Is Visible Infarction on Computed Tomography Associated With an Adverse Prognosis in Acute Ischemic Stroke?

J.M. Wardlaw, MRCP, FRCR, MD; S.C. Lewis, MSc; M.S. Dennis, FRCP, MD; C. Counsell, MRCP; M. McDowall, MSc

**Background and Purpose**—It is unclear whether visible infarction on a CT scan at any time after the stroke is an adverse prognostic factor once other factors such as stroke severity are taken into consideration. We examined whether visible infarction was associated with a poor outcome after stroke using univariate and multivariate analyses, including easily identifiable clinical baseline variables, and adjusting for time from stroke onset to CT.

**Methods**—All inpatients and outpatients with an acute ischemic stroke attending our hospital stroke service were examined by a stroke physician and entered into a register prospectively. The CT scan was coded prospectively for the site and size of any relevant recent visible infarct. The patients were followed up at 6 months to ascertain their functional status with the use of the modified Rankin Scale. Analyses of the effect of visible infarction on the outcomes “dead or dependent” or “dead” at 6 months were performed with adjustment for time from stroke to CT, clinical stroke type (lacunar, hemispheric, or posterior circulation), and in a multiple logistic regression model to adjust for confounding baseline variables such as stroke severity.

**Results**—In 993 patients in the stroke registry, visible infarction increased the risk of being dead or dependent at 6 months (odds ratio [OR], 2.5; 95% confidence interval [CI], 1.9 to 3.3) or dead (OR, 4.5; 95% CI, 2.7 to 7.5), both on its own and after adjustment for time from stroke to CT, stroke symptoms, and other important clinical prognostic variables (OR for death or dependence in the predictive model, 1.5; 95% CI, 1.0 to 2.0; OR for death, 2.4; 95% CI, 1.4 to 4.1).

**Conclusions**—Visible infarction on CT is an adverse prognostic indicator (albeit of borderline significance) even after adjustment for stroke severity and time lapse between the stroke and the CT scan. (Stroke. 1998;29:1315-1319.)

**Key Words:** cerebral infarction ■ cerebrovascular disorders ■ prognosis ■ stroke assessment ■ stroke outcome ■ tomography, x-ray computed

Stroke is a clinical diagnosis. Approximately 50% of all cerebral infarcts are visible on a CT scan at some time, although this varies with the severity of the stroke and the timing of the CT scan. Large cortical infarcts are more often visible than lacunar infarcts. Even MR, while sensitive to infarction, does not visualize all infarcts.

It is not clear whether visible infarction (as opposed to lack of visible infarction) is associated with a poor outcome after stroke or is simply an indicator of a more “severe” stroke or the time lapse between the stroke and the CT scan. Previous studies that examined the association of CT scan findings with outcome and that also took into account clinical variables were either small, examined the effect of infarct size (rather than simply its presence or absence), only examined the effect of a visible infarct on very early CT (ie, within 6 hours of the stroke) rather than over the first week, or only examined the effect on clinical outcome at 1 month rather than in the long term. The largest study by Candelise et al included 1048 patients and examined the association of visible infarction (with other clinical variables), using multiple logistic regression, with death at 1 month and the association in survivors at 1 month with death at 6 months. They found that an infarct on CT was associated with an increased relative risk of death within 6 months in those who survived to 1 month (relative risk, 2.01; 95% CI, 3.3 to 1.2) but not of death within 1 month of the stroke. However, they did not take into account the time lapse from stroke to CT. Other studies have examined the relationship between visible infarction (and its extent) and clinical outcome but without adjustment for confounding factors such as clinical stroke severity.

We wished to examine the specific question of whether visible infarction increased the risk of a poor outcome when other potentially confounding factors (such as time lapse from stroke to CT and clinical severity of the stroke) had been taken into account. We also wanted to determine whether a visible infarct in patients presenting later after the stroke (ie, days to a few weeks), rather than within the first 6 hours, carried an adverse prognosis. In other words, does a patient with, for example, a lacunar syndrome presenting 2 days after the stroke and whose CT scan shows an infarct in the relevant part of the brain have a worse outcome than a patient who is...
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in all ways identical, except for a normal CT scan? Therefore, does a visible infarct on CT reflect some underlying pathophysiological process (such as cellular edema or severity of cell damage) that influences outcome, or is it simply a marker of the severity or size of the stroke?

