6. Imaging in TIA
6.1. What type of brain imaging should be used in suspected TIA
6.2. Which patients with suspected TIA should be referred for urgent brain imaging?

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type Evidence level</th>
<th>Numb of patients</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow-up</th>
<th>Outcome measures</th>
<th>Source of funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redgrave JN, Coutts SB, Schulz UG et al. Systematic review of associations between the presence of acute ischemic lesions on diffusion-weighted imaging and clinical predictors of early stroke risk after transient ischemic attack. Stroke. 2007; 38(S):1482-1488. Ref ID: 2627</td>
<td>Systematic Review last search October 2006 2++</td>
<td>N=12 42 (N=19 studies)</td>
<td>Studies on patients with TIA comparing the results of those with positive and negative DWI Mean age range 58.5 to 73 yrs, male range 44 to 91% Delay to DWI: 6 studies less than 24 hrs, 9 studies greater than 24 hrs, 4 studies not reported.</td>
<td>DWI positive (range of positive scans 16 to 67%)</td>
<td>DWI negative</td>
<td>NA</td>
<td>Clinical and demographic prognostic indicators</td>
<td>None reported</td>
</tr>
</tbody>
</table>
Effect
Time to scan less than 24 hrs
There was a positive association between a positive DWI and motor weakness (DWI + vs – 27/38 vs 52/114; OR 3.49; 95%CI 1.58 to 7.71; p=0.006), and dysphasia (10/34 vs 14/104; OR2.95 (95%CI 1.17 to 7.48; p=0.04).
There were no associations between a positive DWI and age ≥ 60 yrs (NS), previous hypertension (NS), current raised blood pressure (NS), diabetes (NS), dysarthria (NS), duration of symptoms ≥ 60 mins (NS), atrial fibrillation (NS) or ipsilateral carotid stenosis ≥ 50% (NS).

All studies
There was a positive association between a positive DWI and motor weakness (DWI + vs DWI – 151/214 vs 254/505; OR 2.20; 95%CI 1.56 to 3.10; p<0.001), dysphasia (67/220 vs 102/505; OR 2.25; 95%CI 1.57 to 3.22; p<0.001), dysarthria 43/133 vs 81/379; OR 1.73; 95%CI 1.11 to 2.68; p=0.03), duration of symptoms ≥ 60 mins (184/330 vs 321/695; OR 1.50; 95%CI 1.16 to 1.96; p=0.004), atrial fibrillation (55/249 vs 42/518; OR 2.75; 1.78 to 4.25; p<0.001) and ipsilateral carotid stenosis ≥ 50% (73/271 vs 77/563; OR 1.63; 95%CI 1.34 to 2.76; p=0.001).
There were no associations between positive DWI and age ≥ 60 yrs (NS), previous hypertension (NS), current raised blood pressure (NS) or diabetes (NS).

Calvet D.
Management and outcome of patients with transient ischemic attack admitted to a stroke unit. Cerebrovascular Diseases. 2007; 24(1):80-85. Ref ID: 236

<table>
<thead>
<tr>
<th>Calvet D.</th>
<th>Prospective cohort 3</th>
<th>N=203</th>
<th>Patients admitted to a stroke unit within 48 hrs of symptom onset with a diagnosis of probable or possible TIA</th>
</tr>
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<tbody>
<tr>
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<td>Patient population: Median time from TIA onset to first medical management in the emergency departments 180 min (IQR 90 to 540 mins). Median time from TIA onset to stroke unit admission 12 hrs (5 to 25). Media time from TIA onset to MRI 20 hrs (8 to 29). Acute ischemic lesions on DWI 64/203 (32%). Mean age 61 yrs, 61% male, previous TIA 9%, previous stroke 8%, motor weakness 54%, large-artery atherosclerosis 18%, small vessel disease 12% 147/207 (72%) antiplatelet therapy only</td>
</tr>
<tr>
<td>Routine investigations included MRI, 12-lead EKG, prolonged 3-lead cardiac monitoring (93%), Doppler ultrasound, ECG.</td>
<td>NA</td>
<td>3 months</td>
<td>Risk of stroke</td>
</tr>
</tbody>
</table>
Effect
The absolute risk of ischemic stroke was 2.0% (95%CI 0.1 to 3.9) at 48 hrs, 2.5% (0.3 to 4.7) at one week, and 3.5% (1.0 to 6.1) at 3 months.

