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Symptomatologic Versus Neuroimaging Predictors of In-Hospital Survival after Intracerebral Haemorrhage

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Abstract: Symptomatological prediction of Intracerebral haemorrhage (ICH) mortality is a simple and effective method compared to pathological predictors. In this study we considered consciousness level as an easily measurable predictor and compared it to haemorrhage location, intraventricular penetration and haemorrhage size derived from Computerized Tomography (CT) to predict mortality using a parametric survival analysis model. Two hundred and thirty eight ICH patients from a neurology hospital ward were enrolled into this comparative study. Patient history was documented with respect to mortality and a questionnaire outlining background variables and medical history was completed for them. Consciousness level was clinically evaluated by a physician while haemorrhage size and location were determined via computerized tomographic scanning reports. Data were entered into the computer and analyzed according to the Weibull parametric survival analysis model using STATA 8 statistical software. Males constituted 47.1% of the 238 patients, 52.9% were females. The age range of the patients varied from 13 to 88 years, with a mean age of 62.4±13.6 (Mean±SD). Half of the patients survived more than 20 days. Using the Weibull regression model, the only significant independent symptomatological predictor of mortality was found to be the level of consciousness. Cumulative hazard during the 90 days was compared for different levels of consciousness. Application of Weibull to pathological predictors of ICH mortality showed that the two independent predictors were haemorrhage size and intraventricular penetration. Results of statistical modelling didn't provide evidence of priority for pathological predictors of survival compared to easily measurable levels of consciousness as a symptomatological predictor. Easily measurable symptoms of level of consciousness can be used as a survival predictor of stroke due to intra-cerebral haemorrhage when compared to pathological indicators.

Key words: Intracerebral haemorrhage, intraventricular penetration, mortality, parametric survival analysis, survival

INTRODUCTION

Intracerebral hemorrhage (ICH) has the highest mortality rate of all strokes, including ischemic stroke and subarachnoid haemorrhage (Takahashi *et al*., 2006; Togha and Bakhtavar, 2004). At present, there are few effective medical means of treating ICH; thus, the ability to make a prognosis regarding outcome of ICH can be significant in identifying patients for whom surgical procedures might be helpful (Ahmed *et al*., 2001). Relative to moderate success in regeneration of damaged brain tissue post ICH stroke by means of neural stem cell transplantation (NSC) have relied upon accurate evaluation of the extent of intracerebral bleeding within a 2 h period (Chu *et al*., 2007). Hemphill's ICH score is commonly used to predict mortality after ICH. More recently, the ICH grading scale (ICH-GS) has been shown to improve sensitivity of 30 day mortality prediction in this patient group (Clarke *et al*., 2004; Hemphill *et al*., 2001). However, no precise answer has been found to explain how very simple predictors of survival like the Glascow Coma Scale (GCS) or the primary classification of consciousness level can accurately forecast survival compared to more contemporary and complex survival indicators. Computer imaging and measuring volume and location of the haemorrhage are cornerstones of these scales. The aim of this study was to compare the predictive value of consciousness level which is an easily measurable indicator, with more sophisticated imaging measurements.

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MATERIALS AND METHODS

The study was conducted in Ardabil province in northwestern Iran. Study participants were patients with intra-cerebral haemorrhage hospitalized in the neurology and neurosurgery departments of Alavi University Hospital. All of the 238 ICH patients hospitalized in AUH were enrolled in the study during the three year period, 2002-2005. Diagnosis was based on medical history as well as clinical and computerized tomography (CT scan) findings. Those with intracerebral haemorrhage following head trauma were excluded from the study. The main variables measured included age, sex, history of cardiovascular diseases, diabetes, hyperlipidemia, drug history, smoking, alcohol and CT scan findings. At the time of hospitalization, blood pressure, fasting blood glucose, serum lipids, blood urea nitrogen and serum creatinine were measured. Clinical features like consciousness level, electrocardiographic findings and chest x-ray findings were recorded in data collection forms. Where necessary, cardiology and radiology consultations were provided. Recoding of CT scan images facilitated calculation of bleeding size and enabled determination of haemorrhage location. Bleeding size was determined using A*B*C/2 formula where A is the largest diameter in the haemorrhage section of greatest thickness, B is the diameter perpendicular to A and C is derived from multiplying the number of axial haemorrhage sections by the thickness of each section.

The choice to use other predictors than the very commonly referenced Glascow Coma Scale (GCS) was made based on the inherent simplicity of the measurement of consciousness level as well as problems in measuring GCS in the case of aphasic patients. An understanding of what is meant by states of normal and impaired consciousness is instrumental in assessing a patient's likelihood of surviving ICH. In this study mortality predictions were made on the basis of 4 distinct consciousness levels: Normal consciousness, mild, moderate and severe confusion; clinical evaluation of the patient's consciousness level was performed by a nurse and physician.

After completing a questionnaire for each patient, medical staff followed study participants to record the mortality rate. Data entered into the computer were analyzed according to standard survival analysis methods. In accordance with acceptable guidelines for statistical diagnostics, parametric survival analysis methods were used. The Weibull regression model was applied using STATA 8 statistical software package.

