In recent years, it has become clear that the risk of stroke after a transient ischemic attack (TIA) or minor ischemic stroke is higher than was previously supposed, with consistent reports of 7-day stroke risks of up to 10%,1-4 and other evidence of the very short time-window for prevention of stroke after a TIA.5 However, patients with TIA and minor stroke are a highly heterogeneous group in terms of symptoms, risk factors and underlying pathology, and the early risk of recurrent stroke is likely to vary between different clinical and etiological subtypes. In order to appropriately target secondary prevention, we therefore need reliable data on risk in particular subgroups and ideally in individuals. Recent studies have provided some useful data, although many important issues are still unresolved.

There is good evidence that the presenting clinical features of a TIA provide considerable prognostic information. Johnston and colleagues identified 5 risk factors independently associated with a higher 3-month risk of recurrent stroke in a large emergency department–based TIA cohort: age >60 years (OR=1.8; 95% CI, 1.4 to 2.9), symptom duration >10 minutes (2.3, 1.3 to 4.2), weakness (1.9, 1.4 to 2.6), speech impairment (1.5, 1.1 to 2.1), and diabetes mellitus (2.1, 1.1 to 2.7).1 A simple index with 1 point for each risk factor was useful in estimating risk at 3 months, which varied from 0% in patients with no risk factors to 34% in those with 5 risk factors, and also differentiated between risk groups during the first few days after the TIA.1 Isolated sensory or visual symptoms were associated with a low risk of stroke, and sex, ethnicity, previous diagnoses of coronary artery disease or hypertension, current cigarette smoking, antiplatelet or anticoagulant-use at presentation and presentation blood pressure did not predict early stroke.1,6

Rothwell and colleagues studied predictors of stroke during the 7 days after a TIA in 2 independent population-based studies and derived and validated a prognostic score specifically for this very early risk.7 The Table compares the regression model for the 7-day stroke risk derived from the population-based studies7 with the similar model for 90-day risk of stroke derived by Johnston and colleagues.5 The independent predictors are remarkably similar, the main difference being in the size of the hazard ratios for 7-day risk versus 90-day risk.

These risk models clearly demonstrate that the early risk of stroke after a TIA is highly predictable. The models will no doubt be further refined, but the simple scores developed thus far can already be used in routine clinical practice. Rothwell and colleagues developed the 6-point “ABCD” score (Age ≥60 years = 1; Blood pressure: systolic >140 mm Hg and/or diastolic ≥90 mm Hg = 1; Clinical features: unilateral weakness = 2, speech disturbance without weakness = 1, other = 0; Duration of symptoms in minutes: ≥60 = 2, 10 to 59 = 1, <10 = 0), which was highly predictive of the 7-day risk of stroke in 2 independent validation cohorts.7 In a population-based cohort of all referrals with suspected TIA, 19/20 early recurrent strokes occurred in 27% of the patients with a score ≥5: 7-day risk was 0.4% (95% CI, 0 to 1.1) in 274 (73%) patients with a score <5, 12.1% (4.2 to 20.0) in 66 (18%) with score=5, and 31.4% (16.0 to 46.8) in 35 (9%) with score=6. In a hospital-referred weekly clinic cohort, all patients who had a stroke before their scheduled appointment (n=14, 7.5%) had a score of ≥4.7

Weakness or speech disturbance was associated with an increased risk of stroke at 3 months in another study of prognosis after TIA,8 and a recent study of predictors of stroke during the first year after TIA identified hypertension, diabetes and increasing age as independent risk factors but did not collect data on the nature of the presenting symptoms.4

Early risk of stroke after a TIA or minor stroke is also related to the vascular territory of the presenting event. For example, in keeping with the lower long-term risk of stroke after monocular TIs versus carotid territory cerebral TIs,9 the early risk of stroke after monocular events is also low. Posterior circulation territory events, which account for ≈25% of all TIs, have also been thought to have a good prognosis and are often investigated and treated less rigorously than carotid territory events. However, recent evidence suggests that there are no major differences in long-term prognosis and that the early risk of stroke is, in fact, higher after posterior circulation territory events.10 In a meta-analysis of cohort studies in which risks could be compared, studies that recruited during the acute phase after the pres-
Prognostic Model for the 7-day Risk of Stroke in Patients With TIA Derived From Population-Based Studies of TIA in Oxfordshire, UK (Oxfordshire Model) and Equivalent Model for the 90-day Risk of Stroke Derived From an Emergency Department Cohort of Patients With TIA in the USA (California Model)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Oxfordshire Model</th>
<th></th>
<th>California Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥60 y</td>
<td>2.57 (0.75–8.81)</td>
<td>1.8 (1.1–2.7)</td>
<td></td>
</tr>
<tr>
<td>Systolic BP&gt;140 mm Hg or Diastolic BP&gt;90 mm Hg</td>
<td>9.67 (2.23–41.94)</td>
<td>5.02 (1.37 to 18.3; P=0.015)</td>
<td></td>
</tr>
<tr>
<td>Clinical features</td>
<td></td>
<td>5.02; 95% CI, 1.37 to 18.3; P=0.015</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>Unilateral weakness</td>
<td>6.61 (1.53–28.50)</td>
<td>4.39 (1.36–14.22)</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>Speech disturbance without weakness</td>
<td>2.59 (0.50–13.56)</td>
<td>1.5 (1.1–2.1)</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>≥60 min</td>
<td>6.17 (1.43–26.62)</td>
<td>6.17 (1.43–26.62)</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>10–59 min</td>
<td>3.08 (0.64–14.77)</td>
<td>3.08 (0.64–14.77)</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>&lt;10 min</td>
<td>1</td>
<td>1</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4.39 (1.36–14.22)</td>
<td>4.39 (1.36–14.22)</td>
<td>&lt;0.001, 95% CI, 0.7 to 0.8; P=0.0001</td>
</tr>
</tbody>
</table>

