A 5-Item Scale to Predict Stroke Outcome After Cortical Middle Cerebral Artery Territory Infarction

Validation From Results of the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) Study

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Background and Purpose—Various clinical, laboratory, and radiographic parameters have been identified as predictors of outcome for ischemic stroke. The purpose of this study was to combine these parameters into a validated scale for outcome prognostication in patients with a middle cerebral artery territory infarction.

Methods—We retrospectively reviewed 129 patients over a 2-year period and considered demographic, clinical, laboratory, and radiographic parameters as potential predictors of outcome. Inclusion criteria were unilateral hemispheric infarcts within the middle cerebral artery territory >15 mm in diameter. Our primary outcome measure was a favorable recovery defined as a modified Rankin Score was ≤2 at 30 days. A multivariable model was used to determine independent predictors of outcome and weighted to create a 5-item scale to predict stroke recovery. External validation of this model was done using data from the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) study.

Results—The 5 independent predictors of outcome were as follows: age (OR, 1.09; 95% CI, 1.03 to 1.14; P<0.001), National Institutes of Health Stroke Scale score (OR, 1.17; 95% CI, 1.06 to 1.30; P=0.003), infarct volume (OR, 1.01; 95% CI, 1.00 to 1.02; P=0.03), admission white blood cell count (8.5×10^3/mm^3; OR, 1.16; 95% CI, 1.03 to 1.27; P=0.04), and presence of hyperglycemia (OR, 4.2; 95% CI, 1.1 to 16.4; P=0.04). Combining these variables into a point scale significantly improved prediction over the individual variables accounted alone as evidenced by the area underneath the receiver operating curve (OR, 0.91; 95% CI, 0.87 to 0.96; P<0.0001). When applied to the DEFUSE study population for validation, the model achieved a sensitivity of 83% and specificity of 86%.

Conclusions—With validation from a prospective study of similar patients, this model serves as a useful clinical and research tool to predict stroke recovery after cortical middle cerebral artery territory infarction. (Stroke. 2011;42:645-649.)

Key Words: MRI ■ stroke models ■ stroke outcome

Prognostication of functional outcome after ischemic stroke is an important but difficult task. Early stroke models have determined that patient age, baseline National Institutes of Health Stroke Scale (NIHSS) score, and medical comorbidities are factors that impact outcome.1,2 In addition to these clinical parameters, volume of infarction measured on CT1 or diffusion-weighted imaging (DWI) MRI4 in the subacute period after stroke has also been shown to have predictive value. The combination of clinical and imaging parameters has been suggested to synergistically improve outcome prognostication.5,6

However, existing models are limited by their small sample size and heterogeneous populations, including varied infarct locations from which they were derived. In this study, we sought to devise a statistical model using clinical, laboratory, and imaging parameters from a homogeneous population of patients with cortical middle cerebral artery (MCA) stroke with validation from the subjects of the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) study, a separate but similar prospective data set.7

Methods

Patients

With institutional approval, we retrospectively reviewed all inpatients diagnosed with an ischemic stroke from June 2002 to June 2004 in a heterogeneous group of 129 patients with unilateral hemispheric infarcts within the MCA territory >15 mm in diameter. The primary outcome measure was a favorable recovery defined as a modified Rankin Score ≤2 at 30 days. The multivariable model was used to determine independent predictors of outcome and weighted to create a 5-item scale to predict stroke recovery. External validation of this model was done using data from the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) study, a separate but similar prospective data set.7

Results

The 5 independent predictors of outcome were as follows: age (OR, 1.09; 95% CI, 1.03 to 1.14; P<0.001), National Institutes of Health Stroke Scale score (OR, 1.17; 95% CI, 1.06 to 1.30; P=0.003), infarct volume (OR, 1.01; 95% CI, 1.00 to 1.02; P=0.03), admission white blood cell count (8.5×10^3/mm^3; OR, 1.16; 95% CI, 1.03 to 1.27; P=0.04), and presence of hyperglycemia (OR, 4.2; 95% CI, 1.1 to 16.4; P=0.04). Combining these variables into a point scale significantly improved prediction over the individual variables accounted alone as evidenced by the area underneath the receiver operating curve (OR, 0.91; 95% CI, 0.87 to 0.96; P<0.0001). When applied to the DEFUSE study population for validation, the model achieved a sensitivity of 83% and specificity of 86%.

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2004. All patients at our institution were further evaluated with DWI unless they had contraindications for MRI.

