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Clinical commentary

Prognostic value of peripheral leukocyte counts and plasma glucose in intracerebral haemorrhage

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ABSTRACT

Introduction: The value of routine blood markers as prognostic indicators is increasingly established in acute ischaemic stroke. The relationship is less well defined in haemorrhagic stroke. In this study, we examined routine admission blood markers and applied a logistic regression model to predict outcome in haemorrhagic stroke.

Method: A retrospective study was performed between September 2009–2011 in a general admission stroke unit in the UK. 1400 patients were admitted with stroke during this period, of which 117 were haemorrhagic. Admission systolic and diastolic blood pressure, venous blood samples and pre- and post-morbid (i.e. at discharge or death) modified Rankin scores were also recorded. Patients were controlled for age, sex, smoking status, hypertension status and co-morbidities (using Charleson Comorbidity Index scores). Logistic regression models were generated using SPSS.

Results: 113 patients were analysed (58 male/55 female). Lower admission blood glucose ($p = 0.009$), lower total leukocyte count ($p = 0.001$) and lower neutrophil count ($p = 0.021$) were found to be significantly associated with survival vs. death. 90 patients with complete glucose, leukocyte count, sex (forced) and pre-morbid Rankin score (forced) data were entered into a logistic regression model. This predicted correct group membership (survived/deceased) in 72.2% of cases (83.9% survivors/52.9% deceased correctly predicted). In females with normal leukocyte count and glucose, survival was predicted with 68% accuracy.

Conclusion: These results suggest that a logistic regression model using low admission glucose and low total leukocyte count may be markers of better prognosis in acute haemorrhagic stroke with a differential effect between sexes.

1. Introduction

Acute non-traumatic intracerebral haemorrhage (ICH) is a major public health problem with an incidence that has remained unchanged over the past thirty years [1]. It currently accounts for only about one-fifth of the 16.8 million strokes that occur annually but is known to have a higher mortality than other stroke subtypes and, unlike ischaemic stroke, mortality from this disease has not improved over the past decade [2–4]. It also accounts for a disproportionately greater number of the "productive life years lost" due to strokes since it tends to affect people at earlier ages compared with acute ischaemic stroke [2].

The treatment options for ICH range from supportive care to more aggressive interventions such as decompressive surgery. These interventions may carry a significantly higher risk to the patient yet it is not currently possible to clearly identify which patients should be treated most intensively.

A reliable and accurate prognostic biomarker in ICH would be valuable for a number of reasons. Firstly, it would allow patients to be stratified according to their expected clinical outcomes. This would be enormously useful in informing clinical decision-making as well as by aiding in the selection of patients for trials of new treatments. A routine marker that gives an early impression of prognosis would also be useful to clinicians when counselling patients and their families. Moreover, since the pathophysiology of neuronal damage in ICH is poorly understood, new biomarkers

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may direct and inform studies to understand the disease mechanisms of this devastating condition.

Various biomarkers for brain injury have been extensively studied in recent decades, with recognition that these could revolutionise the delivery of care post-injury [5]. However, relatively few studies have focused on biomarkers for non-traumatic brain injuries. In this retrospective study, we aimed to identify markers that could be suitable in offering predictive value for mortality during hospital-stay. We only examined clinical parameters that would be routinely available for every patient who is admitted to hospital.

2. Methods

2.1. Patient selection

We retrospectively reviewed of all cases of stroke admitted to Queen Elizabeth Hospital, King's Lynn between 2009 and 2011, and selected all radiologically confirmed cases of haemorrhagic stroke (intracerebral haemorrhage) for further analysis. Cases of acute ischaemic stroke, sub-arachnoid and sub-dural haemorrhage were excluded.

Routine data on demographics and co-morbidities were obtained. Additionally, other baseline parameters including systolic and diastolic blood pressure and highest values of peripheral leukocyte count and plasma glucose within 24 h of admission were extracted. A Charleson Co-morbidity Index (CCI) score was calculated for each patient to provide an aggregate measure of co-morbidity. Pre- and post-morbid (i.e. at discharge or death) modified Rankin scores were also calculated. The outcome measured was in-hospital mortality.

2.2. Statistical analysis

Statistical analysis was undertaken using IBM SPSS Statistics for Windows version 19 (IBM Corporation, New York, USA). Baseline data was compared across the outcome (mortality) for differences in baseline demographics, co-morbidities (as CCI) and baseline parameters. Significant differentiators, along with sex and pre-morbid modified Rankin Score were forced into a logistic regression model to predict survival.

Comparison of means (for normal data) was performed using *t*-tests, comparison of medians (for non-normal data) was performed using Mann–Whitney *U* tests and proportions compared with Pearson chi-squared tests.

3. Results

113 patients were analysed (55 female), of whom 73 survived the admission and 40 were deceased. There was no significant difference in age, sex nor co-morbidity across survival (Table 1), although sex is of borderline non-significance ($p = 0.079$).

Comparison of admission clinical and laboratory parameters (Table 2) revealed admission plasma glucose, leukocyte and neutrophil counts to be significantly higher in patients who died.

Patients with complete sets of plasma glucose, leukocyte count, sex and pre-morbid modified Rankin Scores (as a control for baseline morbidity) was entered into a logistic regression model predicting survival ($n = 90$). Sex was entered as a categorical covariate, with a value of 0 representing male and 1 representing female patients. Neutrophil count was not entered as its effect was found to account for a significant proportion of variability in survival attributed to leukocyte count. Increased leukocyte count (OR 1.189), glucose (OR 1.243), pre-morbid modified Rankin score (OR 1.513) and male sex (OR 0.257) increased risk of mortality (Table 3).

Model accuracy was variable; overall, the outcome of 72.2% of cases was predicted correctly (Table 4). Prediction of survival was more accurate (83.9%) than death (52.9%).

There was no statistically significant difference in pre-morbid modified Rankin scores between male and female patients in either the total cohort ($p = 0.282$) nor when subgrouped into deceased ($p = 0.193$) and survivors ($p = 0.585$). Similarly, there were no differences for leukocyte count nor plasma glucose between sexes.

Table 1
Demographics and co-morbidities of patients presenting with intracerebral haemorrhage.

	Survived		Deceased		*p* value
		Quartiles		Quartiles	
Age	78	(73,85)	82	(80,85)	0.551
Sex, male	26		21		0.158
CCI*	1	(0,2)	3	(1,4)	0.062
Smoking**	15		13		0.610
Premorbid Rankin Score	0.00	(0.00,2.00)	2.50	(1.00,4.00)	0.163

* CCI at time of admission.
** Smoker at time of admission.

Table 2
Admission clinical and laboratory data of patients presenting with intracerebral haemorrhage.

	Survived		Deceased		*p* value
		Quartiles		Quartiles	
Glucose	6.75	(5.65,8.30)	8.85	(6.15,10.13)	0.009*
BP (systolic)	168	(150.0,189.0)	177	(146.8,209.5)	0.129
BP (diastolic)	84	(75.0,99.0)	89	(80.0,107.0)	0.174
Leukocyte count	9.48	(8.42,12.48)	12.15	(9.58,15.79)	0.001*
Neutrophil count	7.17	(5.91,10.14)	8.19	(6.85,15.13)	0.021*
Lymphocyte count	1.60	(1.19,1.98)	1.67	(0.90,2.60)	0.598
Basophil count	0.05	(0.03,0.07)	0.06	(0.03,0.09)	0.318
Eosinophil count	0.19	(0.10,0.28)	0.10	(0.07,0.20)	0.090
Monocyte count	0.61	(0.46,0.80)	0.63	(0.47,0.85)	0.507

* Significant value.