The study was approved by the Research Committee of Ardabil University of Medical Sciences and the University's Ethical Committee.

RESULTS AND DISCUSSION

Males constituted 47.1% of the 238 patients, 52.9% were females. The age range of the patients varied from 13 to 88 years with a mean age of 62.4±13.6 (Mean±SD). A mean fasting blood sugar of 144.1±47.8 mg dL^{-1} for the patients was noted; mean serum cholesterol and mean triglyceride serum levels of 204.2±66.2 mg/100 mL and 116±53.8 mg/100 mL, respectively, were recorded.

Symptoms of the disease were identified in 52.9% of patients who were awake, 4.2% of sleeping patients, in the early stage of sleep in 10.1% of patients and in 28.6% of resting subjects. A brief medical history of the patients is given in Table 1, which shows that nearly two third of the patients were hypertensive while only 10% of them were diabetic.

Total hospital case fatality rate was 36.3%. As shown in Table 2, the survival rate after one week was 24% among the low consciousness level patients compared to 95% for normal consciousness level group. Among all fatal cases 12.8 and 23.4% occurred within the first and second days of hospitalization, respectively. Mean length of stay was 10.1 days for patients discharged and 5.4 days for those who died in hospital. Overall length of stay was 8.4±5.7 (±SD) days.

Using a Weibull regression model to detect symptomatological predictors of ICH mortality, the significant independent symptomatological predictor was

Table 1: A brief medical history of the patients intracerebral haemorrhage

Medical history item		Frequency of positive answer	Relative frequency of positive answer
History of hypertension?	Yes	162	68.1
	No	72	30.2
	Missing	4	1.7
History of heart disease?	Yes	45	18.9
	No	181	76.0
	Missing	12	5.0
History of diabetes?	Yes	24	10.1
	No	201	84.4
	Missing	13	5.5
Does he/she smoke?	Yes	34	14.3
	No	189	79.4
	Missing	15	6.3
Was she/he a smoker before?	Yes	31	13.0
	No	168	70.6
	Missing	39	16.4
Does she/he live with a regular smoker?	Yes	33	13.9
	No	179	75.2
	Missing	26	10.9
Does she/he drink alcohol?	Yes	5	2.1
	No	194	81.5
	Missing	39	16.4

Table 2: Survival during hospitalization compared for different consciousness levels

Consciousness level	Hospitalization time	Observed survival probability	Survival confidence interval (95%)
Normal consciousness	Second day	0.99	0.92 (0.99)
	Fifth day	0.96	0.89 (0.99)
	One week	0.95	0.87 (0.98)
Mild confusion	Second day	0.96	0.86 (0.99)
	Fifth day	0.90	0.78 (0.96)
	One week	0.88	0.76 (0.94)
Moderate confusion	Second day	1.00	----
	Fifth day	0.92	0.7 (0.98)
	One week	0.78	0.56 (0.9)
Severe confusion	Second day	0.69	0.56 (0.79)
	Fifth day	0.40	0.27 (0.53)
	One week	0.28	0.16 (0.4)

found to be the level of consciousness. The hazard ratio for each unit of increment in consciousness was 2.6 (95% CI: 2.1-3.2).

The same model-analyzing imaging predictors of ICH mortality showed that the two independent predictors were hemorrhage size and intraventricular penetration. The hazard ratio for each unit of increment in bleeding size was 1.018 (95% CI: 1.012-1.024) and 1.7 (95% CI: 1.01-2.9) for patients with intraventricular penetration compared to those without it. When both symptomatological and imaging predictors were entered into a common model only consciousness level and bleeding size remained.

Based on the combined Weibull regression model, hazard function graphs of the first to third cartelist and 90% of consciousness level and bleeding size are compared in Fig. 1 which shows similar patterns in both variables but higher hazard for the lower consciousness levels. Survival is more significantly affected at a higher level of bleeding volume and lower stage of consciousness.

We also used Receiver Operating Curve (ROC) sensitivity and specificity analysis to compare the bleeding size and consciousness variables in diagnosing mortality. Results were consistent with the survival analysis method. The ROC curve shows that sensitivity and specificity are high both for consciousness level and bleeding size. The area under ROC curve was 0.86 (95% CI) for consciousness, a greater value than that of bleeding size at 0.8 (95% CI). Comparative ROC curves are given in Fig. 2.

The present study was performed to identify and compare selected simple clinical versus neuroimaging predictors of in-hospital mortality due to non-traumatic intracerebral hemorrhage. To make the comparison more logical, consciousness was selected as the simplest clinical status evaluation measure compared to computerized tomographic scan (CT scan) neuroimaging findings including hemorrhage size and location. Assessing consciousness status doesn't require that the evaluator is a physician and limiting consciousness grading to four levels simplifies the assessment process further.

Overall mortality in this study was 36.3%. Mortality rates in research literature vary between 20 and 65%, whereas the majority of studies report an overall mortality rate in the 20-35% range .