Inclusion criteria were: patients presenting with a MCA territorial infarction with corresponding hypertensive and hypotensive lesions on DWI and acquired diffusion coefficient, respectively, within 48 hours of symptoms onset. We excluded patients with a baseline disability, those with MRI completed >48 hours after symptom onset, those patients with MCA infarcts <15 mm in diameter, those with bihemispheric infarcts, those with hemorrhagic transformation of the infarct present on the MRI, and those with any infarct outside the MCA territory. Patients were also excluded if they had missing data such as a baseline stroke score, DWI volume of infarction, and 30-day follow-up.

Demographic information included gender and age. Medical history including presence or absence of hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, smoking, prior stroke, ipsilateral transient ischemic attack within the 4 weeks before the incident event, and coronary artery disease was obtained. Patient admission histories were retrospectively assessed, and the authors identified these conditions as present if mentioned and absent if not mentioned. Discharge summaries were also used to document whether these medical conditions were present or absent during the hospitalization. Medication use at the time of stroke, including HMG-CoA reductase inhibitors, angiotensin-converting enzyme inhibitors, aspirin, clopidogrel, and/or warfarin, was also collected. Laboratory parameters such as admission white blood cell count and presence of hyperglycemia (predefined as any single blood glucose level >200 mg/dL within the first 48 hours of admission) were recorded. Clinical stroke severity was determined based on the NIHSS at the time of initial neurological consultation. The use of intravenous and/or intra-arterial thrombolysis along with time from the onset of stroke symptoms to MRI was noted.

MRI Studies

All patients were examined with a clinical 1.5-T MR imager (Symphony or Vision; Siemens, Erlangen, Germany) equipped with enhanced gradients for echoplanar imaging using a standard head coil. The stroke MRI protocol included a 3-dimensional time-of-flight MR angiography of the intracranial circulation and axial DWI spin echo echoplanar imaging sequence (b=0, 500, 1000 s/mm²) in 3 gradient directions. Trace DWI images and calculated maps of the acquired diffusion coefficient were generated online by the scanner. Infarct volume and intracranial MR angiography were measured retrospectively and independently in a blinded manner by 3 authors (S.J.S., N.A.V., A.L.T.) on a standard Siemens MV1000 workstation from trace DWI images and acquired diffusion coefficient maps. DWI abnormalities corresponded to areas of decreased signal intensity on acquired diffusion coefficient maps in all cases. Infarct area of each imaging slice was calculated by tracing the DWI lesion perimeter with a graphing tool available on the Siemens workstation. The product of the slice thickness and the summation of infarct areas gave the infarct volume with the average volume measurement by 2 authors used as the final volume of the ischemic lesion.

MR angiography studies were examined for the presence of a large artery occlusion or near occlusion. These 3 blinded authors also scored MCA vessel patency based on the following criteria. A score of 0 or 1 was ascribed to absent or minimal signal of the M1 MCA, respectively. A score of 2 was given to those vessels with normal M1 MCA signal but decreased M2 signal. A score of 3 represented normal signal in both M1 and M2 MCA.

End Points

Patients were seen in our outpatient neurology clinic 30 days after stroke as part of routine follow-up and were assessed for their level of disability as a standard practice. Modified Rankin Scores were extracted from chart review of the outpatient or rehabilitation clinic note and dichotomized to favorable (modified Rankin Score 0–2) or unfavorable (modified Rankin Score >2) outcomes as our end point.6,9

Statistical Analysis

All analyses were performed using SPSS Version 13.0. A univariate analysis was performed to determine the potential predictors of 30-day outcomes. Categorical variables were analyzed using a χ² test, whereas continuous variables were analyzed with a Student t test. Variables with a probability value <0.10 were entered into a binary logistic regression model to determine the independent predictors of favorable outcome at 30-day follow-up with statistical significance defined as a probability value of <0.05.

A clinical point scale was derived using the independent variables found in the multivariable model. Using a weighted average based on our results, the significant variables were assigned point values. The maximum points assigned to a patient were 9 based on the variables in the multivariable analysis. The total points were then categorized into 3 scoring categories to predict 30-day clinical outcome.

Receiver operator characteristic curves were also generated for each of the independent variables. The area under the curve was tabulated and recorded for each independent variable and also for the combined point scale variable to determine if the combined scale had a higher sensitivity in determining outcomes in comparison to the individual variables. A Spearman correlation was also performed to confirm that the combined point scale had a stronger association to outcome when compared with each of the significantly independent variables.