The risk of ischemic stroke or TIA was 2.5% (0.3 to 4.6) at 48 hrs, 5.0% (2.0 to 8.0) at one week, and 9.9% (5.6 to 14.1) at 3 months.

The Cox analysis showed that presence of DWI abnormalities (HR 10.3; 95%CI 1.2 to 86.7; p=0.032) was independently associated with the risk of stroke at three months.


Prospective cohort 3
N=184
Patients with TIA (N=152)
Patients with amaurosis fugax (N=32) (results not reported)
Mean age 73 yrs*, male 44%* and mean duration of symptoms 179 minutes
*Significant difference at baseline between patients with a positive and negative scan
CT
Observer blind to clinical data
The median time interval between the last TIA and the scan was 11 days.
NA
Mean 3.7 yrs
CT findings
Medical Research Council and Chest, Heart and Stroke Association

IMAG1:
*CT findings
Of the 120 patients scanned, 93 (78%) presented with carotid attacks, 18 (15%) with vertebrobasilar attacks and 9 (8%) uncertain location. 32/120 patients had a positive scan. 14/320 (12%) were judged to be related to the clinical symptoms.
*CT and risk factors

There were no statistical factors associated with a positive scan including age, mean number of attacks, mean duration of attacks, duration greater than or equal to one hour, hypertension, ischemic heart disease, diabetes and atrial fibrillation.

7/32 patients with an ischemic lesion died during follow-up compared with 20/88 with no ischemic lesions (NS).


Retrospective cohort 3

N=322

Patients with TIA.

Patient population: median age 73 yrs, 50% male, TIA symptoms > 10 mins 84% and 20% admitted to hospital

Patients with positive CT scan (N=322)

(within 48 hrs of their presentation and within the first 24 hrs in 96%)

The scans were reviewed by physicians blinded to patient characteristics and outcome

Patients with negative CT scan (N=156)

Time to scan as for positive group

90 days

IMAG1: Imaging findings

IMAG2: Independent predictors of stroke/ mortality

None reported

Effect

*CT results

Of the CT scans performed with 48 hrs, no abnormality was present in 148 (46%) of patients. There was evidence of new infarction in 13 (4%), old infarction in 69 (21%) and periventricular white matter disease in 75 (23%). Cerebral atrophy was reported in 96 (30%) and vascular calcifications in 8 scans (2.5%). In the 13 patients with new infarctions, all of their symptoms had resolved in 24 hrs. All new infarctions were located on the side of the brain appropriate to the symptoms manifested.

*Risk of stroke at 90-day follow-up

Stroke occurred in 5/13 (38%) patients. Evidence of a new infarction statistically increased the odds of having a stroke within the next 90-days (adjusted OR 4.06; 95%CI 1.16 to 14.14; p=0.028).

Periventricular white-matter disease, old infarctions, atrophy or vascular calcification were not statistically associated with an increased risk of stroke.

<table>
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<tr>
<th>Effect</th>
<th>IMAG1:</th>
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<tbody>
<tr>
<td></td>
<td><em>CT</em> 114/176 (64.8%) patients with high-grade stenosis and presenting with TIA had negative CTs. Appropriate brain infarctions were detected in 50 patients (28.4%), and of these 18 (36.0%) had bilateral lesions. The remaining 12 patients had infarcts not relating to their symptoms (excluded from analysis).</td>
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<td></td>
<td>11 patients had cortical infarcts only, 10 had deep infarcts only and 22 had subcortical infarcts.</td>
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<td></td>
<td><em>Relationship between clinical variables and a positive scan</em>  Patients with a positive CT scan were older than patients with a negative scan (66.6 vs 63.1 yrs).</td>
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<td></td>
<td>IMAG2:</td>
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<tr>
<td></td>
<td><em>Follow-up</em> 24 patients (12 in the infarction-absent and 12 in the infarction-present group) had ipsilateral strokes, and six patients (two from the infarction-absent and four from the infarction-present group).</td>
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<tr>
<td></td>
<td>The univariate (adjusted) analysis revealed no statistical relationship between CT infarction and the risk of stroke.</td>
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<tr>
<td>Prospective cohort 3</td>
<td>N=564</td>
</tr>
<tr>
<td>Patients with TIA during the 30 days prior to admission. 350/564 patients were evaluated ≤ 4 weeks after the ictus</td>
<td>CT scan (90% contrast enhanced)</td>
</tr>
<tr>
<td>IMAG1: Imaging findings</td>
<td>IMAG2: Independent predictors of stroke/mortality</td>
</tr>
</tbody>
</table>

**Effect**

**IMAG1:**

A history of prior stroke statistically increased the chances of finding a cerebral infarction on CT (OR 5.11; p=0.0001).