Subjects and Methods

The study was approved by the Lothian Area Ethics of Medical Research Committee. From May 1992 to April 1997, data from all patients admitted to our hospital with a stroke (first or recurrent) were entered prospectively into a local stroke registry, the Lothian Stroke Register. From November 1994 onward, all outpatients attending the neurovascular clinic with a stroke were also included. The patients were examined by a stroke physician who documented the clinical findings and stroke severity and classified the stroke type according to the OCSP into either TACS, PACS, LACS, POCS, or uncertain (for those who did not fit clearly into one of the other types). If the patient had been scanned and the CT was normal or showed an infarct, the abbreviation “I” (infarction) was substituted for “S” (syndrome). The clinical characteristics of the patients were recorded, including age and prestroke disability. If patients had a history of more than one stroke, the first stroke was used in the present analysis. In patients who presented to the stroke physician at 3 weeks or later, the history and blood test results performed by the family physician at the time of symptom onset were available so that the stroke physician was able to make a clinical diagnosis of stroke based on common sense. Patients thought to have had migraine or an epileptic seizure, vasovagal attack, or other noncerebrovascular cause of the symptoms were excluded. Between May 1992 and September 1996, some patients received antithrombotic treatments in a randomized trial. From September 1996 onward, most patients received aspirin for their stroke.

Most patients had a standard CT brain scan (without contrast) as soon as possible after the clinical examination (same or next day for inpatients, but usually later in outpatients). We attempted to scan all patients, using an IGE 8800 scanner with fast upgrade (up to August 1996) and thereafter an IGE High Speed CTI spiral scanner. Approximately 3% of stroke patients were scanned with MRI rather than CT and therefore were excluded from the present analysis. The site of the infarction considered to be the cause of symptoms was classified according to a previously described and validated template.3 From April 1994, all the scans were classified by a neuroradiologist. Before that they were classified by a consensus of neurologists with an interest in stroke. The clinical information was available to the person reading the scan, ie, the readers were not deliberately blinded. We have previously validated our method of categorizing the scans and found it to be reliable even when used by nonneuroradiologists.4 In patients who had more than one CT scan (eg, because they deteriorated neurologically), only the first CT was used in the present analysis.

Patients with intracerebral hemorrhage or other nonstroke pathologies were excluded, and in the remaining patients, those with a visible infarct considered appropriate to the stroke symptoms were compared with patients without such a lesion (ie, patients with a normal CT or with an old infarct in the wrong part of the brain to be the cause of symptoms). A “visible infarct” was defined as any area in the brain with lower density than normal brain and either wedge-shaped or rounded and occupying a recognized vascular territory. Furthermore, the classification of site and size of infarct was used to determine the relevance to the site of stroke predicted by the clinical features. The age of the lesion, and hence its relevance to the present clinical symptoms, was judged from the degree of mass effect, clarity of margins, degree of hypodensity, and presence of hemorrhagic transformation. In patients presenting beyond 3 weeks, when the age of the lesion would be more difficult to judge, a “recent” infaract was determined from its site in the brain (hence its relevance to the presenting symptoms) and absence from any brain scan before the recent stroke. If there was any doubt as to the relevance of an infarct, it was classified as “no visible infarct.” Subtle early signs of infarction were classified as a “visible infarction” (loss of outline of basal ganglia, effacement of sulci, loss of insular ribbon) but not a hyperdense artery in the absence of any brain parenchymal change.

Clinical follow-up was by telephone at 6 months and was performed blinded to the patients’ clinical features and CT results. Each patient’s disability was categorized according to the modified Rankin Scale5 (with ≥3 indicating a poor outcome [dead or dependent] and 6 indicating death). Because choosing between a modified Rankin Scale score of 2 and a modified Rankin Scale score of 3 may be difficult, a secondary analysis of death at up to 6 months versus survival at 6 months was also performed, with death being a more objective end point. Deaths included those from any cause up to exactly 6 months after stroke onset. All data were entered into the stroke registry, double punched and checked for consistency, and analyzed in SAS6 with the use of logistic regression.

We first examined the effect of visible infarction on clinical outcome at 6 months in a univariate analysis. To determine whether visible infarction was an independent predictor of outcome over and above any influence of the clinical severity of the stroke or age of the patient (which might be more powerful confounding outcome predictors) or time lapse to the CT scan, we performed a multiple logistic regression using a previously developed statistical model (see Appendix). This was derived from the OCSP data set7 and externally validated with the use of the Lothian Stroke Register and other community-based cohorts; it predicted poor functional outcome at 6 months on the basis of clinical features at the time of stroke.8 The effects of visible infarction and time lapse between stroke and CT on outcome at 6 months were examined by including them in the logistic regression model to which the linear predictor (the “equation” that pulls together the key clinical variables that predict stroke outcome) of the model from the OCSP had already been included (Table 1). This analysis was checked by recalculating the linear predictor with the Lothian Stroke Register data and fitting that in place of the OCSP linear predictor. The same modeling process was used with the outcome of death within 6 months. The model of Counsell et al9 has also been validated for prediction of death and works well. It was also the best statistical predictor of outcome after stroke that was available to us.