Subsequently, the clinical point score was used to predict outcome in patients with MCA cortical infarctions from the prospective DEFUSE registry outcomes at the time of analysis. The DEFUSE registry consisted of 74 patients presenting with MCA cortical strokes within 3 to 6 hours. These patients provided informed consent and then underwent subsequent diffusion-perfusion weighted MRI before and 3 to 6 hours after the administration of intravenous thrombolysis. A third MRI was also obtained at 30 days. The subject’s second MRI infarct volume (after thrombolysis) and stroke score just before this scan were considered for model validation.

Based on the multivariable analysis results and point scale described, each DEFUSE registry subject’s prognosis was predicted and compared with their actual outcome. The authors were blinded to the DEFUSE registry outcomes at the time of analysis.

Results

A total of 129 patients was analyzed. The mean age, NIHSS, and time to MRI for this cohort were 66±14 years, 10±6, and 24±13 hours, respectively. The etiology for ischemic stroke was as follows: 60 (46%) large artery atherosclerosis, 41 (32%) cardioembolic, 20 (16%) cryptogenic, and 8 (6%) other causes. A total of 61 (47%) patients had the infarct on the right side and 68 (53%) patients were women. Fifteen (12%) patients received intravenous or intra-arterial thrombolitics with only 5 of those achieving a favorable outcome. In total, 58 (45%) patients from our series achieved a good functional outcome, whereas 34 of 74 patients from the DEFUSE registry (46%) were independent at 30 days. Table 1 summarizes the univariate analysis comparing demographic information, medication usage before hospitalization, clinical, laboratory, and radiographic parameters. Time to MRI, use of thrombolytics, or prior use of any medication class did not significantly impact outcome findings. Table 2 summarizes the independent predictors of a favorable outcome at 30-day follow-up. Patients with atrial fibrillation and/or poor MCA patency (score of 0 or 1) on MR angiography were not found to have a significant association with outcomes in multivariable modeling.

The 5 items found to be significant in multivariable modeling were assigned point values to help clinicians tabulate an outcome probability score (Table 3). The area under the
receiver operator characteristic curves are reported for each variable individually and for the aggregate total of all variables combined. There is a higher sensitivity in predicting clinical outcomes using the combination of all variables in comparison to the individual variables. The area under the receiver operator characteristic curve using the clinical scale was 0.91 (95% CI, 0.87 to 0.96, \( P = 0.0001 \)). The total point values were broken down into 3 ranges (Table 4) with a lower score in the 0- to 2-point range highly predictive of a favorable 30-day outcome. Patients in the 3 to 4 total point range had a 50% chance of a good recovery, whereas those with point totals \( >5 \) points were unlikely to make an independent recovery in our cohort.

Validation was accomplished by comparing the prognosticated outcomes using the previously described point scale with the actual functional status of patients in the DEFUSE study. The sensitivity of the point scale was 83% with a specificity of 86%.

### Discussion

Several prediction models have been developed to prognosticate outcome for patients with stroke. Our model is unique in that clinical, laboratory, and radiographic parameters were combined to identify the factors that impact recovery. Patients with increased age, higher baseline NIHSS, larger DWI infarct volume, early hyperglycemia, and admission leukocytosis have greater odds of poor recovery from MCA cortical strokes.

Early predictive models did not include laboratory parameters such as white blood cell count and hyperglycemia, despite the fact they influence outcome in prospective studies.\(^{10-12}\) Hyperglycemia is known to exacerbate neuronal death due to impaired metabolism during focal ischemia.\(^{10}\) Leukocytosis has been proposed to affect stroke outcome through microvascular thrombosis and hyperviscosity but more likely is a surrogate marker for fever and infection.
which causes clinical deterioration after stroke.\textsuperscript{2,12} Both hyperglycemia and leukocytosis can predispose to a more lengthy or complex hospitalization, which may have an impact on long-term recovery. The statistical significance in our multivariable analysis for these laboratory parameters highlights the necessity for defining their role in clinical deterioration because they can serve as a target for medical therapies post-stroke.

