergus N Doubal, Martin S Dennis, Joanna M Wardlaw

ABSTRACT

Background Diffusion-weighted (DWI) MRI is recommended in UK guidelines to evaluate minor strokes, yet can produce negative results.

Objective The authors determined the rate of negative MRI (including DWI) and associated features in patients presenting to hospital with minor strokes.

Methods The authors performed a prospective observational cross-sectional study in a teaching hospital of patients with a clinical diagnosis of ischaemic lacunar or minor cortical stroke. The authors performed multivariate analysis to determine predictors of negative DWI and MRI (all sequences). Gold standard for clinical diagnosis of stroke was the opinion of an expert panel.

Results The authors recruited 246 patients, mean age 68.1 years (SD 11.6 years), 162 were males (66%), and the median NIHSS was 2 (range 0 to 8). The median time from stroke onset to MR scan was 12 days (IQR 4–27 days). Eighty-one patients (33%) did not show any ischaemia on DWI. Sixty patients (24%) did not show the recent infarct on MRI (DWI/T2/FLAIR). With multivariate analysis, less severe stroke, younger age, female gender and increased time from stroke onset to scan were associated with negative DWI. With multivariate analysis, younger age and female gender were associated with negative MRI (DWI or T2 or FLAIR) scans.

Conclusions There is a high rate of negative MRI and DWI among patients with minor stroke (a third) which has important management and research implications. A negative MRI or DWI does not exclude the diagnosis of stroke.

INTRODUCTION

UK guidelines recommend MRI in patients presenting with minor stroke. Diffusion-weighted MR imaging (DWI) is more sensitive than CT scanning at detecting acute cerebral ischaemia in minor stroke. DWI can be positive for ischaemia for several weeks after minor stroke, but there is also a negative rate for DWI in patients with clinically definite stroke. It is unclear which features are associated with negative DWI. We investigated the rate and associations of negative DWI and MRI in patients presenting with minor ischaemic stroke.

METHODS

We recruited patients prospectively between April 2005 and December 2007. We included patients presenting to our teaching hospital (which sees 550 patients/year with stroke) with a clinical diagnosis of minor ischaemic stroke (defined as lacunar or partial anterior circulation stroke). We defined stroke if it was diagnosed by a panel of experts (neuroradiologist, vascular neurologist and stroke physician all blinded to the study hypothesis) with full access to MRI (to exclude other structural causes of the symptoms) and other investigation results. We excluded patients with transient ischaemic attacks (symptom duration <24 h), contraindications to MRI and those without a clinical diagnosis of minor ischaemic stroke. In August 2009, we reviewed all case records in those with negative imaging, to see if an alternative diagnosis had emerged, and re-reviewed the initial diagnosis of stroke. The follow-up period ranged from 21 to 52 months.

Patients had MRI after presentation on a 1.5 T MR scanner (Signa LX; General Electric, Milwaukee, Wisconsin) with 22 mT m⁻¹ maximum strength gradients, including axial DWI, T2-weighted, fluid-attenuated inversion recovery (FLAIR), T2* and sagittal T1 weighted sequences. A consultant neuroradiologist, blinded to the study hypothesis but not clinical information, coded acute relevant infarcts (DWI increased signal, reduced signal on apparent diffusion coefficient map, or increased signal with/without swelling without evidence of cavitation on FLAIR/T2) using a validated morphological schema. Patients had carotid Doppler ultrasound, electrocardiogram, routine blood tests and further clinical investigations as indicated. We defined time to scan as the time from stroke onset to scan, the persistence of symptoms was recorded at the time of the scan and age at presentation to hospital. We recorded stroke severity (NIHSS) and gender.

We defined minor cortical and lacunar stroke syndromes as previously (but did not use a subclassification system to diagnose stroke). We further classified stroke subtype using radiological criteria, that is whether any recent infarct on MRI was cortical or lacunar, and used both clinical and radiological classification to subtype stroke. Where classifications differed, the radiological classification was used.

