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Review Article

Ischemic stroke outcome: A review of the influence of post-stroke complications within the different scenarios of stroke care

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ABSTRACT

Stroke remains one of the main causes of death and disability worldwide. The challenge of predicting stroke outcome has been traditionally assessed from a general point of view, where baseline non-modifiable factors such as age or stroke severity are considered the most relevant factors. However, after stroke occurrence, some specific complications such as hemorrhagic transformations or post stroke infections, which lead to a poor outcome, could be developed. An early prediction or identification of these circumstances, based on predictive models including clinical information, could be useful for physicians to individualize and improve stroke care. Furthermore, the addition of biological information such as blood biomarkers or genetic polymorphisms over these predictive models could improve their prognostic value. In this review, we focus on describing the different post-stroke complications that have an impact in short and long-term outcome across different time points in its natural history and on the clinical-biological information that might be useful in their prediction.

1. Introduction

The latest advances in cardiovascular and stroke prevention and care have been able to significantly reduce stroke incidence and mortality in developed countries. However, the absolute number of people who have strokes annually, as well as related deaths and disability-adjusted life years (DALYs) lost have increased, being the majority of global stroke burden in low- and middle-income countries [1,2]. Stroke prognosis could be understood under three different and complementary points of view: vital, neurological and functional outcome. Stroke represents currently the fourth cause of death worldwide [3] and in-hospital mortality rates for ischemic stroke have been estimated between 11 and 15% and increase with age, while both genders are equally affected [4].

A global monitoring of the neurological function is of special interest during the acute and subacute phase of stroke, by providing an objective measure that alert physicians about neurological worsening. The National Institutes of Health Stroke Scale (NIHSS) is the most widely used scale for this purpose [5]. It is usually evaluated at least every 24 h in the acute stroke setting, as well as before and after revascularization procedures. Variations in four points or more in the score along time are usually considered as neurological improvement, when the score decreases, or deterioration, when there is an increment [6]. Incidence of neurological deterioration within the first 24 h after stroke has been estimated in 13.8% for patients treated with thrombolysis, strongly predicting poor functional outcome [7]. It has also been demonstrated to be an indicator of underlying infarct progression [8], or post-stroke deleterious processes such as cerebral edema or hemorrhagic transformation [9,10].

Nonetheless, perhaps the most important issue in the prediction of stroke outcome and the main end-point for stroke clinical trials is the functional status [11]. Data from the World Health Organization indicates that about half of stroke survivors are left with some degree of physical or cognitive impairment, and a 20% of them will require institutional care. This situation ranks stroke to the second leading cause of disability in Europe, which entails a 6.3% of total DALYs [12]. The modified Rankin Scale (mRS) [13] is a 7-point scale grading the capacity of performing basic activities of daily living, recommended as clinical end-point for stroke trials [14]. The mRS score is usually dichotomized into ≤2 or >2 points to report good or poor functional outcome, respectively.

Stroke prognosis is highly dependent on the interaction between baseline characteristics of the patient, such as age, gender or stroke severity [15,16]. It has been postulated that prediction of stroke outcome by physicians, which is commonly based on their own expertise and data reported by clinical trials, generates a bias by the overestimation of good outcome rates [17,18]. The presence of a wide variability among stroke patients in both baseline characteristics and factors derived from the stroke itself, makes the search for multivariate outcome

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Table 1
Predictive scores in general stroke outcome.

No ref	Name	Endpoint	Sample size derivation cohort	Sample size validation cohort	Variables	Points	Accuracy (C-statistic)
[130–132]	ASTRAL	Disability (mRS>2)	1645	1659 + 653 + 3755 + 1520	- Age - NIHSS - Time from symptoms onset - Visual field impairment - Blood glucose - Level of consciousness	8 + age + NIHSS	Derivation: 0.85 Validations: 0.90 + 0.81 + 0.89
[133]	BOAS	Disability (mRS>2)	221	100	- Age - Upper limb paralysis - NIHSS - Oxigen - Urinary catheter	5	Derivation: 0.89 Validation: 0.85
[134–136]	DRAGON	Good-Poor-Miserable (mRS<3->4)	1319	333 + 4519 + 297	- Early CT signs - Previous disability - Age - Glucose - Time to tPA - NIHSS	10	Derivation: 0.84 Validation: 0.80 + 0.84 + 0.84
[137–138]	G Score	Functional independency (BI<13/20)	137	314	- Complete limb paralysis - Hemiplegia + hemianopia + higher cerebral dysfunction - Drowsiness - Age - Level of consciousness - Hemiparesis	7	Validation: 0.64
[139–140]	iScore	Disability (mRS>2)	3818	4635 + 4061	- Age - Gender - CNS - Stroke subtype - AF - CHF - Cancer - Dialysis - Previous disability - Glucose	245 + age	Derivation: 0.79 Validation: 0.679
[141–142]	Johnston KC	Good Outcome (BI>95, GOS = 1, NIHSS<2)	256	299	- Age - NIHSS - Infarct volume - Lacunar etiology - Previous stroke - Diabetes - Previous disability		Derivation: 0.84 Validation: 0.83
[143]	PLAN	Poor Outcome (mRS<4)	4943	4904	- Previous Disability - Cancer - CHF - AF - Age - Lower limb weakness - Upper limb weakness - Aphasia or inattention	25	Validation: 0.88
[144]	Reid JM	Disability (mRS>2)	538	530 + 1330	- Age - Previous disability - Verbal GCS - Upper limb function - Gate		Derivation: 0.87 Validation: 0.78
[145–147]	SSV	Independency (OHS<3, mRS<3)	530	538 + 1330 + 538 + 537	- Age - Living alone pre-stroke - Independent pre-stroke - Verbal GCS - Upper limb function - Gate		Validation: 0.84 + 0.84 + 0.79 + 0.82
[148–149]	s-TPI	Good Outcome (mRS<2)	2184	301	- tPA - Age - Diabetes - NIHSS - Gender - Previous stroke - SBP - Time to tPA		Derivation: 079 Validation: 0.80
[148–149]	s-TPI	Catastrophic (mRS>4)	2184	301	- Age - NIHSS - Glucose - ASPECTS		Derivation: 0.78 Validation: 0.78
[150–151]	Weimar C	Poor outcome (BI<95)	1754	1470	- Neurological complications		Derivation: 0.88