Our findings are consistent with those of prior studies. Age has consistently been linked to neurological recovery after stroke as has the initial NIHSS. Patients with lower NIHSS scores have been shown to have a better prognosis.\textsuperscript{1} This is due to the fact that the NIHSS represents an objective description of the extent of neurological deficit,\textsuperscript{13} hence its inclusion in existing outcome prediction models.\textsuperscript{4,6,14}

However, the NIHSS does have a hemispheric bias, and higher NIHSS scores do not necessarily mean larger territorial infarcts because right and left hemispheric infarctions can have disparate scores when linked to stroke size.\textsuperscript{15} Hence, a volumetric measurement of infarct size may also add predictive power in addition to stroke scales. DWI MRI infarct volume has been suggested because of its advantages over infarcts seen on CT and fluid-assisted inversion recovery MRI. Although there is evidence of diffusion reversibility\textsuperscript{16} and fluid-assisted inversion recovery MRI infarcts are used as a standard for measurement for chronic infarct size,\textsuperscript{17} infarcts on DWI are better visualized than on CT and correlate better with earlier infarction than fluid-assisted inversion recovery MRI for the purpose of prognostication.

MRI stroke volume models have inconsistently shown a correlation between outcome and DWI infarct size.\textsuperscript{18,19} Our results are consistent with 2 retrospective studies correlating DWI stroke volumes with outcome based on clinical scales but differ in that a larger sample size with a homogeneous population was used.\textsuperscript{4,6,19} We believe that our sample thus allows for better prediction in moderate-sized infarcts in which prognostication may be equivocal and in a population restricted only to MCA cortical infarcts.

Other advantages of our model compared with existing ones include the homogeneity of our population.\textsuperscript{5} Also, compared with other MRI-based volumetric outcome studies, validation was done using a separate prospective data set with a similar imaging protocol and with similar vascular lesions like in our study.\textsuperscript{7} Previous CT-based outcome studies identified that combining clinical and radiographic parameters strengthens prognostication.\textsuperscript{14} We believe the present study also offers improvements over existing models largely due to the inclusion of hyperglycemia and leukocytosis for prognostication. Our statistical analysis did suggest that the combination of these parameters was better for prognostication than the variables considered alone.

Although thrombolysis impacts outcome, few patients in our sample received this therapy, hence its nonstatistical relationship to outcome in our univariate model. Thrombolysis was not considered in the multivariable analysis because of our small numbers and our findings that vessel patency had a greater impact in the univariate analysis. There is good rationale to believe that vessel patency has prognostic value but probably failed due to the MRI timing in our model. Late MRI may identify larger infarct volumes due to stroke evolution compared with hyperacute MRI in which vessel patency and perfusion parameters may be more significant. With total or near-total occlusion, we presume that infarct volume will increase as a function of time from stroke onset. Hence, our delayed MRI scan time could have revealed larger stroke volumes that statistically outweighed any predictive value for the patency in the MCA in the multivariable analysis.

Our study’s main limitation is the retrospective design from a single center. Approximately 20\% of screened patients were excluded because of missing data or late MRI. We do not know the ultimate outcomes of these patients and how they may have impacted our model had they been included. The same can be said for those without 30-day follow-up at our institution. Data from these patients would also have provided a larger sample to adequately analyze our large number of univariates. Another consideration with our sample is the time of our data collection. Our initial goal was to replicate our model with a similar prospective data set with a more recent timeframe. However, we felt that prospective validation from a formal registry such as DEFUSE would strengthen our model instead. Unfortunately, the timeframe of this study does not include important findings from newer studies including perfusion MRI data, which could have importance. Earlier investigations using perfusion MRI suggested that the volume of perfusion deficit correlated with clinical outcome.\textsuperscript{20} Newer evidence does corroborate these findings with poor outcomes despite recanalization in the setting of large volumes of hypoperfused tissue.\textsuperscript{21}

Our findings need further prospective validation. This is currently being investigated prospectively with more sophisticated outcome measures to confirm our model. Once validated, we do feel this will be a useful tool for clinical decision, quality assessment, and research methodologies in patients with cortical MCA infarcts.

**Disclosures**

R.G. is on the scientific advisory board/consultant for Concentric Medical, CoAxia Inc, and Rapid Medical.

**References**


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背景与目的：很多临床、实验室以及影像学参数是缺血性卒中预后的预测因子，本研究的目的就是将这些参
数加入到有效的量表中来预测大脑中动脉供血区皮质梗死患者的结局。

方法：两年时间我们回顾性调查了 129 例患者，将人口学、临床、实验室以及影像学参数作为潜在的预测因子。
入选标准为直径 >15 mm 大脑中动脉单侧半球梗死。最主要的评价为 30 天改良的 Rankin 评分 ≤2。运用多因
素模型确定卒中后的独立预测因子，通过加权创建预测卒中恢复的 5 个条目量表。运用 DEFUSE 研究 (the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution Study) 数据评估模型的外部效度。

