Predictors of outcome for non-traumatic intracerebral hemorrhage

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ABSTRACT

الأهداف: لتقييم الإنذار والنتيجة العصبية ومشعرات البقاء للمرضى المصابين بنزف داخل المخ الغير ناتج عن رض.

الطريقة: تم تقييم 96 مريض سعودي (ذكر وأنثى) مصابين بالسكتة في قسم جراحة المخ و الأعصاب في مستشفى عرعر المركزي – عرعر – بمنطقة الحدود الشمالية – المملكة العربية السعودية، خلال شهر يوليو 2005م. في هذه الدراسة تم تضمين 96 مريضاً من المصابين بنزف مخي غير رضي من أصل 103. ادخلوا في البداية إلى قسم الطوارء كمرضى مصابين بنزف دماغي. أستبعد منهم من كان لديه خلل في الأوعية الدموية الدماغية (AVM) والإصابات الدماغية والإصابات المتكررة بالسكتات الدماغية وإعتلالات أخرى.

النتائج: تم تحليل نتائج 96 مريض، متوسط أعمار المصابين بالسكتة الدماغية كان 67.20 (± 14.7) عام، أعمارهم تتراوح مابين 30 – 100 عام، متوسط مقياس جلاسقو كوما (GCS) عند دخول المرضى 8.42 (±1.73) أي بين (4 – 13)، وكمية النزف الدماغي بالأشعة الصوتية 10.61 (±14.01) ml^3، أي بين (1–36)، كان مستوى ضغط الدم لدى المرضى عند دخولهم المستشفى 81.9 (±22.8) mm – Hg، اي بين (70 – 130 mm – Hg). كان معدل الوفيات خلال 30 يوما 17.7%. العوامل المستقلة غير المرتبطة خلال هذه الفترة هي مقياس جلاسقو كوما جلاسقو كوما (GCS) الذي أعطى (p=0.001)، وأعطى تمدد النزف البطيني (p=0.001) (Intraventricular Extension of Hemorrhage).

خاتمة: ساهمت هذه الدراسة في التمييز بين المرضى الذين يحتمل لهم الموت أو البقاء خلال 30 يوما من السكتة الدماغية، كما يمكن أن تساعد في اتخاذ القرارات فيما يتعلق بتقديم العناية المناسبة للمرضى المصابين بالنزيف المخي.

Objective: To evaluate the prognosis, neurologic outcome, and predictors of survival in patients with non-traumatic intracerebral hemorrhage.

Methods: We evaluated prospectively a cohort of 96 Saudi adult males and females with stroke during the month of July 2005 at Arar Central Hospital, Riyadh, Kingdom of Saudi Arabia. Out of 103 patients, 96 patients, who were diagnosed as having intracerebral hemorrhage (ICH) presenting to the emergency department for initial evaluation, were included, except those with recurrent intracerebral hemorrhage, arteriovenous malformation, subarachnoid hemorrhage, traumatic brain injury, hemorrhagic infarctions, and patients receiving anticoagulant therapy. No patient underwent any neurosurgical procedure.

Results: The results of 96 patients were analyzed. The mean age at ICH was 67.2 (±14.7) years (range, 30-100 years), and mean Glasgow coma scale (GCS) score on admission was 8.42 (±1.73) and (range, 4-13). Mean ICH volume on initial CT scan was 10.61 (±14.01) ml^3 (range, 1-63). Mean pulse pressure on hospital arrival was 81.9 (±22.8) mm Hg (range, 70-120 mm Hg). In uni-variate analysis, GCS score (p=0.0005), ICH volume (p=0.001), mass effect (p=0.001), and presence of intraventricular hemorrhage (p=0.0005) were all associated with 30-days mortality, while in multivariable analysis, the most significant independent predictors of 30-day mortality were, GCS score and the intraventricular extension of hemorrhage.

Conclusions: This model may aid in making decisions quickly and easily regarding the appropriate level of care for such patients with intracerebral hemorrhage.

