Acute stroke is a leading cause of death and due to fears of haemorrhagic complications. The advent of thrombolytic therapy for acute ischaemic stroke arguably represents the most important advance in modern neurology. 

**Table 1 | The SEDAN score**

<table>
<thead>
<tr>
<th>Item</th>
<th>Value</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood sugar</td>
<td>≤8.0 mmol/l</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(≥14.4 mg/dl)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.1–12.0 mmol/l</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(≥145–216 mg/dl)</td>
<td></td>
</tr>
<tr>
<td>Early ischaemic signs on CT</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Hyperdense artery sign</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Age</td>
<td>≤75 years</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;75 years</td>
<td>1</td>
</tr>
<tr>
<td>NIH Stroke Scale score</td>
<td>0–9 points</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥10 points</td>
<td>1</td>
</tr>
</tbody>
</table>

To minimize risk of haemorrhagic transformation after rtPA, the clinician would hope to identify patients at particularly elevated risk and either exclude them from treatment or take measures to mitigate risk. Patient characteristics such as age and stroke severity associate strongly with haemorrhagic risk. Several investiga-tive groups, including the original National Institute of Neurological Disorders and Stroke (NINDS) tPA Stroke Study Group, have published lists of variables that correlate with haemorrhagic risk. A few groups have attempted to distill these lists into digestible scoring systems that could prove useful at the bedside. One such system, the SEDAN score, was recently presented by Daniel Strbian and colleagues in *Annals of Neurology*. Scoring systems for any aspect of clinical medicine face substantial hurdles. First, the derivation of the scoring system must be rigorous, and must adhere to accepted clinimetric standards. Scoring systems derived from expert consensus may overlook critical variables, and overestimate or underestimate their relevance. Use of a large number of patients and a stepwise or other logistic regression approach usually yields not only all the critical variables but also some estimate of their relative weight in determining the outcome of interest. A second hurdle is the need for rigorous validation of the scoring system. No regression analysis proves a relationship—only prospective validation in a second large data set serves to validate the predictive value of the scoring system.

Strbian *et al.* successfully cleared the key hurdles, using a rigorous approach in a derivation cohort (974 patients with ischaemic stroke who received intravenous thrombolysis at the Helsinki University Central Hospital), followed by a validation cohort (828 stroke patients from three Swiss cohorts). The SEDAN score—blood Sugar, Early ischaemic changes, HyperDense artery sign, Age, and NIH Stroke Scale (NIHSS) score—is quite simple and easily determined from data that always should be rigorous, and must adhere to accepted clinimetric standards. To derive the scoring system must be rigorous, and must adhere to accepted clinimetric standards.

Patrick D. Lyden

Despite the proven favourable risk–benefit ratio, thrombolytic therapy for acute stroke is perceived to carry a grave risk. A simple risk-rating system, the SEDAN score, allows clinicians to quantify elevated risk. Whether effective thrombolytic therapy should be withheld from any particular patient requires further study, including randomized trials of patients with elevated risk scores.

**STROKE**

Haemorrhage risk after thrombolysis—the SEDAN score

The advent of thrombolytic therapy for acute ischaemic stroke arguably represents the most important advance in modern neurological therapeutics. Wide dissemination of this therapy lags, however, in part due to fears of haemorrhagic complications. Acute stroke is a leading cause of death and the number one cause of disability globally. Bringing thrombolytic therapy to more patients will require improvements in stroke centre infrastructure; widespread public education; and some reassurance to clinicians that the risk of haemorrhagic transformation is acceptable given the potential benefits. To address this latter point, investigators have taken one of two approaches: to search for safer lytic agents, or to attempt to minimize risk with the currently available agent, recombinant tissue plasminogen activator (rtPA).
scan interpretation falls within the scope of practice for certified vascular neurologists, although many centres provide urgent neuroradiological interpretation for non-neurologists who must finalize a thrombolytic decision. Nevertheless, agreement on subtle early signs of ischaemia on CT scan remains far from perfect. The SEDAN score, therefore, contains some inherent uncertainty, but generally should be easily done in any centre qualified to administer rtPA to stroke patients.