There is also evidence that the early risk of stroke depends on the underlying causal pathology. For example, a recent meta-analysis of data from 1709 patients in 4 population-based studies of stroke showed that the risks of recurrent stroke were 4.0% (95% CI, 0.2 to 7.8) at 7 days and 12.6% (5.9 to 19.3) at 30 days in patients with large artery atherosclerotic etiology compared with 0% and 2% (0 to 4.2), respectively, in patients with lacunar stroke. Although documented large artery atherosclerosis accounted for only 14% of the 1709 initial strokes, this group represented 37% of the recurrences at 7 days. It should be stressed, however, that subtype differences are likely to be less marked in patients presenting with TIA only, where for example some patients with underlying small vessel disease can have a very high risk of early stroke. Nevertheless, the high risk of stroke in patients with large artery atherosclerosis is likely to be generalizable. A recent population-based study of prognosis of patients with TIA and ≥50% symptomatic carotid stenosis reported risks of stroke in the region of 20% during the 2 weeks before endarterectomy, and other studies have highlighted the high risk of stroke if endarterectomy is delayed, and the rapid fall-off in benefit with time since event in patients who get to surgery.

Brain imaging also appears likely to be of prognostic value. The presence of infarction on computed tomography (CT) brain scanning in patients with TIA or minor stroke has been found to be associated with an increased risk of stroke recurrence in the medium and long term, and a recent study of TIA patients who had CT scans performed within 48 hours of their clinical event showed that new infarction on CT was potentially highly predictive of recurrent stroke (OR=4.06; 95% CI, 1.16 to 14.14; P=0.028). However, diffusion-weighted MRI (DWI) is of greater clinical usefulness, and also appears to be of similar prognostic value. In a recent study of DWI in patients with TIA, the combination of abnormalities on DWI and symptoms lasting ≥1 hour was an independent predictor of further cerebral ischemic events (OR=5.02; 95% CI, 1.37 to 18.3; P=0.015). Another study reported an interaction between the presence of an acute lesion on DWI and evidence of a vessel occlusion, with a 32.6% risk of recurrent stroke at 90 days in those patients with both an ischemic lesion and an occlusion. Another study of 119 patients with nondisabling stroke who had DWI performed within 24 hours of symptom onset showed that the presence of multiple acute cerebral infarcts on DWI was an independent predictor of stroke recurrence, vascular events and death compared with a single acute infarct only.

Brain imaging with CT or DWI could therefore be a useful prognostic tool, but further studies are required to determine whether the presence of an acute ischemic lesion predicts stroke independently of the simple clinical characteristics in the risk scores. For example, focal weakness, speech disturbance and symptoms lasting ≥1 hour have all been associated with acute ischemic lesions on DWI in patients with TIA. Large prospective studies are required in which detailed data on the clinical characteristics, event characteristics, time since event, and results of brain and vascular imaging are combined and the optimal prognostic strategy determined. Experience with prognostic modeling in patients with recently symptomatic carotid stenosis suggests that all of these different elements might well be independently predictive of outcome. Detection of cerebral microemboli might also be of value in certain subgroups, and research is required to determine whether newer technologies, such as biomarkers of cerebral ischemia and molecular imaging of the cerebral vessels, can add additional clinically useful information.

In conclusion, the early risk of stroke after a TIA or minor stroke is related to the nature of the initial event, including both the type of symptoms and the vascular territory, as well as to the underlying etiology and the appearances on brain imaging. Simple risk scores to predict stroke during the first few days after a TIA have been developed and will allow primary care and other front-line physicians to identify which of the patients in whom they suspect a diagnosis of TIA should be referred-on for assessment as an emergency.
Further research will allow the results of acute brain and vascular imaging and other technologies to be incorporated into such scores, where appropriate, so that physicians can make treatment decisions based on as reliable and accurate a knowledge of prognosis as possible. Finally, all stroke physicians need to be aware of the limited public recognition of the symptoms of TIA and of the widespread lack of appreciation of the need to seek medical attention urgently.27 The simple risk scores will allow the necessary public education to be focused on the specific symptoms and characteristics of TIs that indicate a very high early risk of stroke.

References
2. Lovett J, Dennis M, Sandercock PAG, Bamford J, Warlow CP, Rothwell PM. The very early risk of stroke following a TIA. Stroke. 2003;34:e138–e140.

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