结果：5 个独立的预测因子是：年龄 (OR, 1.09; 95% CI, 1.03-1.14; P =0.001)，美国国立卫生研究院卒中量表
(NIHSS) 评分 (OR, 1.17; 95% CI, 1.06-1.30; P =0.003)，梗死体积 (OR, 1.01; 95% CI, 1.00-1.02; P =0.03)，入院时
的白细胞计数 (8.5×10²/mm³; OR, 1.16; 95% CI, 1.03-1.27; P =0.04) 和高血糖 (OR, 4.2; 95% CI, 1.1-16.4; P =0.04)。
将这些变量综合成一个积分量表的预测能力显著高于单个变量。其预测能力由受试者操作特征曲线下面积
(AUC)(OR, 0.91; 95% CI, 0.87-0.96; P =0.0001) 得到证实。借助 DEFUSE 研究人群数据验证其效度，模型的敏
g感度和特异度分别达到 83% 和 86%。

结论：从类似病例的前瞻性研究资料所检验效度看，本模型可以作为评估大脑中动脉供血区皮质梗死预后的
有价值的临床和研究预测工具。

关键词：磁共振成像，卒中模型，卒中预后

(Stroke. 2011;42:645-649. 北京市神经外科研究所 茹小娟 译 江滨 王文志 校)
MRI 禁忌症，所有患者均进行了 DWI 进一步检查。

入选标准为：发病 48 小时内 DWI 检查出现对应 MCA 供血梗死区高信号和低信号及各自弥散系数的患者。

排除了基线时有残疾的患者，用 MRI 排除了症状出现 >48 小时，MCA 梗死直径 <15 mm、双侧半球梗死、梗死灶的出血转变以及 MCA 区之外的其他部位梗死的患者。也排除了缺失基线卒中评分、DWI 梗死体积和 30 天随访数据的患者。

人口学信息包括性别和年龄。疾病史包括是否高血压、糖尿病、高脂血症、房颤、吸烟、卒中史、发生卒中前 4 周出现同侧短暂性脑缺血发作 (TIA) 以及冠心病。作者通过回顾性地调查了解患者入院时有无上述病史，出院小结也用来证明住院治疗期间是否有过这些疾病。收集了治疗卒中所用的药物，包括羟甲基戊二酰辅酶 A (HMG-CoA) 还原酶抑制剂、血管紧张素转换酶抑制剂 (ACEI)、阿司匹林、氯吡格雷和/或华法林。记录了实验室参数，如入院白细胞计数和高血糖 (定义为入院 48 小时内任一单次血糖水平 >200 mg/dL)。卒中严重程度由最初就诊时的 NIHSS 评分决定。记录了从发病到 MRI 检查期间静脉注射和/或动脉内溶栓剂的使用情况。

MRI 研究

所有的患者接受了 1.5-T MR 图像仪 (Symphony or Vision; Siemens, Erlangen, Germany) 检查，配备有标准头部线圈的加强梯度回波平面成像。卒中 MRI 诊断记录包括颅内循环三维时间飞跃法 MRA 和 3 个梯度方向的轴向 DWI 自旋回波平面成像序列 (b=0, 500, 1000 s/mm²)。跟踪 DWI 成像和得到的弥散系数计算图由扫描仪在线产生。

按盲法原则，在标准的西门子 MV1000 终端机上，3 名作者依据跟踪 DWI 成像和得到的弥散系数计算图事前独立地测量了梗死体积和颅内 MRA。在所有病例，DWI 异常要与获得的弥散系数图上的低信号区域相对应。

每个成像面的梗死面积用西门子终端机的绘图工具通过追踪 DWI 病灶周长计算得到。层厚和梗死面积之和的乘积是梗死体积，2 名作者分别测量到的梗死体积的平均数作为最终梗死体积。

MRA 检查了大动脉闭塞或近似闭塞。按盲法原则，3 名作者基于以下标准，为 MCA 血管开放状况评分。MCA M1 段无信号或低信号分别记 0 或 1。MCA M1 段正常信号而 M2 段低信号记 2 分。MCA M1 和 M2 段均正常信号记 3 分。

终点

卒中后 30 天的神经内科门诊患者，评价他们的残疾程度。从门诊或康复门诊的记录中摘录出改良 Rankin 评分 (mRS)。以预后良好 (mRS≤2) 和预后不良 (mRS>2) 作为研究终点 [8,9]。