After controlling for stroke history, both age and sex were statistically associated a CT-verified infarct. The odds of finding a infarct on CT by 50% for each 10 yrs of age (p=0.003) and were 2.17 times greater for males than females (p=0.013).

There were statistical associated between CT-verified lesions and ethnicity, smoking history, hypertension, diabetes, ischemic cardiac disease, TIA distribution or admission date.

**IMAG2:**

A proportional hazards analysis, adjusted for age, race, sex, smoking history, ischemic cardiac disease, hypertension, diabetes, TIA distribution and admission date and clinical history of stroke indicated that CT-verified infarction increased the risk of death by 70% (p=0.035). In contrast, after controlling for CT results, a clinical history of stroke increased the risk of death by 3% (p=0.924). There was no evidence that the effect of CT-verified infarction differed in patients with and without a clinical history of stroke (p=0.27).

98 patients evaluated by CT patients were followed-up. The odds of death attributed to stroke were 2.19 times greater for patients with CT-verified infarcts than those without (N=10 38.5% vs 2.2%). This was no longer significant after adjusting for clinical history of stroke.

<table>
<thead>
<tr>
<th>Fazekas F, Fazekas G, Schmidt R et al.</th>
<th>Prospective cohort 3</th>
<th>N=62</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient with TIA</td>
<td>MRI (N=62) Contrast enhanced MRI (N=45)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Patient population: mean age 61 yrs

Time to scan not specified

Interpreted by one examiner blinded to clinical information

**Effect**

*MRI*

50/62 (81%) patients demonstrated some evidence of a focal cerebral lesion. Acute infarcts related symptoms were detected in 19/62 (31%) patients. Old infarcts and/or lacunes were present in 15/24 (63%) patients with previous cerebrovascular attacks and seen in 17/38 (45%) patients previously asymptomatic. The majority of these were cortical 14/19 (73.7%) and were smaller than 1.5 cm 13/19 (68.4%). Contrast enhancement helped to delineate of an acute lesion in 2/45 (4%).

*Clinical findings and potential causes for cerebrovascular attack between TIA patients with and without acute infarction*

There was no statistical difference between the time to scan (mean 3.5 days) and symptom duration (mean 120 minutes) in patients with, and those without, an acute lesion. The only clinical variable associated an acute lesion was in patients with an identifiable vascular or cardiac aetiology (OR 5.2; 95%CI 1.6 to 17.3)


<table>
<thead>
<tr>
<th>Prospective cohort 3</th>
<th>N=31 27 (N=99 7 TIA N=21 30 minor stroke)</th>
<th>Patients with TIA or minor stroke (grade 3 or better on the mRS)</th>
<th>CT</th>
<th>NA</th>
<th>Mean 2.6 yrs</th>
<th>IMAG2: Independent predictors of stroke/ mortality</th>
<th>Netherlands Heart Foundation and pharmaceutical companies</th>
</tr>
</thead>
</table>

**Effect**

*Mortality and Stroke*

302/3127 (9.7%) patients died, 212/302 (70.2%) died from vascular causes. 200/3127 (6.4%) died had a major cardiac event. 469 (15%) had the combined outcome of nonfatal stroke, nonfatal myocardial infarction or vascular death.
**Predictors of death and vascular events**

Independent predictors of the combined outcome vascular death, stroke or myocardial infarction were a border zone infarct (HR 2.1; 95%CI 1.3 to 3.5), any other infarct (1.3; 95%CI 1.1 to 1.5) and white matter hypodensity (HR 1.4; 95%CI 1.1 to 1.8). The following CT findings were independent predictors of new stroke (fatal and nonfatal); border zone infarct (HR 3.5; 95%CI 2.0 to 6.0), any other infarct (HR 1.6; 95%CI 1.2 to 2.0) and white matter hypodensity (HR 1.6; 95%CI 1.2 to 2.2).