Results

From May 1992 until April 1997, 1302 inpatients and outpatients with probable or definite stroke had their data entered into the Lothian Stroke Register. The following were excluded from analysis: 83 patients (6%) with an intracerebral hemorrhage and 124 patients (10%) who did not have a CT scan within 99 days of the stroke (primarily because of late presentation to the outpatient clinic), of whom 38 (3%) had an MRI scan instead of a CT scan. Sixty-four patients were known to be alive 6 months after their stroke, but their modified Rankin score at 6 months could not be ascertained. These patients were removed from the analyses that used

Selected Abbreviations and Acronyms

CI = confidence interval
LACI = lacunar infarct(s)
LACS = lacunar syndrome
OCSP = Oxfordshire Community Stroke Project
OR = odds ratio
PACI = partial anterior circulation infarct(s)
PACS = partial anterior circulation system
POCI = posterior circulation infarct(s)
POCS = posterior circulation syndrome
TACI = total anterior circulation infarct(s)
TACS = total anterior circulation syndrome
death or dependence at 6 months as an outcome but were retained in the analyses that used death as an outcome.

To determine whether excluding the 124 patients who did not have a CT scan (10% of our registry) had introduced bias, we examined their baseline characteristics and outcome to see whether there were any significant differences between those with and without a CT scan. Patients who did not have a CT scan were more likely to be outpatients (ie, they were examined too late after their stroke for CT to be considered useful by the clinician, who sometimes arranged an MR scan instead) (OR, 3.5; 95% CI, 2.4 to 5.1) or to have died within 14 days of stroke onset (OR, 6.9; 95% CI, 3.9 to 12.2) (the clinician considered the patient very likely to die very quickly and therefore did not scan the patient for humane reasons). Twenty-four (15%) of those who did not have a CT scan died within 14 days of stroke onset compared with 48 (5%) of those who did have a CT scan.

Of the 993 patients with fully analyzable data, 64% were scanned within a week; 136 (14%) were scanned on the day of the stroke, 212 (21%) the day after, 159 (16%) between 2 and 3 days, 132 (13%) between 4 and 7 days, and 167 (17%) between 7 and 21 days (ie, 81% within 3 weeks); and the remaining 187 patients (19%) were scanned after 21 days (the later times primarily involved outpatients who did not attend the outpatient clinic until several weeks after their stroke).

The percentage of patients with a visible infarct fell in patients CT scanned later than a week after the stroke, mainly because most of the late-presenting patients were outpatients with milder strokes (Figure 1).

There were 133 TACI (13%), 397 PACI (40%), 258 LACI (26%), and 158 POCI (16%) strokes, and 47 (5%) were classified as "uncertain." The proportion of patients with a relevant visible infarct in each subtype of ischemic stroke (eg, TACI, LACI) is shown in Figure 2. A greater proportion of the patients with a TACI had an infarct visible at all stages compared with patients with a PACI, LACI, or POCI, as expected from previous studies.1

In the univariate analysis, the outcome at 6 months in patients with a relevant visible infarct was significantly worse than in those without: 53% of those with a visible infarct were dead or dependent compared with 31% of those without (OR, 2.5; 95% CI, 1.9 to 3.3). Seventeen percent of those with a visible infarct died within 6 months of the stroke compared with 4% of those without (OR, 4.5; 95% CI, 2.7 to 7.5).

Outcome at 6 months also varied depending on the time lapse between stroke onset and CT. Patients who had a CT scan within a week of the stroke were more likely to be dead or dependent at 6 months than those scanned later (OR, 4.8; 95% CI, 3.5 to 6.4). This was partly because patients with milder strokes were more likely to stay at home, arrive at the

