Five-Simple-Variables Risk Score Predicts Good and Devastating Outcome after Stroke

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Abstract

**Background:** Predicting outcome after stroke may have utility in providing prognostic information to patients and relatives, and informing treatment decisions. We aimed to develop predictive risk scores derived from outcome prediction models for outcomes 6 months post-stroke.

**Methods:** The Stroke Outcome Study (2001-2) enrolled 538 ischaemic and haemorrhagic stroke patients admitted to the Halifax Infirmary, Nova Scotia, Canada. Baseline variables were collected and modified Rankin score (mRS) assessed 6 months after stroke. Previously published models for excellent (mRS<2), good (mRS<3) and devastating outcomes (mRS>4) were used.

**Results:** From previously published models, Five Simple Variables (FSV) were used; age<80 years, pre-stroke functional status, normal verbal Glasgow coma score, ability to walk unaided, and lift both arms. Predictive scores developed for excellent and good outcomes were identical with a range of 7 points for previously independent individuals. The devastating outcome score (a 14 point score, FSVDEV) included total anterior circulation stroke, and excluded ability to walk. Area under curve (AUC) values of 0.859-0.886 were observed for all three outcomes (AUCs of 0.847-0.884 in an external dataset). An FSV score ≥4 and FSVDEV scores ≥6 showed sensitivities of 64-70% and specificities of 83-91% to predict each outcome.

**Conclusions:** FSV scores can be used to predict outcomes 6 months post-stroke with external validity. Whether such scores offer clinical utility over and above informal physician prediction requires further study.

**Keywords:** Stroke outcome; Prognosis, Risk score

Introduction

Predicting outcome after stroke may have utility in providing prognostic information to patients and relatives, and informing treatment decisions. Age, stroke severity, prior functional status and comorbidity are important clinical predictors of outcome [1,2]. Several prognostic models and recently some predictive scores have been developed [3-11] although none has been widely adopted in routine clinical use. Ideally, clinical prediction models or scores should include relevant variables that are readily available with high reliability, and are simple to calculate, increasing the likelihood of utilisation [12]. In particular, a six simple variable (SSV) model has been developed [10] and used for stratification in randomised trials [13] and for adjustment of case mix in comparing outcomes between stroke units [14]. More recently, it is recognised that one of the variables from this model, living alone prior to stroke, is a less robust predictor of independent survival, leading to a five simple variable (FSV) model excluding this variable [7-9]. Our previous studies developed outcome prediction models based on the FSV model variables to predict excellent, good or devastating outcomes defined as a modified Rankin score (mRS) <2, <3 and >4 respectively, six months after ischaemic or haemorrhagic stroke [8,9]. The aim of this study was to derive simple clinical prediction scores from previously developed stroke outcome models and to externally test their accuracy.

**Methods**

**Study population**

Outcome prediction models were used in this study which were previously developed from the Stroke Outcome Study (SOS) as previously described [7,8]. Patients presenting with ischaemic and haemorrhagic stroke between 2001 and 2002 and admitted to the Halifax Infirmary, Nova Scotia, Canada, were consecutively enrolled. In brief, patients with a clinical diagnosis of stroke were consented to join the study. Written consent for study participation was obtained from each patient or his/her surrogate decision maker, which was approved by the Capital Health Research Ethics Board, Halifax, Nova Scotia, Canada. All patients were assessed acutely by a member of the
neurology team and had imaging (majority CT) on arrival in the emergency department. The clinical parameters recorded relevant to this study at the time of first neurological assessment included the FSV model variables; age, pre-stroke functional status (Oxford handicap score), whether the patient could lift both arms off the bed, walk without the assistance of another person, had a normal verbal component of the Glasgow coma score (GCS), and also Oxfordshire community stroke project (OCSP) subtype. Of a total of 598 patients, 38 refused consent, 9 were lost to follow-up and 13 with repeat presentations had the second admission excluded, leaving a final study population of 538. No significant differences between excluded and included patients were noted regarding age, gender and stroke severity [7]. Outcome was measured at six months by telephone interview by a single author (YR) trained in administering the mRS (all clinical variables previously source referenced) [7].

