

# Predictors of one-year survival after ischaemic stroke



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*Predicting the outcome of ischaemic stroke (IS) is a complex task, as mortality and disability depend on many factors, including age, gender, type and severity of stroke, and comorbidities. Survival rates also vary between countries depending on genetic characteristics and differences in the organisation of healthcare systems.*

**Objective:** to search for predictors of one-year survival after IS in a sample of patients from the Perm region.

**Material and methods.** The study included 254 patients who had suffered an IS. Seventy-five parameters obtained during routine clinical examination were analysed, including information on the subtype and severity of the stroke, the size and location of the lesion, neurological disorders, comorbidities, and other factors. Relevant features were selected using the WEKA programme, and the selected features were used in a predictive model based on logistic regression.

**Results.** The following factors have been identified as significant predictors of annual survival in patients who have undergone IS (the sign of the coefficient reflects the relative contribution of the factor to the model and its positive or negative effect): age (-0.02), degree of neurological deficit on the NIHSS scale at discharge (-0.06), haemoglobin level (0.01), infarction in the anterior choroidal artery basin (0.74), recurrent stroke within the following year (-0.02) and cardioembolic stroke subtype (-0.32). The accuracy of the logistic model was 84% with 10-fold cross-validation.

**Conclusion.** In the model predicting one-year survival after IS, other factors have been identified in addition to age, which is usually associated with a less favourable prognosis. Further multicentre studies are needed to confirm the reliability of the proposed model.

**Keywords:** ischaemic stroke; predictive model; outcome; magnetic resonance imaging; NIHSS; blood test.

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**Introduction.** Stroke is a severe neurological disorder, characterized by a high-level of mortality and chronic disabilities among survivors [1]. Given the enormous economic and social consequences of stroke, identifying predictors of its outcome is an important task. However, the etiology and clinical presentation of stroke are extremely diverse, complicating the prediction of outcome.

Recent models predicting unfavourable stroke outcome include a 30-day mortality risk prediction model [2], a nomogram for predicting death within 6 months of stroke [3], the PLAN score [4], the IScore [5], the Ischaemic Stroke Survival Score [6], various scores and models for predicting survival up to 1 year [7–9], including a dynamic prediction model suggested by Huang et al. [10], and a 10-year mortality model proposed by Szlachetka et al. [11]. Despite the differences in the proposed models, there is a common evidence that certain factors may be considered as promising predictors of stroke survival, including age [4, 10, 11], sex [5, 10, 11], stroke severity [2, 5, 10], stroke type [4, 7, 10] and various comorbidities [4, 5, 7], such as heart-related diseases, diabetes, renal dysfunction, etc. However, the exact combination of these factors in the proposed prediction models varies across the studies (a detailed comparison of these studies is given in Tab. 1). This fact may

reflect not only the differences in the prediction models used but also different mortality levels from stroke across the countries [12], which may stem from multiple factors such as race [13], lifestyle [14], genetics [15, 16] and differences in the organization of the national health care systems with respect to stroke treatment [17].

Taking these factors into account and the fact that most prediction models were developed based on Western populations, our goal was to identify factors that could be used to predict mortality rates 1 year after stroke in the Russian population.

**Materials and methods.** The study included 254 patients (mean age  $65.8 \pm 10.2$  years, min. age – 28 years old., max. – 90 years old.; 140 male / 114 female) with acute ischemic stroke who were followed up for at least one year after their initial hospitalization to the Neurology Department of Perm City Clinical Hospital No. 4.

#### Inclusion criteria:

- 1) acute ischemic stroke confirmed by CT and/or MRI;
- 2) complete clinical, laboratory and instrumental examination in accordance with the current clinical guidelines;
- 3) given informed consent.

Over the following year, 54 patients died, representing a mortality rate of 21%. During routine clinical examinations, data

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containing 75 clinical parameters were collected for each patient. All clinical examinations were conducted in accordance with the national healthcare guidelines and protocols. The recorded parameters included both numerical (Table 2) and binary (Table 3) variables, grouped for better interpretation.

Binary variables were used to describe: 1) stroke etiology – atherothrombotic, cardioembolic, embolic stroke of undetermined source (ESUS) or other; 2) localization of stroke lesion in specific brain regions or arterial territories; 3) presence of various comorbidities (e.g., coronary heart disease, cancer, etc.); 4) presence of stroke-related disorders (e.g., hemiparesis, aphasia, etc.) and 5) smoking status.