统计分析

所有的分析使用 SPSS 13.0 完成。单因素分析确定 30 天预后的潜在预测因子。分类变量分析用 χ² 检验，连续变量分析用 Student t 检验。P<0.10 的变量进入二元 logistic 回归模型作为随访 30 天预后良好的独立预测因子，P<0.05 被认为具有统计学显著意义。

由多因素模型中的独立变量衍生出一个临床积分量表。基于我们研究结果的加权平均值，有显著意义的变量赋予分值。在多因素分析中赋予的最大分值是 9。总分被分为 3 类以预测 30 天临床预后。每个独立变量均绘制了受试者操作特征曲线，计算了曲线下面积。同时也计算了组合变量积分量表的曲线下面积，用来明确是否组合变量量表比单一变量预测预后有更高的敏感度。Spearman 秩相关用来证实，与单个独立变量比较，组合变量量表和预后的关系更为密切。

随后，将临床积分量表运用到前瞻性 DEFUSE 登记在册的 MCA 供血区皮质梗死患者预测卒中预后。登记在册的 DEFUSE 研究包括 74 名 3-6 小时内发病的 MCA 皮质梗死患者。这些患者签署了知情同意书，在静脉溶栓后 3-6 小时行弥散-灌注加权 MRI 检查。1/3 的患者 30 天后做了再次 MRI 检查。患者的第二次 MRI 梗死体积 (溶栓后) 和此次扫描前的卒中评分用于验证模型的效度。

基于多因素分析结果和积分量表，预测每个 DEFUSE 登记在册患者的预后，和他们实际的预后进行比较。作者采用盲法分析 DEFUSE 登记在册患者的实际预后。

结果

本组分析了 129 名患者，其平均年龄、NIHSS 评分和行 MRI 时间分别为 66±14 年、10±6 和 24±13 小时。缺血性卒中的病因学分类如下：60 例 (46%) 大动脉粥样硬化，41 例 (32%) 心源性栓塞，20 例 (16%) 原因不明和 8 例 (6%) 其他原因导致。61 例
(47%) 患者右侧梗死，68例（53%）是女性患者。15例（12%）患者接受了静脉注射或动脉内溶栓剂治疗，溶栓后预后良好的仅有5例。整体来讲，我们的研究对象中有58例（45%）功能预后良好，DEFUSE 登记在册的74例患者中有34例（46%）在30天时预后良好。表1概述了人口学信息、入院前的药物治疗情况、临床、实验室以及影像学参数等因素比较的单因素分析结果。行MRI检查的时间、溶栓剂的使用、其他药物的治疗史对预后没有显著影响。表2概述了随访30天预后良好的独立预测因子。在多因素模型中没有发现房颤或MRA显示MCA开放差（得分为0或1）和预后有明显联系。对多因素模型中具有统计学显著意义的5个因素赋值帮助临床医生制定预后概率分数（表3）。给出了每个变量和组合变量量表的受试者操作特征曲线下面积。与单个独立变量比较，组合变量量表预测预后有更高的敏感度。临床量表的曲线下面积为0.91（95% CI, 0.87-0.96, P=0.0001）。总积分值分为3个范围（表4），0-2的较低的分值对30天良好预后具有较高的预测价值。3-4分的患者有50%好转的机会，而那些积分>5的患者不太可能恢复自理。与DEFUSE患者的实际功能状态比较，用上述积分量表预测卒中预后得到了验证。积分量表的敏感度和特异度分别为83%和86%。

### 讨论

目前已有的一些预测卒中预后的模型。而本研究模型的独到之处在于结合临床、实验室以及影像学参数来识别影响卒中恢复的因素。那些年龄大、基线NIHSS评分高、DWI梗死体积大、高血糖以及入院时白细胞增多的MCA皮质梗死的患者更不易康复。

早期的预测模型不包括实验室参数如白细胞计数和高血糖，尽管事实表明在前瞻性研究中这些参数影响预后[10-12]。众所周知由于脑缺血使新陈代谢表1 随访30天预后良好的预测因子单因素分析

