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Early Prediction of Outcome of Activities of Daily Living After Stroke : A Systematic Review

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Early Prediction of Outcome of Activities of Daily Living After Stroke

A Systematic Review

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Background and Purpose—Knowledge about robust and unbiased factors that predict outcome of activities of daily living (ADL) is paramount in stroke management. This review investigates the methodological quality of prognostic studies in the early poststroke phase for final ADL to identify variables that are predictive or not predictive for outcome of ADL after stroke.

Methods—PubMed, Ebsco/Cinahl and Embase were systematically searched for prognostic studies in which stroke patients were included ≤2 weeks after onset and final outcome of ADL was determined ≥3 months poststroke. Risk of bias scores were used to distinguish high- and low-quality studies and a qualitative synthesis was performed.

Results—Forty-eight of 8425 identified citations were included. The median risk of bias score was 17 out of 27 (range, 6–22) points. Most studies failed to report medical treatment applied, management of missing data, rationale for candidate determinants and outcome cut-offs, results of univariable analysis, and validation and performance of the model, making the predictive value of most determinants indistinct. Six high-quality studies showed strong evidence for baseline neurological status, upper limb paresis, and age as predictors for outcome of ADL. Gender and risk factors such as atrial fibrillation were unrelated to this outcome.

Conclusions—Because of insufficient methodological quality of most prognostic studies, the predictive value of many clinical determinants for outcome of ADL remains unclear. Future cohort studies should focus on early prediction using simple models with good clinical performance to enhance application in stroke management and research. **(*Stroke*. 2011;42:1482-1488.)**

Key Words: activities of daily living ■ prognosis ■ review ■ stroke

Stroke recovery is heterogeneous in terms of outcome, and it is estimated that 25% to 74% of the 50 million stroke survivors worldwide require some assistance or are fully dependent on caregivers for activities of daily living (ADL) after stroke.[1] In addition to medical management after acute stroke to prevent further cerebral damage, stroke rehabilitation is initiated early with the ultimate goal of achieving better recovery in the first months after stroke and reducing disability during the years that follow.[2] The current trend to shorten the length of stay in hospital stroke units and the increasing demand for efficiency in the continuum of stroke care imply that knowledge about the prognosis for outcome in terms of basic ADL, such as dressing, mobility, and bathing, is crucial to optimize stroke management in the first months. In addition, it guides realistic goal-setting, enables early discharge planning, and correctly informs patients and relatives. This knowledge is also important for adequately designing future trials in stroke rehabilitation. In particular, identifying subgroups of patients who may benefit most from a particular intervention[3] and stratifying patients into prognostically comparable groups[4] will prevent underpowered studies (ie, type II error), especially because the effects of stroke rehabilitation are relatively small when compared to the prognostic variability across included patients.[5,6]

Unfortunately, prognostic models have not gained much acceptance in clinical practice due to doubts about their

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predictive accuracy because of issues such as observation bias, problems with generalization of results, and the complexity of algorithms that hamper practical implementation.[7,8] Previous systematic reviews have shown that a high proportion of prognostic studies in stroke is methodologically poor.[7,8] However, the most recent review of this topic dates back to March 2002.[9] Since the past decade, emphasis is given to improve prognostic research by developing guidelines for the reporting of prognostic studies in health care.[10–12]

The purpose of the present systematic review was to investigate the methodological quality of prognostic studies in the early poststroke phase for outcome of ADL and to identify early clinical factors that are predictive or not predictive for outcome of basic ADL beyond 3 months.

Materials and Methods

Study Identification

The following databases were searched for relevant studies by 2 researchers (J.V. and J.K.) from inception to October 2010: PubMed (October 18), Ebsco/Cinahl (October 12) and Embase (October 19). The following terms were used (with synonyms and closely related words): "cerebrovascular accident" or "stroke," and "activities of daily living" or "walking" or "gait" or "mobility," and "prognosis"[10–13] or "systematic review" or "meta-analysis." The search strategies in the electronic databases and the full logbook of all the searches are available on request. Studies were included when: (1) they aimed to identify prognostic studies and combined at least 2 separate variables that were used to predict the future outcome in individuals;[3,13] (2) stroke patients aged 18 years or older had been recruited within 2 weeks after onset. In accordance with the World Health Organization, stroke was defined as "rapidly developing clinical symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin."[14] Transient ischemic attacks (ICD-10 G45) and subarachnoidal bleeding (ICD-10 I60) were excluded; (3) they were designed as a longitudinal cohort study, which tracks a specific group of people in time from exposure to outcome to identify incidence, natural history, and prognosis of a disease;[15] (4) they had final outcome defined as basic ADL measured at least 3 months after stroke and included the ability to perform basic activities of self-care and mobility. These activities are captured by a combination of codes d510 (washing oneself), d530 (toileting), d550 (eating), d540 (dressing), b5253 (fecal continence) and b6202 (urinary continence), d410 (changing basic body position), d420 (transferring oneself), and d450 (walking) from the International Classification of Functioning, disability and health;[16] (5) the article was written in English, German, French, or Dutch, because these are the most common languages in peer-reviewed journals.[17] Reference lists were checked for other relevant studies or reviews and personal bibliographies were consulted.

Data Abstraction

One reviewer (J.V.) extracted relevant characteristics of each cohort study with respect to numbers recruited, timing of initial and final observations, outcomes used, included and excluded variables for multivariable modeling, and model performance.

Quality Appraisal

The methodological quality of reports of prognostic studies was assessed by a developed 27-item checklist that addressed 6 major risks of bias: study participation, study attrition, predictor measurement, outcome measurement, statistical analysis, and clinical performance/validity.[7,8,10,18] As shown in Supplemental Table I (http://stroke.ahajournals.org), each item was graded positive (sufficient information: low risk of bias, 1 point assigned), negative (sufficient information: potential risk of bias, 0 points assigned), or partial/unknown (insufficient information: ? assigned). A total score was obtained by summing all items that were scored as positive. This list was pilot-tested on 3 different prognostic studies that did not meet the study inclusion criteria to reach consensus about each checklist item. A priori, we considered a study to be at low risk for bias when it scored ≥20 points (75% of the maximum score)[8] and at high risk for bias when it scored ≤19 points. Two reviewers (J.V. and M.H.) independently assessed the risk of bias of the included studies. They were not blinded to author names, institutions, or journal of publication. Disagreements were resolved in a consensus meeting.

Analysis

We were unable to perform a quantitative analysis (statistical pooling) of the data because of heterogeneity in terms of study design, moment of inception and follow-up, and the composition and analytical methods of the multivariable models. Consequently, a best-evidence synthesis was performed independently by J.V. and E.W. to summarize the findings of the included studies. Based on the number, quality (ie, low- or high-risk of bias), and results of these cohort studies, 4 levels of evidence for a particular predictor variable were distinguished: (1) strong evidence: generally consistent findings in multiple (≥2) studies with low risk of bias; (2) moderate evidence: generally consistent findings in 1 study with low risk of bias and ≥1 studies with high risk of bias; (3) limited evidence: only 1 study with low risk of bias is available; and (4) insufficient or no evidence: consistent findings in multiple studies with high risk of bias, inconsistent findings in multiple studies, inconsistent findings within 1 study, or no significant result with outcome of interest is present.[19,20]

Generally consistent findings means that the number of studies showing evidence was >50% of the total number of studies within the same methodological quality category. Otherwise, insufficient or no evidence was allocated. Subsequently, predictors and nonpredictors were classified according to the International Classification of Functioning Disability and Health in terms of body structures, body functions, activities and participation, and personal and environmental factors.

Results

Study Identification

The Figure shows that the electronic search resulted in 8425 citations. On the basis of this search and checking references, a total of 48 studies were included.[21–71] Contacting authors for further information did not result in additional inclusions. A list of excluded studies can be obtained from the corresponding author on request.