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**TABLE 1. Logistic Regression Model to Predict Dead or Dependent Patients at 6 Months Generated in the Oxford Community Stroke Project Using Baseline Clinical Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Log (OR)</th>
<th>SD of Log (OR)</th>
<th>OR</th>
<th>95% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>12.34</td>
<td>1.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (increment per year)</td>
<td>0.06</td>
<td>0.01</td>
<td>1.06</td>
<td>1.03–1.09</td>
</tr>
<tr>
<td>Poor or no arm power</td>
<td>1.71</td>
<td>0.50</td>
<td>5.51</td>
<td>2.09–14.53</td>
</tr>
<tr>
<td>Modified Rankin score &gt;2 before stroke</td>
<td>2.92</td>
<td>0.54</td>
<td>18.56</td>
<td>6.48–53.14</td>
</tr>
<tr>
<td>Living alone</td>
<td>0.65</td>
<td>0.27</td>
<td>1.92</td>
<td>1.13–3.27</td>
</tr>
<tr>
<td>Abnormal verbal score on Glasgow</td>
<td>1.75</td>
<td>0.50</td>
<td>5.78</td>
<td>2.15–15.49</td>
</tr>
<tr>
<td>Coma Scale (&lt;5)</td>
<td>1.24</td>
<td>0.40</td>
<td>3.46</td>
<td>1.59–7.56</td>
</tr>
<tr>
<td>Unable to walk</td>
<td>0.60</td>
<td>0.29</td>
<td>1.83</td>
<td>1.04–3.22</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.35</td>
<td>0.32</td>
<td>3.86</td>
<td>2.07–7.20</td>
</tr>
</tbody>
</table>

Adapted from Counsell et al.12

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Figure 1. Percentage of patients with visible infarction at various times after the start of stroke symptoms.
hospital as outpatients, and therefore be scanned later. In addition, those scanned after 1 week had to have survived 1 week and therefore were self-selected patients with better prognoses. After adjustment for the time lapse between stroke onset and CT, patients with a visible infarct were still more likely to be dead or dependent at 6 months (OR, 2.1; 95% CI, 1.6 to 2.8) or to have died within 6 months of the stroke (OR, 3.8; 95% CI, 2.3 to 6.3). The effect of visible infarction on the risk of a poor outcome did not vary over time, ie, patients with a relevant visible infarct on CT had a worse prognosis at 6 months than those without a relevant infarct regardless of when the CT was performed. The effect of fewer infarcts being visible at later times was influenced by the fact that the later scans were performed on patients with milder strokes; it was therefore important to perform a multivariate analysis to adjust for these confounding factors.

Eighty-nine percent of the subjects with TACI, 40% of those with PACI, 33% of those with LACI, 30% of those with POCI, and 55% of the patients classified as uncertain were dead or dependent by 6 months after the stroke. Thirty-six percent (TACI), 9% (PACI), 4% (LACI), 10% (LACI), and 22% (uncertain) had died within 6 months of the stroke. After the clinical stroke syndrome and time between stroke onset and CT were taken into account, visible infarction was still associated with a poor outcome (dead or dependent: OR, 1.7; 95% CI, 1.3 to 2.3 [Table 2]; dead within 6 months: OR, 3.0; 95% CI, 1.8 to 5.2). There was no evidence that the influence of visible infarction on outcome was any different in TACI, LACI, PACI, POCI, or uncertain clinical stroke types.

In the multivariate analysis, which included and adjusted for all possible confounding clinical baseline prognostic variables with the use of the prediction model generated in the OCSP (Table 1), patients with a visible infarct were still more likely to be dead or dependent at 6 months, although this was of borderline significance (OR, 1.5; 95% CI, 1.0 to 2.0) (Table 2) or to have died within 6 months (OR, 2.4; 95% CI, 1.4 to 4.1). There were no significant interactions between the variables. Adjusting for the time between CT and onset of symptoms did not change the results.

**Discussion**

We have demonstrated that stroke patients with a visible infarct on their CT scan (even those few scanned late after the stroke) are more likely to be dead or dependent at 6 months than otherwise identical patients scanned at the same time after the stroke but whose scan does not show a recent infarct. In previous studies, the predictive value of a visible infarct was not clear because factors such as the time lapse from stroke onset or stroke severity, site, or type had not been taken into account. In other words, visible infarction might just have been a surrogate marker for stroke severity or time lapse rather than an independent indicator of poor prognosis. Some previous studies have concentrated on the effect of visible infarction within 6 hours or very soon after the stroke, which gives no information about the influence of visible infarction as a prognostic factor in the majority of patients who present at later times. In the present study, when time from stroke onset, stroke syndrome, and stroke severity were taken into account, visible infarction appropriate to the symptoms still increased the risk of a poor outcome. Thus, a LACI patient with a relevant visible infarct is more likely to have a poor outcome than a LACI patient with identical clinical features but a normal CT brain scan; similarly, for PACI, TACI, POCI, and uncertain stroke types, the presence of a relevant visible infarct on the CT scan carries an adverse prognosis.