Another Iranian study conducted in Tehran reported the in-hospital mortality or case fatality to be 46.7%, a figure considerably higher than in this study and other published reports. The Tehran study was conducted in a reputable University hospital which receives patients both directly and as secondary/tertiary referrals from other general private or state hospitals in the area. The difference maybe due to the fact that some nearby general hospitals refer their severe cases or cases with lowest consciousness levels to the aforementioned hospital, resulting in possible overestimation of ICH case fatality (Togha and Bakhtavar, 2004).

A mean length of stay for all cases was 8.4 days and a 10.1 day mean length of stay for live discharges was reported in our study. Length of stay is reported with high variation in literature, a difference that may reflect inherent heterogeneity in the distribution of mortality and length of stay predictors in research. However, based on the fact that many studies only report the overall length of stay including deceased study participants with a shorter length of stay, a plausible explanation for different reports of hospitalization length may be the variation in fatality proportions. In cases where there is a high incidence of disease-related fatality, authors of medical research articles should attempt to provide detailed information about length of stay.

Consistent with our findings Takahashi *et al.* found that level of consciousness was the best single predictor for mortality, followed by high ICH volume (Takahashi *et al*., 2006). They compared prediction by ICH volume and lower levels of consciousness but neglected to make an evaluation of fatality inside the cartelist, a measurement that yields more detailed information. We found that although upper cartelist of low consciousness and ICH volume resulted in similar predictions for mortality, with ICH volume being a slightly better indicator, overall mortality prediction, particularly in the case of good consciousness, was better for level of consciousness.

Mortality prediction models have been developed and improved in recent years. Although, there is need of further research in some areas, many of them have

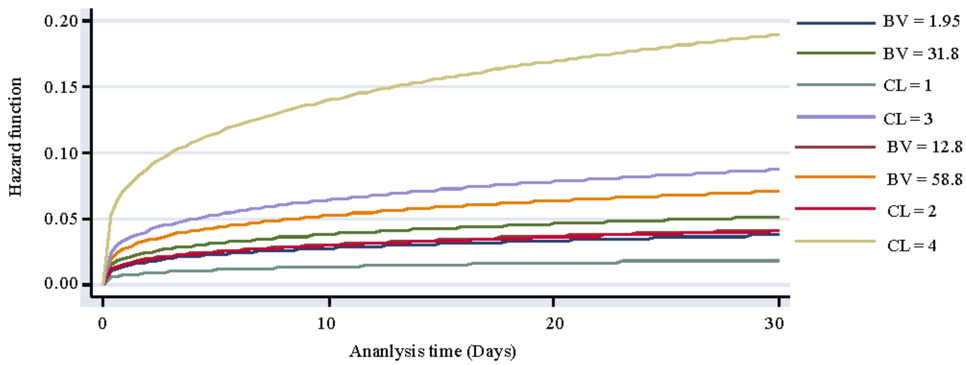

Fig. 1: Hazard function based on weibul regression Cartelist of bleeding size (BV) and consciousness level (CL)

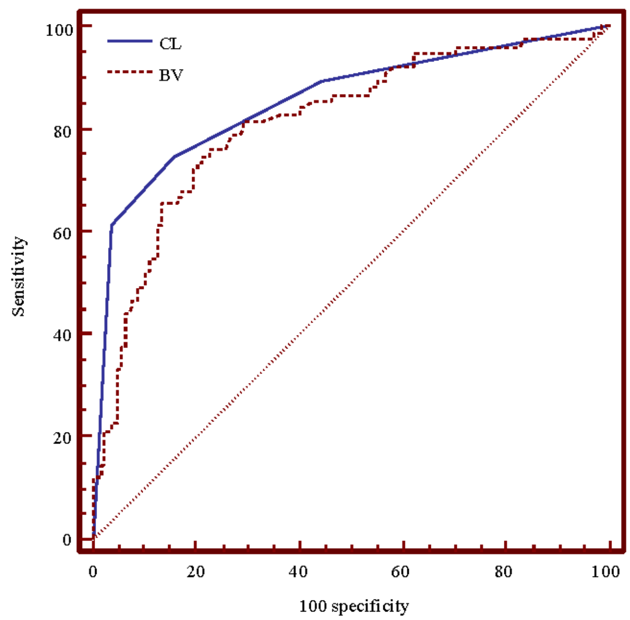

Fig. 2: Receiver operating curves (ROC) for consciousness level (CL) and bleeding size (BV) in predicting hospital mortality

been shown to be quite reliable in different settings (Berwaerts *et al*., 2000; Hemphil *et al*., 2001; Naval *et al*., 2008; Chiquete *et al*., 2007; Takashi *et al*., 2006). However, the main idea supported by the findings of this research focuses on : 1- simplicity in applying a method of evaluating level of consciousness that nurses as well as more specialized medical staff can use. 2-level of consciousness is a general predictor of survival for many diseases. 3-evaluation by means of consciousness levels can be made relatively quickly and still meet requirements for acceptable test sensitivity and specificity.

Although it is generally true that more complex prediction models yield more precise results, this research shows that a higher level of technical sophistication contributes very little to survival prediction in the case of ICH.

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