Study Characteristics

A description of the main characteristics of the included prognostic studies can be found in Supplemental Table II. The number of participants in the 48 inception cohorts ranged from 41[34] to 4499,[64] and amounted to a total of 25 843 subjects. Forty-two of the 48 studies recruited immediately after hospital admission (ie, hospital-based).[21–26,29,31,32,34–40,42,44–54,56–59,61,62,64–71] Twenty-one studies included patients with ischemic and hemorrhagic strokes,[21,27a,30,31,33,35,38,39,41,46,49,52,58,62–67,69,70] whereas 13 studies were restricted to first-ever strokes.[22,29–31,37,41,45,48,50,53,64,66] The mean time that had elapsed between stroke onset and initial observation was 5.4 days, ranging from 136.6 minutes[48] to 14 days.[33,38,44,52] All studies defined final outcome of ADL at a fixed moment after onset, with the exception of two.[45,69] Some studies used >1 ADL measurement in their

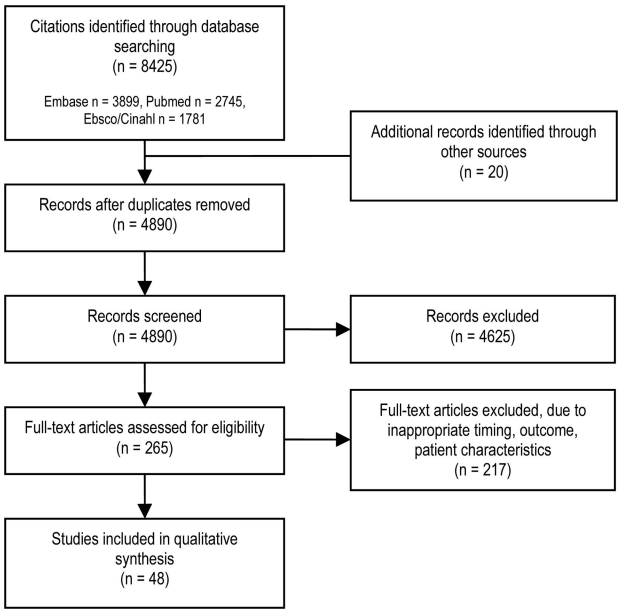

Figure. Flow diagram of literature search.

prognostic investigations.[23,42,61] The Barthel Index (BI; K=24) [23,24,26,29,31,32,34,37,41,42,45,46,51–53,58–62,64–66,68] was the most frequently used scale to assess ADL outcome, followed by the modified Rankin scale (K=18),[21–23,25,30,35,37,38,42,44,47,49,50,57,67,70,71] the Glasgow Outcome scale (K=4),[40,42,56,61] the Functional Independence Measure (K=2),[38,54] the Oxford Handicap Scale (K=1),[27a] the Katz scale (K=1),[63] and other less known ADL assessment instruments (K=2).[39,69] Thirty-six studies dichotomized[21–26,27a,29–33,35–37,40,42–51,53,56,59–62,64,65] or classified[41,58] outcome of ADL, with cut-off scores ranging from 60[23,42] to 95,[23,24,26,33,42,45,62] for the 100-point version of the BI, and from 12[59,65] to 19[29] for the 20-point BI version. The modified Rankin scale cut-off scores varied from 1[23,37,42] to 5.[23]

Quality Appraisal

As shown in Supplemental Table III (http://stroke.ahajournals.org), the median risk of bias scores of the included studies was 17 points (range, 6[71]–22[21,22]). Six of the 48 studies were of high methodological quality and scored ≥20 out of 27 available points.[21–26]

Study Design

Eighty-three percent of the included studies clearly stated the inclusion and exclusion criteria, and 48% described baseline key characteristics of the study sample. A prospective design was used in 77% of the studies. Twenty-seven percent gave information about the medical or paramedical treatment provided.

Study Attrition

The number lost to follow-up was reported in 77% of the articles, reasons were stated in 67%, and adequate methods of dealing with missing data were described in 33% of the studies.

Predictor Measurement

Predictors were well-defined in 92% of the studies, but only 19% reported a clear rationale for the cut-off scores that were used.

Outcome Measurement

The outcome was clearly defined in 96% of the studies, and 42% properly defined both cut-off points and rationale.

Statistical Analysis

All studies reported whether they used linear or logistic regression techniques; however, 38% gave information about variable selection methods and the probability value used for acceptance. Univariable crude estimates and confidence intervals were described in 19% of the studies, whereas 73% reported point estimates with confidence intervals of the multivariable analysis. Finally, 35% did not dichotomize variables of a continuous nature, like age.

Clinical Performance/Validity

Clinical performance was tested in 56% of the studies using explained variance (K=9),[26,34,38,45,54,57,63,69,71] area under the curve (K=7)[21,23–25,27a,29,42] or c-statistic (K=1),[57] overall accuracy (K=6),[22,26,29,31,39,59] sensitivity and specificity (K=5),[22,32,41,44,59] Hosmer-Lemeshow statistic (K=2),[36,44] and calibration (K=1),[23] whereas 1 study just reported the graph of the receiver-operating characteristic curve.[68] The model developed was internally validated in 8% and externally validated in 21% of the studies.

Identified Early Poststroke Predictors of Final Outcome

Six studies showed a low risk of bias and 42 studies a high risk of bias. The Table shows the predictor variables measured early after stroke with their level of evidence, that were predictive for outcome of ADL ≥3 months.

Strong evidence was found for patients' neurological status measured with the National Institutes of Health Stroke Scale (NIHSS) or the Canadian Neurological Scale, with items relating to lower severity of (upper limb) paresis as strong components for better outcome of ADL. In addition, strong evidence was found for older age as a variable disfavoring outcome of ADL. Supplemental Table IV (http://stroke.ahajournals.org) lists those variables that were found not to be predictive for outcome of ADL ≥3 months. Synthesis resulted in strong evidence that gender and risk factors, such as atrial fibrillation, are unrelated to final outcome of ADL ≥3 months.

Discussion

Prediction plays an important role in evidence-based clinical decision-making after stroke by objectifying, simplifying, and increasing the accuracy of forecasting patients' future functioning.[72] The present research synthesis investigated which early measured variables are predictive or not predictive for basic ADL outcome after stroke. A vital aspect herein is the assessment of methodological quality. The large number of studies published in the past decade shows that prognosis in stroke rehabilitation is a growing field of

Table. Best-Evidence Synthesis of Early Measured Variables Predictive for Outcome of Activities of Daily Living ≥3 Months After Stroke According to the International Classification of Functioning, Disability and Health

Variable	Level of Evidence
Body structures	
Stroke classification	IV
Imagine variables	
Stroke volume	IV
Focal computed tomography abnormality	III
Leukoaraiosis	III
Superficial middle cerebral artery	IV
Cortical	IV
Posterolateral extension involving posterior limb of internal capsule	IV
Location (lobar, deep, infratentorial)	IV
Lenticulostriate arteries infarction	III
NIHSS*small vessel occlusion	IV
Days to magnetic resonance imaging	IV
Intima-media thickness	IV
Body functions	
Initial neurological status	I
GCS verbal	IV
Able to talk and oriented	IV
Paresis	IV
Arm	I
Grip strength	IV
Tendon reflexes	IV
Able to swallow	IV
Cognitive deficit*	IV
Dysphasia	IV
Complications	
Neurological complications	III
Fever	III
Orpington prognostic score	IV
Allen prognostic score	IV
Activity and participation	
Trunk control test	IV
Gait	
Ability to walk	IV
Able to walk unaided	II
ADL functioning	IV
Change in ADL at days 2–15	IV
Disability	III
Leg function	IV
Personal factors	
Age	I
Prestroke independence	II
Prestroke mobility	IV
Comorbidity and risk factors	
No. of risk factors	IV
Previous stroke	II
Neurological impairment	IV
Diabetes	IV
Hypertension	IV
Myocardial infarction	IV
Heart failure	IV
Cognitive impairment	IV
Depression	IV
Cardiac, blood, and urine variables	
Urea	IV
CFU-EC increment, week 1	IV
Living alone	IV
Relationship with significant other	IV
Previous Short Form-36 health survey	IV
Prestroke institutionalization	IV
Educational level	IV
Prestroke financial security	IV
Nutrition	
Malnutrition	IV
Undernourished	IV
Undernutrition, week 1	IV
Race	IV
Black*time	IV
Environmental factors	
Time from onset	IV
Time (log function)	IV
Discharge to nursing home or other institution	IV
Inpatient treatment neurologist	IV
Days to rehabilitation initiation	IV
Black*days to rehabilitation*time	IV
Days to rehabilitation*time	IV
Adequacy of home and neighborhood	IV

I, strong evidence: generally consistent findings in multiple (≥2) studies with low risk of bias. II, moderate evidence: generally consistent findings in 1 study with low risk of bias and ≥1 studies with high risk of bias. III, limited evidence: only 1 study with low risk of bias is available. IV, insufficient or no evidence: consistent findings in multiple studies with high risk of bias, inconsistent findings in multiple studies, inconsistent findings within 1 study, or no significant result with outcome of interest is present.