### Statistical analysis

Our previous studies produced several models of varying complexity; models using FSV model variables were non-inferior in performance to more complex models, and were externally validated [7,8]. These included two models utilising the FSV variables for good (independent survival, mRS<3) and excellent outcomes (disability-free survival, mRS<2), and a model for devastating outcome (death or severe dependence, FSV<DEV, mRS>4) [7,8]. The FSV<DEV model included four of the five FSV variables excluding the variable ability to walk unaided, and including the OCSP subtype of total anterior circulation stroke syndrome (TACS). For the FSV<DEV the variables inability to lift both arms, abnormal verbal GCS and age ≥80 were used as predictors of poor outcome. The coefficients for each of the three models are shown in Table 1.

**Table 1: Predictive models and risk score for excellent, good and devastating outcomes.** AUC for the risk score in SOS and OCSP cohorts is shown. * per unit variable. PRE-SFS – pre-stroke functional status.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficient (SE)</th>
<th>Odds Ratio (95% CI)</th>
<th>FSV risk points</th>
<th>AUC (SOS)</th>
<th>AUC (OCSP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent Outcome (mRS&lt;2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age&lt;80</td>
<td>0.80 (0.30)</td>
<td>2.23 (1.23-4.05)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRE-SFS*</td>
<td>-0.87 (0.14)</td>
<td>0.42 (0.32-0.55)</td>
<td>-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Verbal GCS</td>
<td>0.83 (0.31)</td>
<td>2.30 (1.24-4.25)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to lift both arms</td>
<td>1.81 (0.37)</td>
<td>6.08 (2.96-12.5)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to walk unaided</td>
<td>0.99 (0.25)</td>
<td>2.70 (1.65-4.40)</td>
<td>1</td>
<td>0.859</td>
<td>0.847</td>
</tr>
<tr>
<td>Good Outcome (mRS&lt;3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age&lt;80</td>
<td>1.15 (0.29)</td>
<td>3.16 (1.79-5.58)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRE-SFS*</td>
<td>-0.99 (0.13)</td>
<td>0.37 (0.29-0.47)</td>
<td>-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Verbal GCS</td>
<td>1.15 (0.28)</td>
<td>3.16 (1.80-5.53)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to lift both arms</td>
<td>1.77 (0.30)</td>
<td>5.85 (3.23-10.6)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to walk unaided</td>
<td>1.08 (0.27)</td>
<td>2.94 (1.70-5.07)</td>
<td>1</td>
<td>0.886</td>
<td>0.884</td>
</tr>
<tr>
<td>Devastating Outcome (mRS&gt;4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age≥80</td>
<td>1.45 (0.28)</td>
<td>4.28 (2.55-7.19)</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRE-SFS*</td>
<td>0.48 (0.09)</td>
<td>1.61 (1.35-1.93)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal Verbal GCS</td>
<td>1.38 (0.25)</td>
<td>4.28 (2.55-7.19)</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to lift both arms</td>
<td>1.07 (0.28)</td>
<td>2.93 (1.69-5.09)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TACS</td>
<td>1.19 (0.35)</td>
<td>3.29 (1.65-6.57)</td>
<td>2</td>
<td>0.866</td>
<td>0.876</td>
</tr>
</tbody>
</table>

The predictive/risk score was derived using an established method [15-17] in which points were assigned to each variable by dividing each regression β-coefficient by the smallest β-coefficient and rounding to the nearest integer. A predictive/risk score was assigned to each patient by summing the points for each risk factor present. These risk scores were externally tested using the OCSP dataset, [10] a community-based incidence study in the United Kingdom (1981–1986) of first-ever stroke. Risk score performance was assessed using the area under the receiver operator curve [18]. Patients were then divided into approximate quartiles based on their predictive/risk score (discrimination) [18] and comparing predicted vs. observed excellent, good and devastating outcome (calibration) respectively. Each level of the score was tried as a cut-off point and the respective sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) was calculated. The optimum cut-off point was chosen on the basis of optimal sensitivity, specificity and PPV [19,20]. After determining optimal cut points for predicting excellent, good and devastating outcome, the sensitivity, specificity, PPV, NPV in the OCSP cohort was calculated. All analyses were conducted using SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA).
Results