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Intracerebral hemorrhage (ICH) constitutes 10-15% of all strokes and has a higher risk of morbidity and mortality than cerebral infarction or subarachnoid hemorrhage (SAH) in the western world.[1,2] Despite advances in the treatment of cerebral infarction and

SAH, there remains no therapy of proven benefit in improving outcome after ICH.[3] The incidence and prevalence of strokes are low in Saudi Arabia when compared with the western countries, and this is mainly attributed to the younger age of the population. The overall distribution of stroke types are not different from that reported in other communities, with the exception of the low incidence of SAH.[4,5] In Saudi Arabia, most of the hemorrhagic strokes are ICHs and only 2% of all strokes are SAHs. Hypertension (52%), diabetes mellitus (41%) and cardiac disorders were reported common risk factors and atherosclerosis (36%), hypertensive or diabetic arteriolopathy (24%) and cardiac embolisms (19%) are most common causes.[6] These findings are similar to the other parts of the world, as ICH constitutes 10-15% of all strokes and has a higher risk of morbidity and mortality than cerebral infarction or SAH.[1,2] However, in a study carried out in Saudi Arabia[7] it was reported that early mortality (19%) was relatively low compared from the more industrialized world. Several previous studies revealed risk factors for ICH and proposed methods to predict patient outcome. These currently available methods vary in intricacy, and some require even mathematical calculation for prediction of outcome.[8-11] Hence, while these methods may precisely predict outcome, they differ in their simplicity of use. However, the ICH Scoring System[10,12] is a simple clinical grading scale that allows risk stratification on presentation with ICH.

The purpose of this study was to evaluate the prognosis, neurologic outcome, and predictors of survival among patients with non-traumatic intracerebral hemorrhage in Northern Saudi Arabia. We also aimed to define one or 2 simpler clinical criteria that are predictive of outcome and that can swiftly and precisely assess the risk at the time of case presentation, and can also predict the survival of cases.

Methods. Arar is a semi-urban city at the north of Saudi Arabia with 279,286 inhabitants.[13] During the time of this prospective study, Arar Central Hospital, was the only hospital with a neurosurgery unit. One hundred and sixty-five patients were admitted to the emergency unit of Arar Central Hospital, Riyadh, Kingdom of Saudi Arabia during the month of July 2005. One hundred and three patients were diagnosed as having ICH, and 96 were included to the study. Since the purpose of this study was to evaluate prognosis, patients were only included if they received the diagnosis of ICH after presented to the emergency department for initial evaluation at the emergency service. The cases with cerebral trauma as the possible precipitating cause of ICH, and patients who were transferred from other health centers for intensive care or investigation at an outside clinic or hospital were excluded. Informed consent was taken from the patients' attendant, and the study was approved by the Research and Ethical Committee of the hospital. Variables recorded were age, gender, systolic blood pressure, diastolic blood pressure, Glasgow coma scale (GCS),[14] hematoma volume, site of the bleeding, degree of ventricular extension, and presence of mass effect. Pulse pressure (defined as systolic blood pressure minus diastolic blood pressure) was also calculated through the first blood pressure recorded after hospital arrival. The mass effect was graded according to the degree of ventricular compression and cisternal effacement (ambient cistern and, quadrigeminal cistern). Presence of intraventricular hemorrhage (IVH), GCS score, and ICH volume were recorded as these are components of previously validated ICH outcome models,[8,15] and can be accurately assessed by personnel without extensive training in stroke or neurology.[10,16] The GCS score at the time of transfer from the emergency department (to intensive care unit, operating room, or hospital ward) was used as this is the point at which initial acute intervention would be considered. The GCS scores were calculated by the principal researcher from the neurological examination. Final diagnosis of ICH was made on behalf of the findings. The hematoma volume was measured on the initial cerebral head CT scan with the use of the ABC/2 method, in which A is the greatest diameter on the largest hemorrhage slice, B is the diameter perpendicular to A, and C is the approximate number of axial slices with hemorrhage multiplied by the slice thickness.[16] Routine care was provided to all patients according to the guidelines. Patients who were alive at hospital discharge and did not have a recorded date of death in any of the visitor's records were accepted as assumed to have being alive at 30 days after ICH.

Statistical analysis was performed with SPSS (version 10.0), and $p<0.05$ was considered statistically significant. We calculated mean with their 95% confidence interval (CI) of numerical data and carried out uni-variate analyses to check any association, whereas the Cox-regression analyses for survival was applied by entering all variables at once (the Enter method).