ADL indicates activites of daily living; CFU-EC, colony-forming unit-endothelial cell; GCS, Glasgow coma scale; NIHSS, National Institutes of Health Stroke Scale.

*eg, neglect, dyspraxia, visuospatial problems.

interest. However, prognostic research is complex, acknowledging that the generalization is mostly limited. Because of methodological shortcomings and inadequate reporting, the predictive value of most determinants for outcome of ADL after stroke is indistinct. It should be acknowledged, however, that the development of the methodology of prognostic studies is still in progress[10] and that the guidelines for reporting observational studies according to the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement only recently have been established.[12] Fortunately, our review shows a positive evolution of the

methodological quality of prognostic studies because 5 out of the 6 high-quality studies were published in the past decade. This illustrates the growing awareness among investigators that they have to meet the methodological criteria for prediction model development.

Despite the fact that only a small proportion (12.5%) of the included studies were of high quality, we found strong evidence that age and outcomes assessing severity of neurological deficits in the early poststroke phase, such as the NIHSS[23,25,73] and Canadian Neurological Scale,[22] are highly associated with final basic ADL outcome beyond 3 months after stroke. More specifically, items related to severity of motor impairments seem to be the most important components of these scales for predicting outcome of ADL. These findings are largely in line with Counsell et al,[7] who reported these multivariable tested predictors for the outcome in terms of survival in an independent state. In addition, there is strong evidence that gender and the presence of risk factors for stroke, such as atrial fibrillation, do not predict outcome of basic ADL. The present systematic review also shows that the added value of imaging data for the prediction of ADL outcome is limited when compared to the contribution of clinical variables alone.[21,29,74]

Just as in stroke trials, the BI and modified Rankin scale were the two activity-level outcome measures most frequently used in prognostic stroke studies.[75] Both outcomes were dichotomized for regression analysis in many studies, although cut-off points varied. For example, "independent" or "favorable" on the BI was defined as either >60, ≥85, ≥90, >95, or ≥95, hampering a valid comparison across the included studies. The comparability of studies can be improved by using well-established cut-off points.[76] Remarkably, the Functional Independence Measure, which is commonly used to evaluate outcome in terms of ADL dependency after stroke,[77] has barely been used in inception cohorts started from stroke onset (ie, within 2 weeks) for the purpose of making predictions beyond 3 months.[38,54]

Unfortunately, prognostic models are not commonly applied in routine care for a number of reasons. First, successful clinical implementation of the investigated models is hampered by the complexity of the algorithms derived from them. Second, opportunities to generalize the probabilities of derived models are limited because of differences in patient characteristics. The cohorts in the prognostic studies included in our review were often mixed but sometimes restricted to, for example, ischemic or hemorrhagic strokes, or anterior circulation or posterior circulation infarcts. Obviously, the selection of a cohort with a common underlying stroke type increases the precision with which the outcome of interest can be predicted but limits its generalization to other stroke types. This suggests that transparency is needed concerning the criteria used for patient selection. In addition, case-mix adjustment has to be considered to control for differences in sample recruitment. Third, generalization of the probabilities of existing models based on clinical and imaging variables is hampered by differences in the timing of clinical determinant measurement in the early poststroke phase.[6,73,78] For example, in a recent cohort study we found that the earliest time at which an optimal prediction of ADL independency outcome (ie, ≥19 points according to the BI) could be made was at day 5 after stroke, whereas day 2 scores resulted in suboptimal prediction because of an underestimation of patients' abilities when they are still bed-ridden.[78] In contrast, the accuracy of the NIHSS in predicting ADL outcome is almost unaffected by the timing of assessment in the first 9 days after stroke, making this instrument more robust for determining patient prognosis.[73] Finally, prediction models still misclassify a certain amount of patients, but most prognostic studies failed to report information about the performance of the model derived and also failed to verify its internal and external validity, which is important because prediction rules are always less accurate when retested in an independent patient cohort.[8,79]

The present review does have some limitations. First, despite a sensitive search, publications may have been missed because of poor indexation of the literature reporting observational studies including prognostic research.[80] Second, data extraction was performed by 1 reviewer.[81] Third, the scoring list for the assessment of methodological quality was based on recent recommendations for prognostic research as well as criteria used in previous scoring lists for assessment of prognostic stroke research.[10,18] However, there may be room for improvement because the development of criteria for assessing methodological quality is still in progress. For example, the used criteria for defining study characteristics such as an inception cohort (ie, ≤2 weeks) and final outcome (ie, ≥3 months) are based on purely pragmatic grounds.

A future overview of unbiased predictors of ADL outcome will only be possible when the key methodological criteria for prognostic research are met. Besides, future studies should aim for robust but clinically feasible predictors of ADL outcome. For this, consensus about International Classification of Functioning-linked definitions and standardized measurement of these predictors is conditional. Recently, we found in 3 cohorts of patients with a first-ever hemispheric stroke that the baseline value of the dependent variable for measuring ADL is highly predictive of the final outcome.[5,78,82] However, only a few low-quality studies have investigated this relationship so far.[29,31,46,59,62,66] In addition, Stinear[82] recently suggested that the accuracy of prediction might be increased by combining simple bed-side tests of motor impairment with neuroimaging, genotyping, and neurophysiological assessment of neural plasticity. Furthermore, patients preferably should be tested at fixed moments early after stroke, because clinical determinants are time-dependent and nonlinearly related with stroke recovery.[6] Determining the optimal timing for predictions requires studies with an intensive repeated-measurement design.[83] In the same vein, new statistical methods such as random coefficient analysis[52] allow one to investigate how early neurological improvements may affect the accuracy of predicting final outcome after stroke. In addition, an accurate model is of no benefit if it is not generally applicable and is not implemented in practice.[84] This means that implementation studies are needed to investigate the added value of using prediction rules in daily practice for the accuracy of clinical decision-making, compared to clinical expertise alone.[84] Finally, the present systematic review shows that more attention must be given to

a uniform procedure in selecting and dichotomizing determinants to make prognostic models comparable.[75]

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SUPPLEMENTAL MATERIAL

Early Prediction of Outcome of Activities of Daily Living after Stroke: A Systematic Review

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Table I. Quality assessment of reports of prognostic studies[1-4]