Stroke is a clinical diagnosis, made on the basis of clinical features. Imaging with CT is used in patient management largely to differentiate between hemorrhagic and ischemic stroke and to exclude tumors and other nonvascular lesions that occasionally present with stroke-like symptoms. It was not possible to perform CT scans on all patients entering the

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**TABLE 2. Effect of Visible Infarction on 6-Month Outcome Alone and After Adjustment for Clinical Variables at Presentation and Time Lapse Between Stroke and CT Scan**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dead or Dependent</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Visible infarction alone (univariate analysis)</td>
<td>2.5</td>
<td>1.9–3.3</td>
</tr>
<tr>
<td>After adjustment for time from stroke to CT and stroke syndrome</td>
<td>2.2</td>
<td>1.3–3.3</td>
</tr>
<tr>
<td>After adjustment for OCSP baseline variables and time from stroke to CT</td>
<td>1.7</td>
<td>1.0–2.0</td>
</tr>
</tbody>
</table>

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**Figure 2.** Percentage of patients with a visible infarct in each of the stroke subtypes classified according to the OCSP on CT scans in different time periods after stroke onset. Only one person had a TACI and was scanned more than 21 days after stroke onset; this person had a visible infarction.
stroke registry; some had MR scans, some presented too late for it to be clinically worthwhile, and a very few (24/1302, 2%) died before the CT could be performed early after the stroke. However, the omission of these patients is unlikely to have biased the results of the present study because the number of missed scans was so small. Fewer patients scanned after 3 weeks had a visible infarct mainly because patients presenting late tend to have had milder strokes that are less likely to be visible on CT. The patients with severe strokes, like the TACIs, were all scanned earlier, and therefore more infarcts were visible overall in the first few weeks.

The observer reliability for detection of any infarct on the CT scan done days after the stroke is reasonable.\(^{9,14,15}\) The present study was concerned with patients presenting not only within the first 6 hours but at later times after the stroke as well, and it relied on a variety of readers (all of whom had a major interest in stroke) and two CT scanners. Most of the scans were not read with the reader blind to the symptoms, but a previous study suggested that prior knowledge of the symptoms was unlikely to introduce much bias.\(^{16}\) In any case, in the present study it was important to distinguish with certainty the relevant infarct from old irrelevant infarcts.

Multiple logistic regression statistical modeling is a powerful tool with which the independence of a group of variables, which may all be associated or interrelated with some other factor, can be tested. Examination of only one variable (eg, visible infarction) would not determine whether that variable was directly associated with a poor outcome or whether in fact the variable was associated with another feature of the stroke that more closely determined outcome. Thus, to begin to explore causation (not just association) requires determining which variables are closely linked with others and which are independently related to the outcome in question. Visible infarction is more frequent in TACI than in LACI or POCI patients and changes with time lapse from stroke. Thus, an allowance had to be made for both the OCSP classification and time lapse to test for the strength of association between visible infarction and outcome. Furthermore, the OCSP classification is not a stroke severity scale, and therefore a more refined statistical model had to be included to make allowance for stroke severity or we would not have determined the independent prognostic importance of visible infarction.

In conclusion, after all potential confounding factors were taken into account, it appears that visible infarction on CT at any time (up to 3 months) after stroke is associated with a poor outcome.

Appendix

The following variables were considered for inclusion in the multiple regression models used to produce the predictive model of Counsell et al.\(^{12}\) Variables from set 1 (see below) were considered for inclusion first, followed by the variables from set 2. The final model is shown in Table 1. Further details of the model are available from the authors on request.

Set 1 (simple clinical variables) includes age at time of stroke in years, sex, living alone before stroke, employed at time of stroke, modified Rankin score >2 before stroke, history of hypertension, known previous myocardial infarction, diabetes mellitus before stroke, known previous malignancy, seen by neurologist within 2 days of stroke onset, systolic blood pressure >160 mm Hg at baseline examination, systolic blood pressure <120 mm Hg at baseline examination, abnormal Glasgow Coma Scale eye score (<4) at examination, abnormal Glasgow Coma Scale motor score (<6) at examination, abnormal Glasgow Coma Scale verbal score (<5) at examination, poor arm power (unable to lift both arms to horizontal), poor leg power (unable to lift both legs off bed), and cannot walk without the help of another person (even with use of stick or Zimmer walking frame).

Set 2 (more detailed clinical variables) includes current smoker (smoked within 12 months of stroke onset), previous transient ischemic attack, any evidence of peripheral vascular disease, apoplectic onset (headache within 2 hours of onset or vomiting within 6 hours of onset or unconscious within 30 minutes of onset or meningism), cerebral bruit, cardiac failure or murmur, dysphasia, cognitive deficit (dyspraxia, neglect, sensory inattention, visuospatial dysfunction), visual field defect (hemianopia or visual inattention), tonic deviation of eyes to one side or gaze paresis, normal posterior fossa function, and proprioception normal in all four limbs.

References

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