Results. Ninety-six patients were included in the study. Of 96 patients, overall 30-day mortality was 17.7% (n=17). Mean age at ICH was 67.20 (±14.78) years (range, 30-100 years), and mean GCS score on admission was 8.42 (±1.73) and (range, 4-13). Mean ICH volume on initial CT scan was 10.61 (±14.01) ml^3 (range, 1-63). Mean pulse pressure on hospital arrival was 81.9 (±22.8) mm Hg (range, 70-120 mm Hg). The cohort was in a manner similar to that previously described for other series of ICH patients (**Table 1**).[3,15]

Table 1 - Characteristics of the subjects (N=96) by gender.

Patients' characteristics	Males (n=81)	Females (n=15)
Age		
Mean	67.63 (±14.64)	64.87 (±15.8)
Median	70	70
95% Confidence interval	64.3-70.87	56.12-73.61
Range	30-100	40-90
Glasgow coma scale		
Mean	8.27(±1.7)	9.20(±1.7)
Median	8	8
95% Confidence interval	7.89-8.65	8.2-10.4
Range	4-11	6-13
Systolic blood pressure		
Mean	183.6 (±24)	182.4 (±21.9)
Median	190	190
95% Confidence interval	170.2-194.5	170.26-194.5
Range	140-220	60-210
Diastolic blood pressure		
Mean	99.4 (±19.8)	112.9 (±21.9)
Median	90	90
95% Confidence interval	95-103.8	100.7-125.1
Range	80-140	80-140
Hospital stay		
Mean	16.5 (±6.7)	18.33 (±5)
Median	17	17
95% Confidence interval	14.9-17.9	15.5-21.1
Range	30-100	40-90
Hematoma volume		
Mean	11.5 (±14.8)	6 (±7.35)
Median	05	03
95% Confidence interval	8.2-14.7	1.9-10.1
Range	1-63	1-31

In univariate analysis, ICH volume (*p*=0.001), mass effect (*p*=0.001) (**Figure 1**), presence of IVH (*p*=0.0005) (**Figure 2**), and GCS score (*p*=0.0005) (**Figure 3**) were all associated with 30-day mortality. The age, pulse pressure, ICH location, and gender were not associated with the outcome. A regression model was built to check for the independent effects of the different variables on patient survival. **Table 2 & 3** summarize the risk and outcome prediction models, which in turn form the basis for the prediction of outcome in these patients. The GCS score and ventricular extension were the significant independent predictors of outcome.

Discussion. The cohort of this study was in a manner similar to that previously described for other series of ICH patients in other studies,[3,15] and in uni-variate analysis, GCS score, ICH volume, mass effect, and presence of IVH were all associated with 30-day mortality, which was estimated at 18%. However, the age, pulse pressure, ICH location, and gender were not associated with the outcome. Since clinical grading scales play an important role in the evaluation and management of patients with acute neurological disorders, there are several examples of widely used clinical grading scales including the

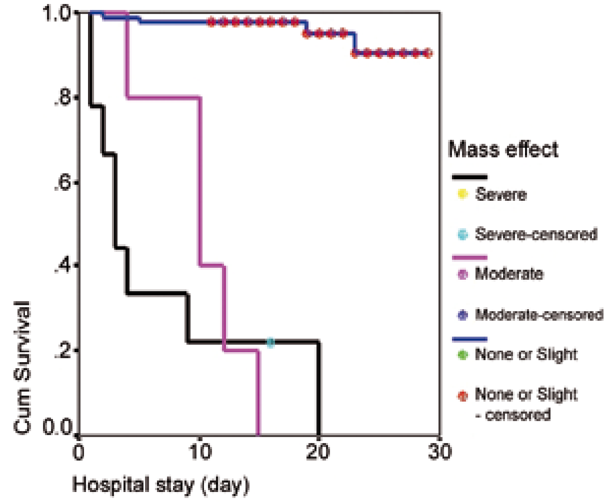

Figure 1 - The effect of mass effect on 30-day survival in non-traumatic intracerebral hemorrhage patients.