OUTCOME STRATEGIES		SCALE	CRITERIA
Evaluation of			
Study design			
D1	Source population and recruitment	Y/N/?	Positive when sampling frame (e.g. hospital-based, community-based, primary care) and recruitment procedure (place and time-period, method used to identify sample) are reported.
D2	Inclusion and exclusion criteria	Y/?	Positive if both the inclusion and exclusion criteria are explicit described.
D3	Important baseline key characteristics of study sample	Y/?	Positive if the following key characteristics of the sample are described: gender, age, type, localization, number of strokes*, stroke severity. *Number of strokes is adequate when at least 'a history of stroke' or 'recurrent stroke' is reported.
D4	Prospective design	Y/N/?	Positive when a prospective design was used, or in case of a historical cohort in which prognostic factors are measured before the outcome is determined.
D5	Inception cohort	Y/N/?	Positive if observation started at a uniform time point within two weeks after stroke onset.
D6	Information about treatment	Y/N/?	Positive if information on treatment during observation period is reported (e.g. (para)medical, usual care, randomized, etc.).
Study attrition			
A1	Number of loss to follow-up	Y/N/?	Positive if number of loss to follow-up during period of observation did not exceed 20%.
A2	Reasons for loss to follow-up	Y/N/?	Positive if reasons for loss to follow-up are specified, or there was no loss to follow-up.
A3	Methods dealing with missing data	Y/N/?	Positive, if in case of missing values the method of dealing with missing values is adequate (e.g. multiple imputation), or there are no missing values.
A4	Comparison completers and non-completers	Y/N/?	Positive if article mentions that there are no significant differences between participants who completed the study and who did not, concerning key characteristics gender, age, type and severity and candidate predictors and outcome, or there was no loss to follow-up.
Predictor measurement			
P1	Definition of predictors	Y/?	Positive if the article clearly defines or describes all candidate predictors (concerning *both* clinical and demographic features).
P2	Measurement of predictors reliable and valid	Y/N/?	Positive if ≥1 candidate predictors are measured in a valid and reliable way, or referral is made to other studies which have established reliability and validity.
P3	Coding scheme and cut-off points	Y/N/?	Positive if coding scheme for candidate predictors were defined, including cut-off points and rationale for cut-off points was given; or if there was no dichotomization or classification.
P4	Data presentation	Y/N/?	Positive if frequencies or percentages or mean (SD/CI), or median (IQR) are reported of all candidate predictors.
Outcome measurement			
O1	Outcome(s) defined	Y/N/?	Positive when a clear definition of the outcome(s) of interest is presented.
O2	Measurement of outcome(s) reliable and valid	Y/N/?	Positive when outcome is measured in a valid and reliable way, or there is referred to other studies which have established reliability and validity.
O3	Coding scheme and cut-off points described	Y/N/?	Positive if coding scheme of the outcome was defined, including cut-off points and rationale for cut-off points was given; or if there was no dichotomization.
O4	Appropriate end-points of observation	Y/N/?	Positive if observation was obtained at a fixed moment after stroke onset, negative when observation was obtained at discharge.
O5	Data presentation	Y/N/?	Positive if frequencies or percentages or mean (SD/CI) or median (IQR) are reported of the outcome measure.
Statistical analysis			
S1	Strategy for model building described	Y/N/?	Positive if the method of the selection process for multivariable analysis is presented (e.g. forward, backward selection, including p-value).
S2	Sufficient sample size	Y/N/?	Positive if in logistic regression analysis number of patients with a positive or negative outcome (event) per variable is adequate, i.e. is equal to or exceeds 10 events per variable in the multivariable model (EPV), or in case of linear regression analysis, N is ≥100.
S3	Presentation univariable analysis	Y/N/?	Positive if univariable crude estimates and confidence intervals (β/SE, OR/CI, RR, HR) are reported. Negative when only p-values or correlation coefficients are given, or if no tests are performed at all.
S4	Presentation multivariable analysis	Y/N/?	Positive if for the multivariable models point estimates with confidence intervals (β/SE, OR/CI, RR, HR,) are reported.
S5	Continuous predictors	Y/N/?	Positive if continuous predictors are not dichotomized in the multivariable model.
Clinical performance/validity			
C1	Clinical performance	Y/?	Positive if article provides information concerning ≥1 of the following performance measures: discrimination (e.g. ROC), calibration (e.g. HL statistic), explained variance, clinical usefulness (e.g. sensitivity, specificity, PPV, NPV)
C2	Internal validation	Y/?	Positive if appropriate techniques are used to assess internal validity (e.g. cross-validation, bootstrapping), negative if split-sample method was used.
C3	External validation	Y/?	Positive if the prediction model was validated in a second independent group of stroke patients.

Y, Positive, 1 point; N, Negative, 0 points; ?, Partial/unknown

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Table II. Characteristics of included prognostic studies

First author year	N	Stroke specification	Sampling frame, mean time poststroke at inclusion	Follow-up poststroke	Outcome	Prognostic variables in final model in hierarchical order (cut-off point)	Variables excluded in multivariable analysis	Model performance
Reid 2010	538	Ischemic, hemorrhagic	H, ?	6 mos	mRS ≤2	*Model 1, clinical variables* Pre-stroke independence * Arm power * Age Stroke severity score	Gender Prior stroke/TIA Atrial fibrillation Presenting <3 hours TACI LACI	AUC 0.882
						Model 2, clinical variables, excluding stroke severity Pre-stroke independence * Arm power * GCS verbal * Able to walk unaided * Age	Posterior circulation stroke Hemorrhagic stroke Left hemisphere Infratentorial localization Dysarthria GCS verbal Walk without assistance rTPA treatment	AUC 0.826
						Model 3, CIVIC and clinical variables Pre-stroke independence * Arm power * Age Leukoaraiosis score Stroke severity score Focal CT abnormality *	Any abnormality Mean number focal lesions Acute infarct present Acute infarct or hemorrhage	AUC 0.901
Fiorelli 1995	300	Ischemic, first-ever hemispheric	H, <6 hours	4 mos	(modified) mRS ≥3	CNS admission (≥7, 5-6.5, ≤4.5) Age (≤70, >70)	Atrial fibrillation Gender	Risk cut-off 0.60: Acc 0.78 Sens 0.61 Spec 0.84
Johnston 2007	382	Ischemic	H, <24 hours	3 mos	BI ≥95	rTPA treatment * DWI stroke volume Age NIHSS baseline Diabetes *	Pre-stroke disability Time×DWI stroke volume	AUC 0.803 Calibration cut-off 0.4: MAE 0.33
					BI ≤60	rTPA treatment * NIHSS baseline Age DWI stroke volume Time to DWI	Pre-stroke disability Time×DWI stroke volume Diabetes	AUC 0.808 MAE 0.24
					mRS <2	Age DWI stroke volume NIHSS baseline	Pre-stroke disability Time×DWI stroke volume Diabetes rTPA treatment	AUC 0.795 MAE 0.37
					mRS ≥5	NIHSS baseline Age DWI stroke volume	Pre-stroke disability Time×DWI stroke volume Diabetes rTPA treatment	AUC 0.832 MAE 0.15
Weimar 2006	303	Hemorrhagic, first-ever	H, <72 hours	6 mos	BI ≥95	Age Initial NIHSS	Gender Coronary heart disease Initial NIHSS consciousness Diameter bleeding Ventricular bleeding and/or hydrocephalus	Cut-off -0.42 AUC 0.861
Sato 2008	310	Ischemic	H, <72 hours	3 mos	mRS ≤2	*Model, anterior circulation* NIHSS admission	Age Gender Ischemic heart disease Atrial fibrillation Stroke etiology (TOAST)	AUC 0.868 (0.818-0.917)
						Model, posterior circulation NIHSS admission Ischemic heart disease *	Age Gender Atrial fibrillation Stroke etiology (TOAST)	AUC 0.867 (0.783-0.951)
Weimar 2002	1754	Ischemic	H, <24 hours	100 days	BI ≥95	Neurological complications * Fever (>38, ≤38 °C) Lenticulostriate arteries infarction * Diabetes *	41 variables in total investigated	R^2=0.554 Acc 0.807 (cut-off 0.437)