The study population had a median age of 74 years (interquartile range 61-80), 47% female, 87% ischaemic, and 13% haemorrhagic stroke [7]. The three outcome models used to derive the prognostic index scores are shown in Table 1. For both excellent and good outcomes, the risk points attributable to each of the FSV model variables using the described method was identical; two points being given for ability to lift both arms and one point for age <80 years, being able to walk unaided and normal verbal GCS, and minus one point per level of pre-stroke functional status. For patients that were previously independent the FSV score ranges from -2 to +5. For devastating outcome (FSV_{DEV}) the risk points attributable were three points for age ≥ 80 and abnormal verbal GCS, two points for TACS and inability to lift both arms, and one point per level of pre-stroke functional status (Table 1) giving an FSV_{DEV} score ranging from 0 to 14 for patients with a pre-stroke mRS<5. The risk scores had good predictive performance as measured by the AUC with only a small decrease compared to the original statistical models from which they were derived (AUC of 0.859 vs. 0.861, 0.886 vs. 0.890, and 0.866 vs. 0.868 for excellent, good and devastating outcome respectively) [7,8]. If age was dichotomized with a cut point of 75, 70 or 60 years, the AUCs for the risk score were lower (data not shown). We also tested sub-divided age into categories of 0-64, 65-79 and >79 years old; this produced a minor improvement in the prediction scores of good (AUC 0.893 vs. 0.886) and devasting (0.869 vs. 0.866) outcome, whereas for excellent outcome age was no longer an independent predictor and was deselected in the risk score. The risk scores performed well in the external OCSP cohort (Table 1 and Figure 1).

The proportion of patients achieving each outcome depending on the risk score for the three outcomes in the SOS and OCSP cohorts is shown in Supplementary File. The optimal cut points in the risk score based on sensitivity and specificity were estimated (Supplementary file). An optimal cut point of the FSV score ≥4 had sensitivities of 70 and 64%, and specificities of 83 and 91% respectively for excellent and good outcomes respectively. In the SOS and OCSP cohorts 4% and 3% respectively of those with an FSV score ≤1 had an excellent outcome, whilst 1% and 2% respectively of those with a FSV score ≥4 had a good outcome. For devastating outcome, the optimal cut point of FSV_{DEV} ≥ 6 produced a sensitivity and specificity of 70 and 87%, 96% and 88% of the SOS and OCSP cohorts respectively with a FSV_{DEV} ≥ 10 had a devastating outcome, whereas this increased to 97% and 100% for a score ≥ 11 (Supplementary file).

Discussion

This study produced simple outcome prediction risk scores for excellent, good (FSV score) and devastating outcomes (FSV_{DEV} score), six months after stroke. The risk scores have comparable predictive accuracy to the models they were derived from and were externally validated. The advantage of these scores is that they are much easier to calculate than those produced from more complex statistical models [7-9], use easily collectable variables with good inter-rater reliability [21], and can be used for estimating the likelihood of different outcomes. The optimal cut-points of FSV ≥ 4 for good and excellent outcomes give reasonable estimates of achieving these outcomes (64-70% sensitivity, and 83-91% specificity). Also an FSV score of 0 or 1 makes good and excellent outcomes extremely unlikely (1-2% or 3-4% respectively). For the FSV_{DEV} score a cut point of ≥6 predicts a devastating outcome with sensitivity of 70% and specificity of 87%, and a score of ≥11 gives a 97% or higher likelihood of a devastating outcome. Such predictions may be useful in discussions with patients and relatives regarding prognosis. Predictive scores will always have some imprecision, and their utility will depend on whether they offer improved predictive capacity over a physician’s informal prediction. The SSV model was previously shown to have a predictive value similar to informal physician prediction [22].

