TIA, RIND, minor stroke: a continuum, or different subgroups?

P J Koudstaal, J van Gijn, C W G M Frenken, A Hijdra, J Lodder, M Vermeulen, C Bulens, C L Franke, (for the Dutch TIA Study Group)

Abstract
The results of CT were studied prospectively in 606 patients with a transient ischaemic attack (TIA), 422 patients with a reversible ischaemic neurological deficit (RIND), and 1054 patients with a minor stroke, were all entered into a multi-centre clinical trial. CT scanning showed a relevant ischaemic lesion in 13% (95% confidence interval 10–16%) of TIAS, 35% (95% confidence interval 30–40%) of RINDs, and 49% (95% confidence interval 46–52%) of minor strokes (p < 0.00001). Even within the 24 hour margin, relevant infarcts occurred more often with longer attacks, but were still found in some patients with attacks lasting less than a minute. The type and location of the infarcts were similar in the three groups. These findings suggest that the differences between TIAS, RINDs, and minor strokes are quantitative rather than qualitative.

It is usual to classify patients with cerebral ischaemia according to the duration of the symptoms: (TIA) completely reversible symptoms, lasting less than 24 hours; RIND, also reversible, but with symptoms lasting up to six weeks; stroke, persisting symptoms or signs.

However, in a proportion of patients with the time course of a TIA, CT shows cerebral infarction in a corresponding area. For this reason, it has been suggested that TIAS, RINDs, and minor strokes should be regarded as a continuum rather than as strictly separated subgroups.

The proportion of cerebral infarction in patients with transient ischaemic attacks is unclear. Some authors did not find any infarcts, others have reported an incidence of up to 50%. It is also not known whether the type of infarction (small deep, cortical or borderzone) differs between patients with transient and those with persistent signs. Such qualitative differences might uncover a different pathogenesis. The only comparative study is that of Calandre et al, who studied 214 patients with transient or non-disabling cerebral ischaemia and found that cerebral infarcts were equally frequent in patients with TIAS and RINDs (25%), and that these occurred only slightly more often in patients with permanent handicap (35%). Disadvantages of this study were, however, that all patients with vertebrobasilar ischaemia were included, that focal dilatation of a ventricle or a cistern was interpreted as an ischaemic lesion, and that the authors did not specify the type of infarct in the three study groups.

We studied the CT findings of 2082 patients with ischaemic attacks of one cerebral hemisphere who were entered into a multi-centre clinical trial. Our aim was to assess the frequency, type, and location of cerebral infarction on CT in patients with a clinical diagnosis of TIA, RIND, or minor stroke.

Patients and methods
The Dutch TIA Trial is a multicentre clinical trial, which aims to investigate the protective effects of low-dose aspirin and atenolol in patients with transient ischaemic attacks (TIA), reversible ischaemic neurological deficits (RIND), or minor strokes. Background and design of the study have been described elsewhere. Patients with minor strokes were included in the study as long as they were still independent in most activities of daily life (Grade 3 or better on the modified Rankin scale).

Between 1 March 1986, and 1 March 1989 a total of 3150 patients were randomised. In 24 patients the diagnosis was evidently wrong at the time of randomisation (for instance, cerebral tumour, intracerebral haemorrhage, or vasculitis); these were excluded from the analysis. We also excluded 54 patients in whom a CT scan was not made, and 268 patients in whom the interval between the CT scan and the neurological symptoms was less than 24 hours (233 patients) or unknown (35 patients). Of the remaining patients we excluded 638 patients with symptoms suggesting ischaemia in the posterior fossa (at least one of the following: rotatory dizziness, nausea, problems with swallowing, diplopia, imbalance, and loss of direction on moving the limbs), and 84 patients with monocular blindness. The clinical data and CT scan findings in the remaining 2082 patients were analysed. Six hundred and six patients had suffered a TIA (symptoms completely reversible within 24 hours), 422 a RIND (symptoms lasting more than 24 hours, but completely reversed within six weeks), and 1054 a minor stroke (persisting symptoms or signs).

All CT scans were reviewed independently and blind by at least two neurologists or by one neurologist and a neuroradiologist. In case of disagreement, a third neurologist or neuroradiologist arbitrated. After this procedure the observers were given access to
cerebral infarction was not significantly different, however, from the mean for any of the intervals between symptoms and CT scanning (Goodness of fit test, p = 0.22).

Cerebral infarction and duration of attack

CT showed a relevant ischaemic lesion in 13% (95% confidence interval [CI] 10–16%) of TIAs, 35% (95% CI 30–40%) of RINDs, and 49% (95% CI 46–52%) of minor strokes (p < 0.000001). Multiple infarcts were found more often in stroke patients compared with those with TIAs and RINDs (11% versus 3, 4%, respectively; p < 0.000001). Irrelevant infarcts as the only abnormality on CT were equally common in the three groups (6, 8, and 7%, respectively; p = 0.68).