						Ranking scale Prior stroke * Left arm weakness Right arm weakness Gender Age NIHSS admission		
Counsell 2002	530	Ischemic, hemorrhagic	C, 4 days	6 mos	OHS <3	*Model 1, simple clinical variables* Independent before stroke (OHS ≤2, >2) * GCS verbal (<5, 5) * Arm power * Ability to walk * Living alone * Age	Gender Employed Hypertension Myocardial infarction Diabetes Malignancy Examined <2 days Systolic blood pressure GCS eye GCS motor Able to lift legs	AUC (SE) 0.839 (0.017)
						Model 2, Model 1 + more detailed clinical variables † Age * Living alone * Independent before stroke * GCS verbal * Arm power * Ability to walk * Current smoker * Cognitive deficit *	Previous TIA Peripheral vascular disease Apoplectic onset Cervical bruit Cardiac disease Dysphasia Visual field defect Gaze palsy Brain stem function Proprioception	AUC (SE) 0.829 (0.017)
						Model 3, Model 1 + 2 + investigation results † Age Living alone * Independent before stroke * GCS verbal * Arm power * Ability to walk * Current smoker * Cognitive deficit * Urea (≤7 mmol/L)	High hemoglobulin level Anemia Platelet count Glucose Atrial fibrillation Abnormal cardiac rhythm	AUC (SE) 0.853 (0.023)
Schiemanck 2006	75	Ischemic, MCA, first-ever	H, 11 days	1 yr	BI ≥19	*Model 1, clinical variables* Initial BI (>9, ≤9) Age	Gender Educational level (high/low) Relationship *	AUC 0.84 Acc 0.77
						Model 2, clinical and MRI variables Initial BI (>9, ≤9) Lesion volume (≤22 mL, >22 mL) Hemisphere (left, right) Age Days poststroke to MRI scan	NIHSS MI (>100, ≤100) Urinary incontinence Sitting balance *	AUC 0.87 Acc 0.83
Appelros 2003	377	Ischemic, hemorrhagic, first-ever	C, <48 hours	1 yr	mRS ≥3	Heart failure * NIHSS Age	Gender Hypertension Diabetes Ischemic heart disease TIA Peripheral atherosclerosis	
Sánchez-Blanco 1999	92	Ischemic, hemorrhagic, first-ever, unilateral	H, 11 days	6 mos	BI ≥85	Stroke clinical classification (M, MS, MSH) Initial BI (>20, ≤20) Prior independence (limited activity, nonlimited)	Gender Age Family support prior to stroke Acute hospital discharge Stroke side Stroke type (ischemic, hemorrhagic) Topographic stoke subtypes Consciousness at 24 hours Mental status Visuospatial perception Comprehension of speech Functional expression Motor loss Sitting balance	Acc 0.79
Baird 2001	66	Ischemic,	H, <48	3 mos	BI ≥90	NIHSS score (≤3, 4-15, >15)	Age	Sens 0.77

		anterior circulation	hours			DWI lesion volume (≤14.1 mL,>14.1 mL) Time from onset (≤3 h, 3< time ≤6 h, >6 h)	Gender Hypertension Heart disease Participation in a drug trial	Spec 0.71
Lai 2002	459	Ischemic, hemorrhagic	C, <14 days	6 mos	BI ≥95	Prior SF-36 Age Orpington prognostic score GDS (<6, ≥6)	Charlson comorbidity index	
Woldag 2006	41	Ischemic, supratentorial	H, <72 hours	6 mos	BI	*Model 1, admission* † BI HAND Age	Disability NIHSS Prior stroke	R^2=0.422
						Model 2, day 7 † NIHSS HAND Age Previous stroke *	Δ NIHSS admission to day 7 Δ HAND admission to day 7 BI	R^2=0.788
Acciarresi 2006	435	Ischemic, hemorrhagic	H, <72 hours	3 mos	mRS >2	NIHSS (<15, ≥15) Age Superficial MCA * Gender	Atrial fibrillation TACI LACI Impaired consciousness Small vessel disease Cardioembolism Undetermined causes Subcortical Entire MCA	
Yoo 2008	131	Ischemic	H, <24 hours	3 mos	mRS responder analysis	Undernutrition wk 1 * NIHSS wk 1 Gender	Cardioembolism Insufficient diet Age Initial NIHSS Initial undernutrition External feed	HL-statistic X^2=3.6 (p=.89)
					mRS ≤2	NIHSS wk 1		
					mRS ≥3	NIHSS wk 1 Age		
Lee 2009	533	Ischemic, first-ever	H, <10 days	6 mos	mRS <2	Diabetes * NIHSS admission Total cholesterol	Serum albumin Fibrinogen Uric acid C-reactive protein Body mass index Gender Heart disease Complications	
Duarte 2010	75	Ischemic, hemorrhagic	H, 14 days	6 mos	Motor FIM	*Model 1, TCT* † Age (<64, 64-74, >74 yr) TCT (<37, 37-74, >74)	Stroke type (ischemic, hemorrhagic) Urinary incontinence Gender	R^2=0.61
						Model 2, NIHSS † Age (<64, 64-74, >74 yr) NIHSS (<5, 5-10, >10) Gender	Stroke type (ischemic, hemorrhagic) Urinary incontinence	R^2=0.58
Fullerton 1988	206	Ischemic, hemorrhagic	H, <48 hours	6 mos	"mRS"	Weighted mental score ECG changes Leg function Level of consciousness Arm power Albert's test score (neglect)	Age Daily cigarettes Hematocrit Erythrocyte sedimentation rate Conjugate eye movement Mental score Speech Vision Leg power Walking/balance Arm function Sensation (light touch) Sensation (proprioception) Denial Disordered spatial orientation Apraxia Continence	Acc 0.68
Daverat 1991	166	Hemorrhagic	H, <24 hours	6 mos	GOS ≤2	Intraventricular hemorrhage * Age (10-yr groups) Limb paresis (4 classes) Hemorrhage size (<10, 10-	Gender Hemorrhage side Hemorrhage location Oral comprehension	

						20, >30%)	Oral expression	
Taub 1994	639	Ischemic, hemorrhagic, first-ever, <75 yr	C, ?	3 mos	BI 0-9, 10-14, 15-19, 20	Initial incontinence * Initial swallowing problems * Initial paralysis *	Age Gender District of residence Ethnic origin Living alone before stroke Premorbid disability (BI) Initial coma Initial speech problems	Sens 0.67 Spec 0.69
Johnston 2000	256	Ischemic	H, <1 week	3 mos	BI ≥95	Initial NIHSS Age Diabetes * Infarct volume (cm^3) Prior disability *	Small vessel Prior stroke Diabetes	AUC 0.84
					BI <60, death	Prior disability * Infarct volume (cm^3) Initial NIHSS Age	Small vessel Prior stroke Diabetes	AUC 0.88
					GOS 1	Age Initial NIHSS Diabetes * Infarct volume (cm^3) Prior disability *	Small vessel Prior stroke	AUC 0.84
					GOS >2	Infarct volume (cm^3) Age Initial NIHSS	Small vessel Prior stroke Diabetes Prior disability	AUC 0.88
Liu 2007	489	Ischemic	H, <14 days	28.3 mos	mRS ≤2	Age (≤60, >60 yr) Educational level (0-5) Prior stroke * NIHSS	Gender Smoking Atrial fibrillation OCSP typing Complications	Sens 0.77 Spec 0.71 HL statistic p=.787
Protopsaltis 2009	105	Ischemic, first-ever, non-embolic	H, ?	6 mos after discharge	BI >95	TACI location * Intima-media thickness Infarct volume		R^2=0.363
Shen 2010	483	Ischemic, hemorrhagic, >50 yr	H, <48 hours	6 mos	BI <75	Malnutrition * NIHSS admission Age	Complications Length of hospital stay Stroke type (ischemic, hemorrhagic) Renal failure BI admission Gender	
Franke 1992	157	Hemorrhagic, supratentorial	H, 72 hours	1 yr	mRS ≥3	Age (<70, ≥70) GCS eye, motor day 3 (<9, ≥9) mRS day 3 (>4, ≤4)	Paresis Blood glucose levels Hematoma volumes	
Censori 1993	172	Ischemic, first-ever, carotid artery area	H, 136.6 min	6 mos	mRS ≤2	CNS (<6.5, ≥6.5)	Atrial fibrillation Age	
FOOD collaboration 2003	3012	Ischemic, hemorrhagic	H, <7 days	6 mos	mRS (alive, independent)	Undernourished * Age Able to talk and oriented * Walk without assistance * Able to swallow * Pre-stroke independent ADL * Able to lift both arms off the bed *	Pre-stroke stroke living alone Overweight	
Sobrino 2007	48	Ischemic, first-ever, nonlancunar	H, <12 hours	3 mos	mRS ≤2	Colony-forming unit-endothelial cell increment first week (≥4,<4) Initial NIHSS Initial ischemic volume	rTPA treatment	
Misra 1996	69	Hemorrhagic, supratentorial	H, 6.5 days	3 mos	BI ≥12	GCS CNS Reflex (hypo, hyper, normal) Ventricular extension * MEP *	Medical complications Incontinence	
Tilling 2001	299	Ischemic, hemorrhagic	H, <14 days	<2, 4, 6, 12 mos	BI	Pre-stroke disability * † Urinary incontinence *		