The SEDAN score, ranging from 0 to 6, clearly and significantly associates with the risk of haemorrhage, with an AUC-ROC of 0.77. Each additional point confers additional risk of symptomatic intracerebral haemorrhage, from 1% for a score of 0 to 28% for a score of 5 in the validation cohort; no patient in either data set scored a full 6 points. Of note, the authors treated a sufficient number of patients with basilar artery territory stroke to show the scoring system valid in that subgroup.

The derivation and validation of the SEDAN score were performed with the highest rigour and state-of-the-art statistical methods. One problem with the data set, however, is that blood pressure did not seem to influence risk of haemorrhage in either the derivation or the validation samples. Previously, elevated blood pressure during treatment associated with risk of such events. From the data presented, the study sites involved in testing the SEDAN score appear to have systematically excluded patients with elevated blood pressure from treatment, as per the standard guidelines. Thus, while elevated blood pressure is not included in the derived SEDAN score, clinicians must adhere scrupulously to the standard blood pressure limits. Importantly, the derivation and validation samples, which were derived from separate populations in medical centres in different countries, closely resembled each other, and yielded quite similar results. Thus, the score enjoys the greatest possible clinimetric endorsement. Clinical endorsement remains quite another matter, however, so how might the SEDAN score actively influence decision-making?

Since the first publication of the NINDS trial results, many have attempted to identify subgroups of patients who could be excluded from treatment. To date, however, thrombolytic therapy for acute stroke has proved sufficiently powerful in all subgroups that no recommendation to exclude from treatment has been supported by evidence. Even the SEDAN score should not drive patient selection. While patients with the highest SEDAN score showed the greatest haemorrhage risk, the available evidence indicates that such patients benefit from treatment despite the haemorrhages. Before the SEDAN score can be used to select patients, a randomized trial including a placebo-treated group must be done, to assure the validity of the score for excluding patients. On the other hand, a larger SEDAN score might be used to drive ancillary management, in particular blood pressure and glucose control. A hypothesis for future study would be that patients with lower SEDAN scores could safely begin antiplatelet therapy sooner than the arbitrary 24h after rtPA treatment.

A final comment must be included for the plaintiffs’ bar: infrequent haemorrhage is expected after thrombolytic therapy for acute ischaemic stroke, even if all known use guidelines are followed scrupulously. An elevated SEDAN score cannot and should not be used retrospectively to conclude that any specific patient should not have been treated, even after a devastating haemorrhagic transformation. Currently available risk–benefit analyses suggest that rtPA treatment should not be withheld from any subgroup: the odds of a favourable outcome still exceed the risks under current guidelines. Future studies may identify a particular subgroup in whom rtPA should be withheld but, until those data become available, clinicians should offer treatment to all patients who fit the accepted criteria.

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Competing interests
The author declares no competing interests.


NEUROMUSCULAR DISEASE

Muscular dystrophy—something new on God’s green earth?

Alessandra Ferlini

Promising results on newborn testing for Duchenne muscular dystrophy indicate that widespread screening could become routinely available. Nevertheless, newborn testing raises ethical, social and scientific concerns that need careful consideration to maximize benefit for patients, their families and health-care providers.

Ferlini, A. Nat. Rev. Neurosci. 8, 247–249 (2012); published online 27 March 2012; doi:10.1038/nrneurol.2012.41

Newborn testing represents an important milestone for medical geneticists, molecular biologists, morphologists, neurologists, paediatricians and pharmaceutical companies, all of whom invest time and effort in combating genetic diseases, such as Duchenne muscular dystrophy (DMD), a rare but debilitating disorder that affects one in 3,500–6,000 male births. Indeed, in a short time, this concerted effort has led the