Figure 1 shows the frequency of a relevant cerebral infarct on CT according to the duration of the symptoms, subdivided into seven time categories: four subgroups within the first day, two in the first six weeks, and one group with persisting symptoms. Cerebral infarcts were found in each time category, even in three of 12 patients (not shown separately in the figure) with attacks lasting less than a minute. The longer the duration of the attack, the more often CT showed a relevant infarct (χ² = 219-30, df = 6; p < 0.000001). The increase in the frequency of infarcts with longer attacks was gradual and not at all related to the “boundaries” at 24 hours and six weeks.

Type of cerebral infarction

Figure 2 shows the type of infarct in patients with a TIA, RIND, or minor stroke. In all three groups infarcts were mostly small deep, followed by cortical and border-zone infarcts. Patients with a RIND had relatively more small deep infarcts (χ² = 8.19, df = 2; p = 0.02), but the absolute difference was very small.

Location of cerebral infarcts

In TIAs patients the cerebral infarcts were located more often in the left hemisphere (64%), whereas in the other two groups both hemispheres were equally involved (χ² = 6.28, p = 0.04). In patients with a relevant infarct on CT, the territory of the posterior cerebral artery was most frequently involved in patients with a minor stroke (18%, against 1% with TIAs and 8% with RINDs, (χ² = 20.44, df = 2; p = 0.00003). The site of symptomatic small deep lesions, within the region of the basal ganglia and internal capsule, was not different among patients with a TIA, RIND, or minor stroke (χ² = 7.85, df = 6; p = 0.79).

Discussion

Our study shows that relevant cerebral infarcts on CT can be found after any attack of cerebral ischaemia, regardless of its duration—even in attacks lasting less than a minute. A relevant cerebral infarct was found in 13% of TIAs, 35% of RINDs, and 49% of minor strokes. The incidence of infarction in patients with TIAs is strikingly similar to the 12% found in a recent population study, but somewhat lower.

Clinical details were assessed to determine the relevance of the CT scan abnormalities.

Cerebral infarcts were defined as well-defined, radiolucent lesions, and were subdivided into small, deep lesions, cortical and end-zone infarcts (superficial radiolucent areas, involving the cortex), and border-zone infarcts (wedge-shaped hypodensities in the boundary zone area between two major cerebral arteries, or between deep and superficial branches of the middle cerebral artery). Small deep infarcts were further subdivided according to their location: anterior limb of the internal capsule, genu, posterior limb, corona radiata, basal ganglia, thalamus, or other. The scans were classified as showing a relevant infarct only, an irrelevant infarct only, or both relevant and irrelevant infarcts, dependent on the clinical symptoms.

The data were analysed by means of the Statistical Package for the Social Sciences (SPSS) and Epistat statistical software. Yates' corrected chi-square test was used where appropriate.

Results

Thirty six per cent of all CT scans showed a relevant infarct. Patients with RINDs and minor strokes were scanned slightly earlier on average than TIAs (χ² = 46, df = 12; p = 0.00006). The proportion of patients with
than most other studies. Yet the mere presence of cerebral infarcts definitely links TIAa to strokes. Infarcts were predominantly of the lacunar type in all three groups. The over-representation of small deep infarcts in the stroke group (about 70%, against 25% in population studies) should be attributed to selection bias, as many patients with cortical infarcts were too severely handicapped to qualify for the clinical trial of secondary prevention from which our comparisons were made.

Only minor qualitative differences between the three groups were found. Firstly, patients with RINDs showed a relatively high proportion of small deep infarcts. Owing to the large number of patients in our study, the difference, although very small, just reached statistical significance. Secondly, in patients with minor strokes the posterior cerebral artery was more frequently involved, but no other differences in location were found. Again, this probably reflects the selection criteria for the study, as patients with middle cerebral artery infarcts are more often dependent on others. The overwhelming similarity of both the type and the location of the cerebral infarcts among TIAa, RINDs, and minor strokes suggests that the differences are quantitative rather than qualitative and support the notion that the three groups should be regarded as a continuum rather than as different subgroups.

Before discarding terms such as TIA, RIND, and stroke, we need more information on the prognosis in each of these groups. Aggregate data from different studies suggests a similar outcome in the three groups, and this has recently been confirmed by a population study. In contrast, others have found a better outcome for stroke patients than for patients with TIAa. We do not know therefore whether long attacks herald more harm in the future than short ones, or whether completely reversible attacks are less often followed by disabling stroke than those with residual deficits. It is also not known whether patients with transient signs, but with a cerebral infarct on CT, have an increased risk of major stroke. These questions are currently being investigated in the Dutch TIA trial, as an adjunct to the main questions regarding the efficacy of low-dose aspirin and of atenolol.