						Dysarthria * Gender Age Dysphasia * Limb deficit baseline *		
Ellul 2004	284	Ischemic, first-ever	H, <7 days	1 yr	BI ≤15	Pre-stroke mRS Age (5-yr groups) Initial SSS (5-points)	Gender Hypertension Diabetes Atrial fibrillation Ischemic heart disease Hypercholesterolemia Current smoking Side of lesion Site/extend lesion Carotid stenosis CCA-IMT	
Hinkle 2006, 2010	100	?	H, <72 hours	3 mos	FIM	NCSE Initial FIM Age	Lesion volume NIHSS	R^2=0.42
				3 yr		NIHSS Age Initial FIM	Cognitive status Lesion volume	
Rost 2008	629	Hemorrhagic	H, ?	90 days	GOS ≥4	ICH volume (<30, 30-60, >60 cm^3) Age (<70, 70-79, ≥80 yr) GCS (≥9, ≤8) ICH location (lobar, deep, infratentorial) Prior cognitive impairment *	Gender Hypertension Diabetes Coronary artery disease Warfarin use	c-statistic 0.88
Hallevi 2009	1798	Ischemic	H, <7 days	3 mos	mRS ≤2	*Model, mRS 3 at day 7, NIHSS total* NIHSS (≤4, >4) Number of risk factors (≤2, >2) Age (≤70, >70)		R^2=0.28
						Model, mRS 3 at day 7, items NIHSS Number of risk factors (≤2, >2) NIHSS motor arm (≤1, >1) Age (≤70, >70) NIHSS language (0, >0)	NIHSS level of consciousness NIHSS facial palsy NIHSS dysarthria	R^2=0.28
						Model, mRS 4 at day 7, NIHSS total NIHSS (≤8, >8) Age (≤70, >70) Gender	rTPA Risk factors	R^2= 0.22
						Model, mRS 4 at day 7, items NIHSS NIHSS motor leg Age (≤70, >70) NIHSS visual fields NIHSS facial palsy Gender NIHSS dysarthria	rTPA Number of risk factors NIHSS consciousness NIHSS gaze NIHSS motor arm NIHSS language NIHSS extinction	R^2= 0.25
						Model, mRS 5 at day 7, NIHSS total NIHSS (≤17, >17) Age (≤70, >70) rTPA	Congestive heart disease	R^2=0.22
						Model, mRS 5 at day 7, items NIHSS NIHSS motor leg (≤2, >2) Age (≤70, >70) rTPA NIHSS dysarthria (0, >0)	NIHSS facial palsy NIHSS visual fields NIHSS motor arm NIHSS sensory NIHSS extinction	R^2=0.25
Stone 1993	171	Ischemic, hemorrhagic, hemispheric	H, <72 hours	3, 6 mos	BI 0-14, 15-19, 20	Age Visual Neglect Recovery Index Initial MI	Hemi inattention Visual extinction Sensory extinction Allesthesia Anosognosia Level of consciousness Gaze paresis Visual field defect Proprioception	Acc 0.75

Chua 1995	51	Ischemic, cortical	H, < 24 hours	3 mos	BI >12	APS	CNS 24 hours BI day 7 Age	Sens 0.82 Spec 0.97
Macciocchi 1998	327	Ischemic, MCA	?, 7-10 days	3 mos	BI >60	Lesion side (left, right) Cortical lesion (cortical, other) Prior stroke * UNSS Age (70 vs. 60, 80 vs. 60 yr)	Comorbid medical disorders	
Adams 2003	1281	Ischemic	H, <24 hours	3 mos	GOS 1/ BI ≥19	Baseline NIHSS Small-artery occlusion * NIHSS×small-artery occlusion Age Race Prior stroke *	Gender	
					GOS ≤2/ BI ≥12	Baseline NIHSS Small-artery occlusion * NIHSS×small-artery occlusion Age Race	Gender Prior stroke	
Studenski 2004	236	Ischemic, hemorrhagic	H, 8 days	3, 6 mos	BI ≥95	Comorbidity burden (CDI) (≤1, 2, ≥3 domains) Baseline NIHSS (<6, ≥6) Age		
Colantonio 1996	63	Ischemic, hemorrhagic, >65 yr	C, ?	6 mos	Katz Scale	Pre-stroke physical function (Katz scale: 0, 1+) Race (white, nonwhite) Stroke severity (0-1, 2-3, 4-5)	Prior gross mobility Age Gender Years of education Housing Comorbidity Prior cognitive impairment Complications	R^2=0.32
Di Carlo 1999	4499	Ischemic, hemorrhagic, first-ever	H, ?	3 mos	BI <15	*Model, Total* Urinary incontinence * Paralysis * Swallowing problems * Hypertension *	Prior institutionalization Atrial fibrillation Diabetes	
						Model, <80 yr Urinary incontinence * Swallowing problems * Paralysis * Diabetes * Atrial fibrillation * Hypertension *	Prior institutionalization	
						Model, ≥80 yr Urinary incontinence * Paralysis * Prior institutionalization * Swallowing problems *	Hypertension Atrial fibrillation Diabetes	
					mRS ≥2	*Model, Total* Urinary incontinence * Paralysis * Prior institutionalization * Swallowing problems * Aphasia * Myocardial infarction * Diabetes * Hypertension *		
						Model, <80 yr Urinary incontinence * Paralysis * Myocardial infarction * Swallowing problems * Aphasia * Diabetes * Hypertension *	Prior institutionalization	
						Model, ≥80 yr Prior institutionalization * Myocardial infarction * Urinary incontinence *	Hypertension Diabetes Myocardial infarction Aphasia Swallowing problems	

Shah 2005	53	Ischemic, hemorrhagic, thalamic	?, <6 days	3 mos	BI ≥12	Type of hematoma * CNS (<3, ≥3)	Size of hematoma Diabetes GOS Pupillary asymmetry MEP SEP	
Daviet 2006	156	Ischemic, hemorrhagic, first-ever, hemispheric	H, <24 hours	1 yr	BI	Initial BI † Δ BI day 2-15 Disorders executive function * Previous neurological impairment *	Myocardial infarct Coma Hemianopsia Motor impairment day 2 Hemineglect Astéreoagnosie MMSE day 15 Incontinence day 15 Swallowing day 2 Age	
Horner 2003	598	Ischemic, hemorrhagic	H, ?	1 yr	mRS	*Model 1, effect race* Black×time Time (log function) *Model 2, effect race + covariates* Discharge to nursing home or other institution Lives alone * Inpatient treatment by neurologist * Time (log function) CNS Days to rehabilitation initiation Black×days to rehabilitation×time Days to rehabilitation×time Age	Black Gender Marital status Living situation at discharge Income level Stroke etiology Mental status Time from onset to admission	
Clavier 1994	177	Ischemic, lacunar	H, ?	1 yr 35 mos	BI	Type lacunar syndrome - sensorimotor * - pure motor * Diabetes * Age (<70, >70 yr) History of stroke/TIA *	Cigarette smoking Ischemic heart disease Hypertension Cardiomegaly Dyslipedemia Number of lacunes on MRI Gender	ROC curve
Robinson 1999	50	Ischemic, hemorrhagic	H, 9.9 days	12-24 mos	JHFI	Pre-stroke financial security † Adequacy home and neighborhood Relationship with significant other NIHSS	Relationship with children Family relationship Home and family responsibilities Work experience Social activities Spiritual beliefs Living environment Health and illness experiences	R^2=0.53
Weir 2005	2709	Ischemic, hemorrhagic	H, 7 days	6 mos	mRS	Age † Prior ADL-independency * Pre-stroke living alone * GCS verbal * Able to lift both arms * Able to walk unaided *	Gender Diabetes Ischemic heart disease Stroke type (ischemic, hemorrhagic) Stroke onset in hospital Admission GCS eye Admission GCS motor High systolic blood pressure Urinary incontinence	
Handschu 2009	159	?	H, <24 hours after admission	3 mos	mRS	NIHSS	Age Gender	R^2=0.37
	Σ 25843							