<table>
<thead>
<tr>
<th>Murros KE, Evans GW, Toole JF et al.</th>
<th>N=284</th>
<th>Patients who had a TIA within the previous 30 days and with no history of previous stroke Carotid TIAs 179/284, 95/284 vertebrobasilar and 10/284 involving both territories</th>
<th>Blinding not reported</th>
<th>NA</th>
<th>NA</th>
<th>CT findings</th>
<th>Supported by USPHS and the C.C Smith Stroke Research Fund</th>
</tr>
</thead>
</table>

*CT findings and risk factors (after controlling for carotid stenosis)*

There was no statistical relationship between a positive CT and age, sex, diabetes, hypertension, TIA location, smoking, cardiac disease and ethnicity.

**Oppenheim C, Lamy C, Touze E et al.** Do transient ischemic attacks with diffusion-weighted imaging abnormalities...

(N=33)

Delay from TIA onset to follow-up scan mean 10.6 months

For patients with a positive DWI, a single neurologist recorded the number of lesions and the affected arterial territory. Blinded to the results of the follow-up scan, a single observer then analysed each DWI lesion separately. On each follow-up scan a single neurologist looked for signal intensity changes or atrophy.

n 11.5 months

Effect

**IMAG1:**

33/103 patients had an initial positive MRI scan. Lesions were solitary in 17/33 patients and multiple in 16/33 patients, with a total of 59 lesions. Lesions were located in the anterior circulation in 22/33 patients, in the posterior circulation in 7/33 patients and involved in both for 4/33 patients. 44 lesions (74.5%) were cortical and 15 (25.4%) were deeply located. Of the latter, there were seven small lesions (volume 0.74) and ADC was moderately decreased (rADC = 82). There was a positive relation between rADC (r=8; p<0.001) in contrast ADC or rADC were negative correlated with initial DWI lesion volume (r=-0.47 and -0.52, respectively; p<0.001).

Follow-up MR imaging

MRI detected no permanent injury in 7 cases and identified a subsequent infarct in regions corresponding to the original to the original DWI abnormalities in 26 (79.6%) of patients. Of the 59 lesions initially identified on DWI, 45 (76.3%) were associated with permanent injury on follow-up MR imaging. If only lesions initially imaged within 12 hrs (n=24) or 24 hrs (n=36) were considered, the rates of permanent injury on follow-up MR imaging 83.3% and 78%, respectively.

The DWI volume was statistically larger (0.91 vs 0.21 cm³, p=0.003) and the ADC values lower (79 vs 91, p=0.001) in lesions with subsequent infarct than in those that were fully reversible.
<table>
<thead>
<tr>
<th>Prabhakaran S, Chong JY, Sacco RL.</th>
<th>Retrospective cohort</th>
<th>N=196</th>
<th>Patients with TIA or stroke</th>
</tr>
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<tbody>
<tr>
<td>TIA</td>
<td>N=146</td>
<td>Exclusion criteria: No MRI within 48 hrs</td>
<td></td>
</tr>
<tr>
<td>Acute ischemic stroke and with infarction (DWI confirmed)</td>
<td>N=50 (from 921 admissions)</td>
<td>TIA patients: 37/146 (25%) had lesions on DWI and 109/146 (75%) normal DWI.</td>
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<tr>
<td>Patient population: TIA with normal DWI results – mean age 67.4, male 33%, white 35%, prior TIA 32%, motor symptoms 39%, mean NIHSS score at 24 hrs 0*, duration of TIA &gt; 1 hr 27%, moderate to severe stenosis or occlusion 15%, mean length of stay 3 days*</td>
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<tr>
<td>TIA with abnormal DWI results - mean age 69.5, male 8%, white 32%, prior TIA 11%, motor symptoms 68%, mean NIHSS score at 24 hrs 0*, duration of TIA &gt; 1 hr 60%, moderate to severe stenosis or occlusion 49%, mean length of stay 5 days*</td>
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<td>Ischemic stroke - mean age 66.5, male 44%, white 28%, prior TIA 14%, motor symptoms 76%, mean NIHSS score at 24 hrs 6*, moderate to severe stenosis or occlusion 40%, mean length of stay 7 days*</td>
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</table>

| TIA patients with normal DWI results | N=109 |
| TIA patients with abnormal DWI results (TSI) | N=37 |
| Ischemic stroke | N=50 |