Other more complex risk scores have been described. The ASTRAL score [3] uses six variables, although the variables have a large complexity producing a score ranging from 0 to 65, including one point for every five years of age and for each point in the NIHSS scale, glucose level, level of consciousness, presence of a visual field deficit, and whether onset to admission time is more than 3 hours. An ASTRAL score>31 gives a 50% chance of an unfavourable outcome and has recently been externally validated in a Chinese cohort (AUC of 0.81-0.82) at 3 and 12 months post-stroke [23-28]. This level of AUC was less than noted in the current study despite using more complex variables. Other recently developed prediction scores include the iScore [29] using the Canadian Neurological scale in addition to age gender, glucose and pre-stroke disability, which appears to have better prediction than physician prediction [30]. The THRIVE score is also described using NIHSS, age and comorbidity [31]. A pre-hospital score used by paramedics can predict excellent outcome (mRS of 0-1) at 3 months after ischaemic stroke with a sensitivity of 67% and specificity of 71%, although the score was developed from a small cohort of patients and was not externally validated [4]. A prognostic score for a poor outcome has been previously described with sensitivity of 72% and specificity of 63% [5]. It is unclear whether increasing model complexity (e.g. using a stroke severity score or a comorbidity index) improves predictive power or unnecessarily adds complexity with possible redundancy of variables. The current and prior studies [7-9] demonstrate the utility and non-inferiority of the

Figure 1: Receiver operating characteristic curve for predictive/risk scores predicating excellent (mRS<2), good (mRS<3), and devastating (mRS >4) outcomes respectively at 6-month follow up in OCSP cohort.

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FSV model variables in predicting excellent and good outcome whether as a statistical model or a risk score, and is applicable to both hemorrhagic and ischaemic stroke. The FSV model has been recently validated in multiple contemporary European stroke populations (2004-6), producing more precise estimates of a good outcome than models using a Barthel index, NIHSS with age or additional comorbidity variables [9]. We previously demonstrated that the addition of more complex clinical or radiological variables did not improve predictive accuracy [7-8]. Use of the NIHSS in outcome prediction models has some limitation in that it requires special training, and has some redundancy in its items, and is often not completed in routine practice [24].

The FSV model variables are age, clinical variables, prior dependency, and comorbid conditions. It uses the clinical variables neglect or aphasia, significant or total arm and leg weakness, and reduced level of consciousness. Verbal GCS used in the FSV and FSV models can be abnormal due to a reduced level of consciousness, aphasia or cognitive impairment; neglect and hemianopia would be encompassed by the variable TACS. In contrast to the FSV model, the FSV and FSV scores use slightly different variables for a good, compared to a devastating, outcome with different weighting to some of the variables (e.g. age and normal verbal GCS having greater weighting for a devastating outcome). Thus although a unifying score for multiple outcomes is attractive, some predictive accuracy may be lost. Although mortality itself can also be modelled [11], we consider it more appropriate to group mortality with a mRS score of 5 since patients describe this level of severe dependence as very undesirable [25].

The limitation of this study is that, despite the good AUC and reasonable sensitivity and specificity, it is not clear whether such simple models are adequate for routine clinical use; direct comparison with informal physician prediction is required to answer this question. Although the external validation dataset is more than two decades old, the utility of the FSV risk score variables is bolstered by their external validity in several European cohorts from 2004-2006 [9]. In the era of intravenous thrombolysis and clot retrieval such scores might have to be adapted. Of note the PLAN score performs less well in patients who showed no benefit of thrombolysis [1]. The Gompertz P, Pound P, Ebrahim S (1994) Predicting stroke outcome: Guy's prognostic score in practice. J Neurol Neurosurg Psychiatry 57: 932-935.

This study describes two externally validated outcome prediction scores based on five simple clinical variables to predict an excellent/good and devastating outcome six months after stroke. Use of these scores may inform discussion with patients and relatives regarding prognosis after stroke. To adopt their use widely would require demonstration of superiority over and above physician prediction, which we plan to test in the future.

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References