To determine which variables were included in the multivariate model, we used parametric and non-parametric tests as appropriate to assess univariate associations between variables and the presence of a negative scan. We used multivariate logistic regression to assess contributing factors with the binary outcome of positive/negative scan as the dependent variable. Calculations were performed with Minitab (version 15; Minitab, State College, Pennsylvania), and the α level for significance was 0.05. We excluded...
DISCUSSION

In patients presenting with minor ischaemic stroke in the anterior circulation, 33% had negative DWI, and 24% had negative MRI (DWI/T2/FLAIR). Negative DWI was associated with increasing time between stroke and scan, less severe stroke, younger age and female gender after correcting for other factors. Negative MRI (DWI/FLAIR/T2) was associated with younger age and female gender after correcting for other factors and time to scan, the presence of persisting symptoms and NIHSS (table 1).

### Table 1 Multivariate associations of a negative diffusion-weighted imaging (DWI) and MRI (T2 or fluid-attenuated inversion recovery (FLAIR) or DWI)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Negative DWI</th>
<th>p Value</th>
<th>Negative MRI (T2/FLAIR/DWI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.97 (0.95 to 1.00)</td>
<td>0.047</td>
<td>0.96 (0.93 to 0.98)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.44 (0.24 to 0.81)</td>
<td>0.008</td>
<td>0.46 (0.24 to 0.87)</td>
<td>0.018</td>
</tr>
<tr>
<td>National Institute for Health Stroke Scale score</td>
<td>0.70 (0.54 to 0.91)</td>
<td>0.008</td>
<td>0.76 (0.58 to 1.01)</td>
<td>0.059</td>
</tr>
<tr>
<td>Persisting symptoms at time of scan (yes/no)</td>
<td>0.61 (0.29 to 1.28)</td>
<td>0.191</td>
<td>0.50 (0.23 to 1.08)</td>
<td>0.077</td>
</tr>
<tr>
<td>Time from stroke to scan (days)</td>
<td>1.02 (1.01 to 1.03)</td>
<td>0.003</td>
<td>1.01 (1.00 to 1.02)</td>
<td>0.132</td>
</tr>
</tbody>
</table>

The odds ratios (ORs) are per unit increase in the explanatory variable, and all ORs are corrected for all explanatory variables in the table.

How do our results compare with other studies? A similar rate of negative DWI (30%) is reported in patients with minor stroke scanned at a median of 17 days poststroke, but this study did not distinguish between stroke and TIA in the multivariate regression. Studies of DWI within 24 h of acute stroke found negative DWI rates ranging from 6% to 17%, but were retrospective or reclassified patients presenting with TIA but who had an acute ischaemic lesion on DWI as stroke. Other studies did not report negative DWI rates in TIA and stroke separately.

Lower NIHSS (lower stroke severity) was associated with negative DWI. In general, small infarcts are less likely to be identified on imaging than large infarcts, and although infarct size was shown in a small longitudinal study not to predict the duration of DWI-visible lesions, it is probable that small infarcts resolve quicker than larger infarcts. Increased time to imaging was associated with negative DWI although not negative T2/FLAIR MRI. This confirms other findings and is attributable to normalisation of the DWI signal as cellular oedema resolves, but this does not mean that the tissue damage has resolved. Consistent with this, we have demonstrated that T2/FLAIR identifies more infarcts than DWI in patients presenting subacutely with minor stroke. Female gender was associated with both negative DWI and negative T2/FLAIR MRI. Gender did not previously predict negative DWI in patients with TIA/minor stroke combined. The cause of this
discrepancy is not clear; possibly, our result was due to residual confounding from baseline imbalances.

We have shown that a third of patients presenting with minor stroke have negative DWI, which is associated with decreased stroke severity, increased time to scan, younger age and female gender. Had we been less critical with our clinical diagnosis of stroke and included even some of the 355 patients with suspected stroke that were initially screened, the proportion with negative DWI would have been higher. These results should alert clinicians about when to expect a negative MRI in a patient with minor stroke and encourage them not to automatically exclude the diagnosis of stroke if DWI is negative.

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Competing interests None.

Patient consent Obtained.

Ethics approval Ethics approval was provided by the Lothian Regional Ethics Committee, UK.

Contributors FND conceived the study, collected and analysed data and wrote the paper. JMW helped conceive the study, collected data and commented on drafts of the paper. JMW is part funded by the Scottish Funding Council through the SINAPSE Collaboration.

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