Numerical variables included age, weight, height, and associated body mass index (BMI) and body surface area, time to hospital admission (in hours), various stroke severity measures (National Institutes of Health Stroke Scale, NIHSS, and Modified Rankin Scale, mRS, scores), lesion size, clinical blood test results (red blood cell, lymphocyte, platelet count, etc.), and

cardiac parameters (ejection fraction, end-systolic volume, end-diastolic volume, etc.) assessed by echocardiography (ECG).

**Statistical analysis.** Data analysis was performed using WEKA v.3.6.13 software [18]. Feature selection was performed on the entire sample using the CfsSubsetEval function. This function implements the approach proposed by Hall and Smith [19], which evaluates the value of a subset of attributes by taking into account the individual predictive values of each feature and the degree of information redundancy between them. As a result, this approach yields a subset of parameters that are highly correlated with the outcome but have little or no correlation with each other. The model for predicting 1-year survival after stroke was built on logistic regression, which takes a linear combination of clinical features and indicators as an argument. Model coefficients were estimated using the maximum likelihood method. Model accuracy was tested using 10-fold cross-validation.

**Results.** Based on the results of the feature selection procedure, 10 potential predictors of stroke survival were identified

Table 1. *Overview of potential predictors of survival after stroke*

Author	Wang	Sha	O'Donnel	Saposnik	Williams	Anderson	Solberg	Wang	Huang	Szlachetka
Year	2022	2021	2012	2011	2000	1994	2007	2003	2020	2022
Sample N	488497	210	4943	12262	453	492	800	440	4315	10366
Country	UK	China	Canada	Canada	USA	Australia	Norway	Australia	UK	UK
Period	2013–2019	2013–2019	2003–2008	2003–2008	1993–1999	1989–1990	1993–1998	1995–1997	1995–2016	2003–2016
Prediction period	1 m.	6 m.	1 year	10 year						
Sex	+	ns.	ns.	++	ns.	ns.	ns.	ns.	++	++
Age	++	+	++	++	++	ns.	++	ns.	++	++
Stroke type	++	ns.	ns.	++	NA	++	++	++	++	++
Severity	++	NA	NA	++	++	++	++	NA	++	++
Level of consciousness	++	NA	++	NA	NA	++	NA	++	++	NA
Dependency	NA	++	++	++	++	++	NA	NA	++	++
Neurological deficits	NA	NA	++	NA	++	++	++	++	++	++
Cardiac diseases	+	+	++	++	NA	++	++	++	NA	++
Hypertension	ns.	+	ns.	NA	NA	ns.	+	ns	NA	++
WBC	NA	+	ns	NA	NA	NA	NA	ns	NA	++
Serum albumin	NA	++	NA							
Serum d-dimer	NA	++	NA							
Smoking	NA	+	ns.	++	ns.	ns	NA	NA	NA	NA
Nutritional status	NA	+	NA							
Diabetes	ns.	ns.	ns	+	NA	ns	++	++	NA	ns.
Glucose level	NA	NA	ns	++	NA	NA	+	ns.	NA	NA
Hypertermia	NA	NA	ns.	NA	NA	NA	ns.	++	NA	NA

**Note:** 'ns.' – the factor was included in the study but was found to be insignificant for predicting stroke outcome; 'NA' – the factor was not taken into account in the study; '+' – the factor had some correlation with survival after stroke but was not included in the final prediction model; '++' – the factor was considered important for predicting stroke outcome.

across the entire sample: age; pathogenetic stroke subtype; NIHSS score at admission and discharge; mRS score at discharge and after 90 days; hemoglobin level; recurrent stroke during the observation period; involvement of the anterior choroidal artery; and left ventricular ejection fraction. Of these parameters, six were included in the final model, which was constructed using logistic regression with 10-fold validation:

$$\text{Survival} = \text{logit} (1,01 - 0,02 \times \text{Age} - 0,06 \times \text{NIHSS} - 0,32 \times \text{Cardioembolic} - 0,02 \times \text{Stroke} + 0,74 \times \text{AntChArt} + 0,01 \times \text{Hb}).$$

where NIHSS stands for NIHSS score at discharge, Cardioembolic is 1 in case of a cardioembolic subtype of stroke, Stroke is 1 in case of a recurrent stroke during the observation

period, AntChArt is 1 in case of involvement of the anterior choroidal artery, Hb stands for hemoglobin level. The accuracy of the proposed model was 84.6%. Detailed information on the model's performance is presented in Table 4.