<table>
<thead>
<tr>
<th>变量</th>
<th>mRS≤2 (N=69)</th>
<th>mRS&gt;2 (N=60)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>年龄</td>
<td>62±14</td>
<td>71±13</td>
<td>0.0001</td>
</tr>
<tr>
<td>女性</td>
<td>29（42%）</td>
<td>33（55%）</td>
<td>0.16</td>
</tr>
<tr>
<td>高血压</td>
<td>49（71%）</td>
<td>46（77%）</td>
<td>0.55</td>
</tr>
<tr>
<td>糖尿病</td>
<td>16（23%）</td>
<td>17（28%）</td>
<td>0.55</td>
</tr>
<tr>
<td>高脂血症</td>
<td>34（49%）</td>
<td>22（37%）</td>
<td>0.16</td>
</tr>
<tr>
<td>吸烟史</td>
<td>35（51%）</td>
<td>24（40%）</td>
<td>0.29</td>
</tr>
<tr>
<td>卒中史</td>
<td>13（19%）</td>
<td>8（13%）</td>
<td>0.29</td>
</tr>
<tr>
<td>同侧TIA史</td>
<td>14（20%）</td>
<td>8（13%）</td>
<td>0.35</td>
</tr>
<tr>
<td>冠心病</td>
<td>20（29%）</td>
<td>14（23%）</td>
<td>0.43</td>
</tr>
<tr>
<td>HMG-CoA还原酶抑制剂</td>
<td>21（30%）</td>
<td>17（25%）</td>
<td>0.43</td>
</tr>
<tr>
<td>抗血小板治疗</td>
<td>31（45%）</td>
<td>28（47%）</td>
<td>0.86</td>
</tr>
<tr>
<td>高血糖</td>
<td>7（10%）</td>
<td>18（30%）</td>
<td>0.007</td>
</tr>
<tr>
<td>同侧MCA</td>
<td>34（49%）</td>
<td>27（45%）</td>
<td>0.86</td>
</tr>
<tr>
<td>MCA动脉评分（0或1）</td>
<td>27（39%）</td>
<td>41（68%）</td>
<td>0.001</td>
</tr>
<tr>
<td>tPA给药方式（IV或IA）</td>
<td>10（14%）</td>
<td>5（8%）</td>
<td>0.11</td>
</tr>
<tr>
<td>DWI体积（cm³，均值±SD）</td>
<td>27.8±39.5</td>
<td>75.9±87.7</td>
<td>0.01</td>
</tr>
<tr>
<td>基线NIHSS评分（中位数）</td>
<td>6</td>
<td>13</td>
<td>0.001</td>
</tr>
<tr>
<td>自细胞计数（均值±SD）</td>
<td>8.0±2.0</td>
<td>9.6±3.6</td>
<td>0.009</td>
</tr>
<tr>
<td>白细胞计数</td>
<td>22（37%）</td>
<td>8.0±16.41</td>
<td>0.03</td>
</tr>
</tbody>
</table>

### 表2 随访30天预后不良的独立预测因子

<table>
<thead>
<tr>
<th>变量</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>年龄</td>
<td>1.09</td>
<td>1.03-1.14</td>
<td>0.001</td>
</tr>
<tr>
<td>NIHSS</td>
<td>1.17</td>
<td>1.06-1.30</td>
<td>0.003</td>
</tr>
<tr>
<td>DWI体积</td>
<td>1.01</td>
<td>1.00-1.02</td>
<td>0.026</td>
</tr>
<tr>
<td>自细胞计数</td>
<td>1.16</td>
<td>1.03-1.27</td>
<td>0.037</td>
</tr>
<tr>
<td>高血糖</td>
<td>4.2</td>
<td>1.09-16.41</td>
<td>0.038</td>
</tr>
</tbody>
</table>

### 表3 MCA皮质梗死的临床量表评分系统

<table>
<thead>
<tr>
<th>变量</th>
<th>赋予分值</th>
<th>ROC曲线下面积</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>DWI体积</td>
<td>0.76(0.68-0.84)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>0-20 cm³</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-50 cm³</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51-99 cm³</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100+ cm³</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>入院NIHSS</td>
<td>0.82(0.75-0.89)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-14</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15+</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>变量</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>年龄</td>
<td>1.09</td>
<td>1.03-1.14</td>
<td>0.001</td>
</tr>
<tr>
<td>NIHSS</td>
<td>1.17</td>
<td>1.06-1.30</td>
<td>0.003</td>
</tr>
<tr>
<td>DWI体积</td>
<td>1.01</td>
<td>1.00-1.02</td>
<td>0.026</td>
</tr>
<tr>
<td>自细胞计数</td>
<td>1.16</td>
<td>1.03-1.27</td>
<td>0.037</td>
</tr>
<tr>
<td>高血糖</td>
<td>4.2</td>
<td>1.09-16.41</td>
<td>0.038</td>
</tr>
</tbody>
</table>