<table>
<thead>
<tr>
<th>Redgrave JN, Schulz UG, Briley D et al.</th>
<th>Prospective</th>
<th>N=200</th>
<th>Patients referred to a TIA and minor stroke clinic (all presented via their GP). All were scanned on the same day (all ≥ 3 days after the most recent TIA).</th>
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</thead>
<tbody>
<tr>
<td>Patients with positive DWI</td>
<td>N=31</td>
<td></td>
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<tr>
<td>Negative DWI</td>
<td>N=169</td>
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</table>

<table>
<thead>
<tr>
<th>Effect</th>
<th>Rate of recurrent TIA or stroke</th>
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<tbody>
<tr>
<td>3/109 (2.8%) of TIA patients without lesions on DWI had a recurrent TIA and there were no strokes. Of the 50 ischemic stroke patients, one (2.0%) had a recurrent ischemic stroke (NIHSS score increased from 5 to 9). In contrast, there were 4/37 recurrent TIAs and 6/37 ischemic strokes (NIHSS 3 to 13) in TIA patients with infarction.</td>
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</table>

Logistic regression analysis (adjusted) showed that TIA with infarction was an independent predictor of recurrent TIA or stroke (OR 11.2; p<0.01). When only patients with mild strokes or TIA (NIHSS < 5) were included (N=184), TIA with infarction was an independent predictor of inpatient recurrence (OR (adjusted) 10.6; p=0.01).

| Patient population: 106 male, mean age 71.2 yrs |

Effect MRI

 MRI scans were performed at a median of 15 days (IQR 10 to 27) after the most recent TIA.

There was no statistical difference in the median delay to scan in patients with positive versus negative DWI.

Factors associated with a positive DWI versus negative DWI:
- Older age (75.6 vs 70.4; p=0.02)
- Longer duration of symptoms (5.3 vs 2.7 hrs; p=0.02)
- Dysarthria (48 vs 23%; OR (adjusted) 3.16; 95%CI 1.43 to 7.01; p=0.005)
- Atrial fibrillation (23 vs 5%; OR (adjusted) 5.78; 95%CI 1.91 to 17.50; p=0.002)

There was no statistical association for:
- Motor weakness
- Prior TIA/CVA
- Magnetic Resonance Angiography >50% symptomatic carotid stenosis
There was a statistical association between the presence of a positive DWI and increasing ABCD score (adjusted $p=0.03$) and California scores (adjusted $p=0.03$). For example, the proportion of patients with a positive DWI with an ABCD score $\geq 5$ was 25% compared with 75%.

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<tbody>
<tr>
<td>Prospective cohort 3</td>
<td>N=337</td>
<td>Patients with TIA or nondisabling ischemic stroke (Rankin grade 3 or less) (patients were part of a trial looking at aspirin in the prevention of stroke) Exclusion criteria: identifiable causes of ischemia except for arterial thrombosis or thromboembolism</td>
<td>CT All scanned within one month of the index event Images reviewed by two observers blinded to the clinical data</td>
<td>NA Up to 40 months</td>
<td>IMAG1: CT findings The Netherlands Heart Foundation</td>
<td></td>
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</tbody>
</table>

**IMAG 1:**
*CT*
CT showed diffuse hypodensity of the cerebral white matter (HWM) in 337/3017 (11%) of patients with a TIA or nondisabling stroke. The HWM was mild in 133 patients (4%) and moderate to severe in 204 patients (7%). The HWM was the only abnormality in 180 patients, while in the remaining 157 patients there was also evidence of an infarction. Patients with HWM differed with those with normal white matter, they were older (71.4 vs 64.4 yrs; $p<0.001$), a higher prevalence of hypertension (50 vs 41%; $p=0.003$) and were more likely to have a lacunar infarct (40% vs 27%; $p=0.006$)

**IMAG 2:**
During the study period, 51 patients (15%) with HWM had a stroke and in 217 (8%) with normal white matter.

*Predictors of stroke*
Hazard ratios (adjusted) showed that the presence HWM was the only independent factor associated with risk of stroke (HR 1.6; 95%CI 1.2 to 2.2; $p=0.004$). The strength of the relationship between HWM and stroke in subgroups differed only in those younger or older than 70 yrs (HR 1.7; 95%CI 1.3 to 2.4; $p=0.01$) respectively ; $p=0.01$) and in those with or without diabetes (HR 1.9; 1.4 to 2.6; $p=0.05$)