**Discussion.** This study presents a model for predicting 1-year survival after ischemic stroke among patients living in Perm Krai. To select the best parameters, all available clinical data were considered. These parameters included data on the pathogenetic subtype and location of the stroke, neurological deficit, stroke severity, comorbidities, as well as the results of laboratory and instrumental examinations.

Of the 75 available characteristics in the final model, six had significant predictive value: age, NIHSS score at discharge, hemoglobin level, recurrent stroke within the following year,

Table 2. *Summary of the numerical variables across the sample*

Characteristics	Mean	Sd
Age	65.83	10.23
Weight (kg)	78.80	15.73
Height (cm)	167.21	9.66
BSA (m <sup>2</sup> )	1.88	0.20
BMI	27.95	5.05
Time to admission (h)	25.23	41.93
Severity		
NIHSS at admission	6.78	5.28
NIHSS at discharge	3.56	4.50
mRS at admission	1.91	1.37
mRS at discharge	1.61	1.37
Lesion size MRI (max. d), mm	34.17	25.68
Blood Tests		
RBC, x10 <sup>12</sup> /L	4.66	0.57
Hematocrit, %	40.87	5.01
Hb, g/L	138.78	18.03
WBC, %	25.03	9.74
Platelets, x10 <sup>9</sup> /L	220.95	71.34
LDL (Low-Density Lipoproteins)	3.11	1.07
HDL (High-Density Lipoproteins)	1.24	0.33
Total Cholesterol	5.06	1.26
Triglycerides	1.59	0.89
GFR (Glomerular Filtration Rate)	73.87	19.42
Cardiac characteristics		
Ejection Fraction (EF), %	57.69	7.41
End-Diastolic Diameter (EDD)	47.17	5.34
Ventricular Septum Size	12.78	1.80
Posterior wall size	11.71	1.44
End-Diastolic Volume (EDV)	101.83	26.06
End-Systolic Volume (ESV)	43.96	18.02
Heart Stroke Volume (SV)	57.87	13.41
SV index	30.81	6.99
LA (Left Atrial) train	20.66	5.42
LA volume	71.21	29.48
LA volume index	38.27	16.24
LA diameter	3.86	0.54
LA 2-nd size	3.93	0.51
LA 3-nd size	5.19	0.70
LADI (Left Atrial Diameter index)	2.08	0.39
Post-Stroke SBP (Systolic Blood Pressure)	148.98	19.59

Table 3. *Summary of the binary parameters across the sample*

Parameters	Male	Female N	Total
Stroke type			
Embolic stroke of undetermined source (ESUS)	70	59	129
Atherothrombotic	36	14	50
Cardioembolic	19	31	50
Other non-ESUS	15	10	25
Lesion localization			
Cortical	63	56	119
Cortico-subcortical	44	40	84
Lacunar	11	2	13
Deep lesion	32	18	50
Insular lesion	17	25	42
Corpus callosum lesion	2	6	8
Brainstem	8	4	12
Anterior cerebral artery	6	6	12
Middle cerebral artery	91	83	174
Posterior cerebral artery	18	9	27
Anterior choroidal artery	12	14	26
Posterior inferior cerebellar artery	22	12	34
Multiple lesions within the same basin	43	24	67
Multiple lesions in different basins	21	9	30
Comorbidities			
Cancer	12	11	23
Obesity	31	47	78
Arterial hypertension	136	110	246
Diabetes mellitus	15	36	51
Acute myocardial infarction	3	3	6
Myocardial infarction (>1 month ago)	21	9	30
Atrial fibrillation	7	7	14
Ischemic heart disease	40	25	65
Previous stroke	38	27	65
Neurological deficits			
Dysphagia	2	2	4
Hemianopsia	14	8	22
Hemihyperesthesia	52	34	86
Hemiparesis	98	77	175
Ataxia	14	14	28
Oculomotor disturbances	10	4	14
Neglect	12	20	32
Motor aphasia	18	17	35
Sensory-motor aphasia	22	29	51
Acute vestibular syndrome	12	8	20
Smoking	65	9	74

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involvement of the anterior choroidal artery, and cardioembolic stroke subtype.