### 表4 不同总评分患者观察到的预后

<table>
<thead>
<tr>
<th>总分</th>
<th>预后良好</th>
<th>预后不良</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>46/50(92%)</td>
<td>4/50(8%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>3-4</td>
<td>23/47(49%)</td>
<td>24/47(51%)</td>
<td>0.72</td>
</tr>
<tr>
<td>5-9</td>
<td>3/32(9%)</td>
<td>29/32(91%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
受损害，高血糖会加剧神经元死亡。白细胞增多可通过微血管血栓形成和高粘血症影响卒中预后，更可能的是它作为发热和感染的替代标志物，导致卒中后临床症状恶化[12]。高血糖和白细胞增多能导致更长时间或更复杂的住院治疗，这影响卒中长期康复。实验室参数在多因素分析中具有统计学意义，提示在导致临床症状恶化中定义它们作用的必要性，因为它们可以作为卒中后药物治疗的目标。本研究发现和以前的研究结果一致。与起始的 NIHSS一样，年龄一直与卒中后神经功能恢复有关。NIHSS评分低的患者预后更好[1]。NIHSS评分是对神经功能缺损程度的客观描述[13]，因此被纳入目前卒中预后的预测模型[4,6,14]。然而，NIHSS评分存在大脑半球偏倚，NIHSS评分高，不一定意味着大面积梗死，因为左右半球梗死可以有不同的卒中评分[15]。除了卒中量表，梗死体积也会增加预测能力。MRI梗死体积因为优于CT和液体辅助反转恢复的梗死体积而被应用。尽管弥散可逆性[16]和液体辅助反转恢复MRI梗死被用作测量慢性梗死灶大小的标准[17]，但DWI梗死比CT有更好的可行性。DWI梗死体积与早期梗死的关系比液体辅助反转恢复磁共振成像体积更为密切。

MRI卒中体积模型显示预后和DWI梗死灶之间的关系是不一致的[18,19]。我们的结果与两个回顾性研究的结果是一致的，他们也发现DWI卒中体积与基于临床量表预后之间有关系。但不同之处在于我们选择了较大样本的同质人群作为研究对象[4,6,19]。本研究样本在预测预后不确定的中等大小梗死灶和仅限于MCA供血区皮质梗死的人群中有更好的预测价值。

和现有的模型比较，本研究模型另外的优点包括研究人群的同质性[9]。和其他以MRI为基础测定体积的预后研究相比，我们发现DWI卒中体积与基于临床量表预后之间有关系。但不同之处在于我们选择了较大样本的同质人群作为研究对象[4,6,9]。本研究样本在预测预后不确定的中等大小梗死灶和仅限于MCA皮质梗死的人群中有更好的预测价值。

尽管溶栓会影响预后，但在本研究样本中很少有人接受溶栓治疗，因此溶栓治疗在单因素模型中没有统计学意义。由于接受溶栓治疗的人少，在多因素分析时也没有将溶栓考虑在内。我们发现单因素分析时血管开放状况有很大的影响作用。有理由相信血管开放状况有预测价值，但在本研究模型中由于MRI检查时间的原因而未能进入模型。与超早期的MRI相比，延迟的MRI会发现由于卒中进展导致的大面积梗死。与完全或近似完全闭塞一样，假定梗死体积随着卒中发病的时间函数而增加。因此，延迟MRI扫描时间就能显示更大的梗死体积，这可能在多因素分析中突出MCA未闭的预测价值。

本研究的主要局限性是单中心的回顾性设计。大约20%的患者由于数据缺失或没有及时进行MRI检查而被排除。我们不知道这些患者的最终结局，如果将他们纳入，是否有影响或如何影响研究模型尚不得而知。同样他们也没有30天的随访记录，这些患者的患者样本足够可以进行单因素分析。另外的因素就是收集数据的时间。本研究最初的目标是用最近时间范围的类似的前瞻性数据集重复本研究模型。然而，我们认为用DEFUSE前瞻性登记在册的数据做效度验证更能增强此模型的预测作用。不幸的是，本研究的时间范围没有包括那些新的研究中发现的数据如重要的灌注MRI数据。使用灌注MRI的早期检查提示灌注不足的体积与临床预后有关[20]。新的证据证实了灌注不足与不良预后有关的发现，即使有血流灌注不足组织的再通[21]。

本研究结果需要进一步前瞻性研究的验证。目前需要更精确的卒中预后调查来证实此模型。一旦被验证，将是MCA供血区皮质梗死患者临床诊断、质量评估和研究方法学的一个有用的工具。

参考文献