H, Hospital-based; ?, unclear; mos, Months; mRS, Modified rankin scale; *, dichotomized i.e. yes/ no; GCS, Glasgow coma scale; CIVIC, Consortium for the investigation of vascular impairment of cognition; CT, Computed tomography scan; TIA, Transient ischemic attack; TACI, total anterior circulation syndrome; LACI, lacunar syndrome; rTPA, Recombinant tissue plasminogen activator; AUC, Area under the curve; CNS, Canadian neurological scale; Acc, Accuracy; Sens, Sensitivity; Spec, Specificity; BI, Barthel index; DWI, Diffusion-weighted magnetic resonance imaging; NIHSS, National institutes of health stroke scale; MAE, Mean absolute error; TOAST, Trial of ORG 10172 in Acute Stroke Treatment; C, community-based; OHS, Oxford handicap scale; SE, Standard error; †, Non hierarchical order; MCA, Middle cerebral artery; yr, Year; MRI, Magnetic resonance imaging; MI, Motricity index; M, Motor; MS, Motor-sensitive; MSH, Motor-sensitive with hemianopsia; SF-36, Short-form (36) health survey; GDS, Geriatric depression scale; HAND, Grips strength using multi myometer×motor evoked potentials (MEP); HL statistic, Hosmer-Lemeshow goodness of fit statistic; FIM, Functional independence measure; TCT, Trunk control test; ECG, Electrocardiograph; GOS, Glasgow outcome scale; OSCP, Oxfordshire Community Stroke Project; ADL, Activities of daily living; SSS, Scandinavian stroke scale; CCA-IMT,

Common carotid artery intima-media thickness; NCSE, Neurobehavioral cognitive status examination; ICH, Intracranial hemorrhage; APS, Allan's prognostic score; UNSS, Unified neurological stroke scale; CDI, Comorbidity disease index; SEP, Somatosensory evoked potentials; Δ, Change; MMSE, Mini-mental state examination; ROC, Receiver operating curve; JHFI, Johns Hopkins functioning inventory

Table III. Risk of bias assessment of included prognostic studies

Reference	Study design						Study attrition				Predictor measurement				Outcome measurement					Statistical analysis					Clinical performance/validity			*Total (/27)*
	D1	D2	D3	D4	D5	D6	A1	A2	A3	A4	P1	P2	P3	P4	O1	O2	O3	O4	O5	S1	S2	S3	S4	S5	C1	C2	C3	
High quality studies																												
Reid 2010	1	1	1	1	0	0	1	1	0	?	1	1	1	1	1	1	1	1	1	?	1	1	1	1	1	1	1	*22*
Fiorielli 1995	1	1	1	0	1	1	1	1	1	1	1	?	0	1	1	1	1	1	1	1	1	1	1	0	1	?	1	*22*
Johnston 2007	1	1	1	1	1	1	1	?	?	0	1	1	1	1	1	1	?	1	1	0	1	0	1	1	1	1	1	*21*
Weimar 2006	1	1	1	1	1	1	0	1	0	1	1	?	?	1	1	1	0	1	1	1	1	0	1	1	1	?	1	*20*
Sato 2008	1	1	1	1	1	0	1	1	1	1	1	1	?	1	1	1	1	1	1	0	0	0	1	1	1	?	?	*20*
Weimar 2002	1	1	1	0	1	0	1	1	0	0	1	0	1	1	1	1	?	1	1	1	1	0	1	1	1	1	1	*20*
Low quality studies																												
Counsell 2002	1	1	1	1	1	?	1	1	1	1	1	1	?	?	1	1	?	1	1	1	?	0	1	?	1	?	1	*19*
Schiemanck 2006	1	1	1	1	?	0	1	1	0	1	1	1	0	1	1	1	1	1	1	1	0	1	1	?	1	?	?	*19*
Appelros 2003	1	1	1	1	?	0	1	1	1	1	1	?	0	1	1	1	1	1	1	0	1	1	1	1	?	?	?	*19*
Sánchez-Blanco 1999	1	1	1	1	0	1	1	1	1	1	1	1	?	1	1	1	0	1	1	1	0	0	1	0	1	?	?	*19*
Baird 2001	1	1	?	?	1	0	1	1	1	1	1	1	?	1	1	1	1	1	1	?	0	0	1	0	1	?	1	*18*
Lai 2002	1	1	?	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	0	0	1	0	1	1	?	?	?	*18*
Woldag 2006	1	1	1	1	1	1	0	1	0	0	1	1	1	1	1	1	1	1	?	1	0	0	0	1	1	?	?	*18*
Acciarresi 2006	1	1	1	1	?	0	1	1	1	1	1	?	?	1	1	1	?	1	1	0	1	1	1	?	?	?	?	*17*
Yoo 2008	1	1	1	1	1	0	0	1	0	?	1	1	?	1	1	1	0	1	1	?	1	0	1	1	1	?	?	*17*
Lee 2009	1	1	?	1	1	0	1	1	0	0	1	1	1	1	1	1	?	1	1	1	1	0	1	?	?	?	?	*17*
Duarte 2010	1	1	1	1	1	1	1	1	0	0	1	1	?	1	1	1	1	1	1	?	?	0	0	0	1	?	?	*17*
Fullerton 1988	?	1	?	1	1	0	1	1	1	1	1	0	1	0	1	0	1	1	0	1	1	0	0	1	1	?	?	*16*
Daverat 1991	?	1	?	1	1	1	1	1	1	1	1	0	?	1	1	1	?	1	1	?	1	0	1	0	?	?	?	*16*
Taub 1994	1	1	?	1	1	0	0	1	0	0	1	0	?	1	1	1	1	1	1	1	1	1	0	0	1	?	?	*16*
Johnston 2000, 2003	1	1	?	0	1	0	1	?	?	0	1	?	?	1	1	1	?	1	1	0	1	0	1	1	1	1	1	*16*
Liu 2007	1	1	?	0	1	0	1	1	0	1	1	?	0	1	1	1	0	0	1	1	1	1	1	?	1	?	?	*16*
Protopsaltis 2009	0	?	1	1	?	1	1	1	1	1	1	0	?	1	1	1	1	0	1	0	1	0	?	1	1	?	?	*16*
Shen 2010	1	1	1	1	1	0	0	?	0	0	1	1	1	1	1	1	1	1	1	?	1	0	1	?	?	?	?	*16*
Franke 1992	1	1	?	1	?	0	1	1	1	1	1	1	0	1	1	1	?	1	1	?	1	0	0	0	?	?	?	*15*
Censori 1993	1	1	?	1	1	0	1	1	1	1	1	?	?	?	1	1	?	1	0	1	1	0	1	0	?	?	?	*15*
FOOD collaboration 2003	1	1	?	1	1	?	1	1	1	0	?	?	?	1	1	1	?	1	1	0	1	?	1	1	?	?	?	*15*
Sobrino 2007	?	1	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0	1	1	0	?	0	1	?	?	?	?	*15*
Misra 1996	?	1	1	1	?	0	1	1	1	0	1	0	0	1	1	1	?	1	1	1	0	0	1	0	?	?	?	*14*
Tilling 2001	1	?	?	0	?	1	1	?	1	0	1	0	?	1	1	1	1	1	1	1	1	?	?	0	?	?	1	*14*
Ellul 2004	?	1	1	1	1	0	1	1	0	0	1	1	?	1	1	1	0	1	0	0	1	?	1	0	?	?	?	*14*
Hinkle 2006, 2010	?	1	1	1	?	?	0	?	0	?	1	0	?	1	1	1	1	1	1	1	1	0	1	?	1	?	?	*14*
Rost 2008	1	1	1	0	0	0	1	0	0	?	1	?	?	1	1	1	?	1	1	?	1	0	1	0	1	?	1	*14*
Hallevi 2009	1	1	?	0	1	?	1	1	0	0	1	0	?	1	1	1	0	1	1	0	1	0	1	0	1	?	?	*14*
Stone 1993	?	1	?	1	1	0	1	1	0	0	1	0	?	?	1	1	1	1	1	1	0	0	?	?	1	?	?	*13*
Chua 1995	0	1	?	1	1	0	1	1	0	0	1	?	?	?	?	1	1	1	0	0	1	1	1	?	1	?	?	*13*
Macciocchi 1998	?	1	?	1	1	1	1	0	0	0	1	1	?	?	1	1	?	1	1	?	1	0	1	?	?	?	?	*13*
Adams 1999	1	1	?	0	1	?	1	1	0	0	1	1	?	0	1	1	?	1	0	0	1	0	1	1	?	?	?	*13*
Studenski 2004	1	?	?	1	1	0	1	0	0	0	1	1	?	1	1	1	1	1	1	0	1	0	?	?	?	?	?	*13*
Colantonio 1996	1	1	1	1	1	0	1	?	0	1	1	0	?	?	1	0	?	0	?	0	0	1	1	0	1	?	?	*12*
Di Carlo 1999	?	1	?	0	?	1	1	0	0	0	1	0	?	?	1	1	?	1	1	1	1	0	1	1	?	?	?	*12*
Shah 2005	?	?	1	1	1	0	1	1	0	0	1	?	?	?	1	1	?	1	1	1	0	0	1	0	?	?	?	*12*
Daviet 2006	1	1	?	1	1	0	0	1	0	0	1	1	?	?	1	1	1	1	0	?	1	0	0	?	?	?	?	*12*
Horner 2003	1	?	?	1	0	1	1	?	0	?	1	?	?	1	1	1	?	1	0	0	1	0	1	?	?	?	?	*11*
Clavier 1994	?	?	?	1	?	0	0	?	0	0	1	0	?	1	1	1	?	1	1	?	?	0	1	0	1	?	?	*9*
Robinson 1999	?	?	?	1	?	0	0	?	0	1	?	0	?	1	1	0	1	1	1	0	0	0	0	1	1	?	?	*9*
Weir 2005	1	1	?	0	0	0	0	0	1	0	?	?	?	1	1	1	?	1	0	0	1	0	0	1	?	?	?	*9*