Although age is negatively associated with stroke survival in almost all existing prediction models, other factors deserve more detailed discussion. Stroke severity, measured by the NIHSS [2], mRS [11], or Canadian Neurological Scale (CNS) [8], is generally considered an indicator of poor prognosis and is widely used in various prediction models. However, the question remains as to which scale better describes outcome, as most studies use only one scale and cannot compare their predictive ability in the same sample. In the present study, both the NIHSS and mRS were considered. Only the NIHSS score at discharge was retained in the final model. When the NIHSS score was replaced with the mRS score at discharge in the final prediction model, the prediction accuracy remained high (83%) but was slightly lower than for the model with the NIHSS score. Adding both scales to the model did not significantly improve its performance, as the NIHSS and mRS scores were correlated. Thus, both scales can be used interchangeably, but the NIHSS score is preferred, at least for this sample.

The pathogenetic subtype of stroke is another important factor that may influence survival. Most studies examine only two types of stroke (ischemic or hemorrhagic), with hemorrhagic stroke being a significant predictor of poor prognosis. Indeed, the 30-day mortality rate after hemorrhagic stroke is twice as high as after ischemic stroke [20]. However, this study focuses only on ischemic stroke, which is a heterogeneous disease [21]. Ischemic stroke subtypes differ in treatment strategies, severity of comorbidities, recurrence rates, and possibly mortality rates. According to the study by L.G. Stead et al. [22], the only subtype included in the final prediction model was the cardioembolic subtype, which has previously been noted to have the worst prognosis among stroke subtypes [23, 24]. Like L.G. Stead et al. [22], we considered the cardioembolic subtype in our model as a separate predictor, independent of age, gender, and NIHSS score. Interestingly, cryptogenic stroke, which was not included in the prediction model, was associated with a less severe outcome than cardioembolic

stroke. Given the diversity of pathological mechanisms underlying different stroke subtypes, it is possible that constructing prediction models separately for each stroke subtype will lead to better prognosis and draw attention to more significant clinical factors for a particular stroke type [25]. However, this task was left beyond the scope of the present study, since the sample size was not large enough to consider each stroke subtype separately.

Recurrent strokes have previously been associated with long-term mortality in patients with ischemic stroke [26–28]. In the final prediction model, recurrent stroke within one year was also considered as a separate predictor of adverse outcome, highlighting the importance of preventing recurrent vascular events. Prevention of recurrent stroke should be tailored to the specific pathogenetic subtype [29]. However, up to 30% of all ischemic stroke cases are cryptogenic [30]. Therefore, the development of new algorithms for identifying stroke subtypes represents an important area of future research aimed at improving long-term outcomes after ischemic stroke.

In the final model, higher hemoglobin levels were considered a favorable predictor of post-stroke survival. Recent reviews and meta-analyses suggest that anemia in stroke may be associated with increased mortality and disability [31, 32]. However, it is possible that the relationship between hemoglobin levels and stroke mortality is not linear [33], and both very low and very high values may increase mortality and lead to worse functional outcomes.

Finally, the involvement of the anterior choroidal artery, which was considered a favorable factor in our model, may reflect the fact that this type of stroke is likely associated with microangiopathy rather than atherosclerosis or other “more serious” causes. Indeed, previous studies indicate that infarctions in the anterior choroidal artery territories have a more favorable outcome compared with other cases of supratentorial ischemic stroke [34]. The relative contribution of the aforementioned factors to stroke survival, as well as their subset, may potentially vary across different clinical centers, regions, and with changes in the prediction period. Therefore, the presented results should be extrapolated with reasonable caution.

**Conclusion.** In addition to age, which is typically associated with a less favorable prognosis, other factors were identified in the model for predicting 1-year survival after ischemic stroke. Further multicenter studies are needed to confirm the reliability of the proposed model.

Table 4. *Model characteristics broken down by class*

Class	TP rate	FP rate	Precision	Recall	F-measure	ROC area
Died	0.426	0.04	0.742	0.426	0.541	0.817
Survived	0.96	0.574	0.86	0.96	0.907	0.802
Weighted Avg.	0.846	0.46	0.836	0.846	0.829	0.805

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### Conflict of Interest Statement

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