Handschu 2009	?	?	?	1	1	0	0	0	0	0	?	0	0	0	?	1	0	1	0	0	1	0	0	0	1	?	?	*6*
% satisfied (1 point)	69	83	48	77	67	27	77	67	33	38	92	42	19	75	96	94	49	94	75	38	71	17	73	35	56	8	21	*17**

D, Study design; A, Study attrition; P, Predictor measurement; O, Outcome measurement; S, Statistical analysis; C, Clinical performance/validity; 1, Positive; 0, Negative; ?, Partial/unknown; D1, Source population and recruitment; D2, Inclusion and exclusion criteria; D3, Important baseline key characteristics of study sample; D4, Prospective design; D5, Inception cohort; D6, Information about treatment; A1, Number of loss to follow-up; A2, Reasons for loss to follow-up; A3, Methods dealing with missing data; A4, Comparison completers and non-completers; P1, Definition of predictors; P2, Measurement of predictors reliable and valid; P3, Coding scheme and cut-off points; P4, Data presentation; O1, Outcome(s) defined; O2, Measurement of outcome(s) reliable and valid; O3, Coding scheme and cut-off points described; O4, Appropriate end-points of observation; O5, Data presentation; S1, Strategy for model building described; S2, Sufficient sample size; S3, Presentation univariable analysis; S4, Presentation multivariable analysis; S5, Continuous predictors; C1, Clinical performance; C2, Internal validation; C3, External validation; *, Median

Table IV. Evidence synthesis of variables measured early after stroke which are *not predictive* for outcome of ADL ≥3 months poststroke, according to the ICF classification

Variable	Level of evidence
Body structures	
Ischemic/hemorrhagic	II
Topographic stroke subtype (OCSP)	IV
· LACI	II
· TACI	II
Imagine variables	
· Number focal lesions	II
· Ventricular bleeding and/or hydrocephalus	II
· Any computed tomography abnormality	III
· Acute infarct	III
· Acute infarct or hemorrhage	III
· Posterior circulation	III
· Subcortical	IV
· Entire middle cerebral artery	IV
· Infratentorial	II
· Putamen, thalamus, lobe	IV
Time×DWI stroke volume	III
Stroke etiology (TOAST)	II
· Small vessel occlusion	IV
· Cardioembolism	IV
· Undetermined causes	IV
NIHSS×small vessel occlusion	IV
Days to MRI	IV
IMT	IV
Carotid stenosis	IV
Body functions	
· Consciousness (e.g. GCS)	II
· GCS eye	IV
· GCS motor	IV
· Paresis	
· Leg paresis	IV
· Δ Gripstrength×MEP	IV
· MEP	IV
· SEP	IV
· Hemianopsia	IV
· Gaze palsy	IV
· Facial palsy	IV
· Brain stem function	IV
· Sensory function	IV
· Vital	IV
· Proprioception	IV
· Dysarthria	II
· Cognitive deficit	
· Neglect	IV
· Spatial orientation	IV
· Apraxia	IV
· Anosognosia	IV
· Astéreoagnosie	IV
· Extinction	IV
· Visual extinction	IV
· Sensory extinction	IV
· Allesthesia	IV
· Comprehension of speech	IV
· Functional/oral expression	IV
· Denial	IV
Δ Stroke severity admission – day 7	IV
Complications	IV
Mental status	IV
Urinary incontinence	IV
Renal failure	IV
Activity and participation	
Sitting balance	IV
Gait	
· Walking/balance	IV
· Walk without assistance	III
Arm function	IV

Variable	Level of evidence
Personal factors	
Gender	I
Pre-stroke disability	II
Comorbidity and riskfactors	IV
· Number of riskfactors	IV
· Prior stroke/TIA	III
· Prior TIA	IV
· Neurological impairment	IV
· ***Atrial fibrillation***	I
· Hypertension	IV
· Myocardial infarction	IV
· Ischemic heart disease	IV
· Heart failure	IV
· Congestive heart disease	IV
· Cardiogmegaly	IV
· Malignancy	IV
· Current smoker	IV
· Peripheral vascular disease	IV
· Peripheral atherosclerosis	IV
· Cervical bruit	IV
· Health and illness experiences	IV
Cardiac, blood and urine variables	
· Systolic blood pressure	IV
· ECG changes	IV
· High hemoglobulin level	IV
· Anemia	IV
· Glucose	IV
· High systolic blood pressure	IV
· Apoplectic onset	IV
· Hematocrit	IV
· Erythrocyte sedimentation rate	IV
· Pupillary asymmetry	IV
· Cholesterol	IV
· Serum albumin	IV
· Fibrinogen	IV
· C-reactive protein	IV
Marital status	IV
Relationship	IV
Family support	IV
Relationship with children	IV
Family relationship	IV
Home and family responsibilities	IV
Social activities	IV
Years of education	IV
Employed	IV
Work experience	IV
Income level	IV
Nutrition	
· Initial undernutrition	IV
· Overweight	IV
· Insufficient diet	IV
· External feed	IV
Body mass index	IV
Ethnic origin	IV
Black	IV
Spiritual beliefs	IV
Environmental factors	
Presenting <3 hours	III
Examined <2 days	IV
Stroke onset in hospital	IV
Platelet count	IV
Participation drug trial	IV
Warfarin use	IV
Time from onset to admission	IV
Length of hospital stay	IV
Acute hospital discharge	IV
District of residence	IV
Living environment	IV
Living situation at discharge	IV
Housing	IV

I, Strong evidence; II, Moderate evidence; III, Limited evidence; IV, Insufficient/no evidence; OCSP, Oxfordshire community stroke project; LACI, lacunar syndrome; TACI, total anterior circulation syndrome; DWI, Diffusion-weighted imaging; TOAST, Trial of ORG 10172 in acute stroke treatment ; GCS, Glasgow coma scale; MEP, Motor evoked potentials; SEP, sensory invoked potentials; Δ, Change; TIA, Transient ischemic attack; ECG, Electrocardiograph