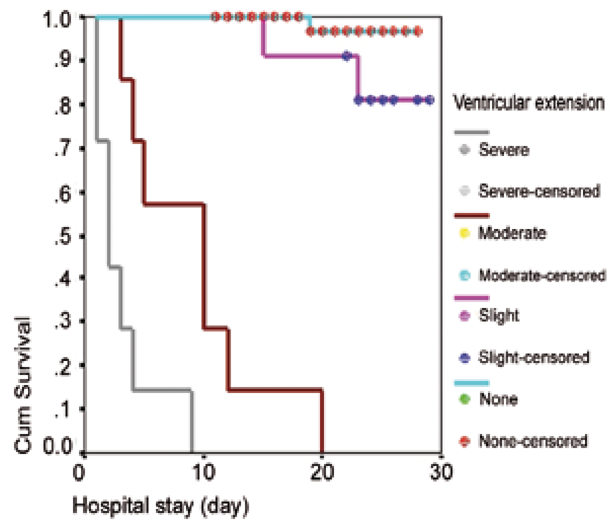

Figure 2 - The effect of ventricular extension on 30-day survival in non-traumatic intracerebral hemorrhage patients.

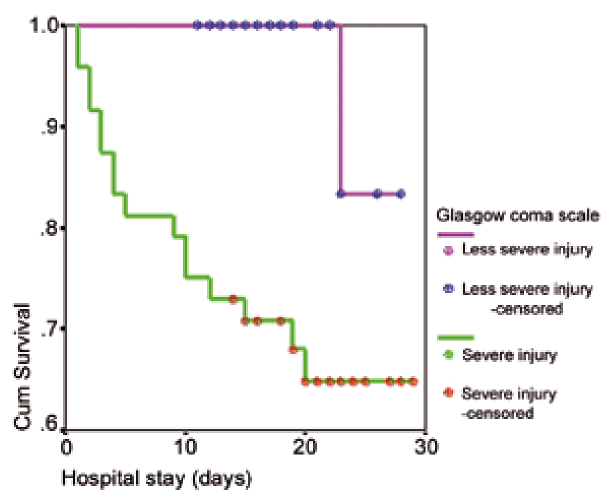

Figure 3 - The effect of Glasgow coma scale on 30-day survival in non-traumatic intracerebral hemorrhage patients.

Table 2 - Uni-variate analysis comparing the effect of patient characteristics on survival (N=96).

Patients' characteristics	30-days mortality n (%)	Odds ratio (95% CI)	*P*-value
Age (≥76 years)			
Yes (n=23)	7 (30.4)	2.7 (0.90-8.37)	0.067
No (n=73)	10 (13.7)		
Gender			
Male (n=81)	16 (19.8)	0.029 (0.035-2.37)	0.223
Female (n=15)	1 (6.7)		
Glasgow coma scale			
Severe damage (n=48)	16 (33.3)	0.04 (0.005-0.33)	0.0005
Less severe damage (n=48)	1 (2.1)		
Hematoma volume (≥31ml³)			
Yes (n=11)			
No (n=85)	9 (81.8)	0.11 (0.05-0.23)	0.0005
	8 (9.4)		
Ventricular extension			
Yes (n=26)	16 (61.5)	0.023 (0.003-0.166)	0.0005
No (n=70)	1 (1.4)		
Mass effect			
Yes (n=14)	14 (31.8)	0.181 (0.056-0.59)	0.001
No (n=82)	3 (5.8)		
Hospital stay(≤10 days)			
Yes (n=12)	12 (100)	16.8 (7.18-39.3)	0.0005
No (n=84)	5 (6)		

CI - confidence interval

Table 3 - Variables predicting 30-days survival in the multivariate Cox-regression analysis for outcome (N=96).

Variables	*P*-value	Odds ratio	95% CI	
			Lower	Upper
Age	0.553	0.981	0.921	1.045
Gender	0.674	0.548	0.033	9.035
Systolic blood pressure	0.316	1.022	0.979	1.067
Diastolic blood pressure	0.381	0.977	0.928	1.029
Glasgow coma scale	0.024	0.511	0.285	0.917
Hematoma volume (ml³)	0.441	0.959	0.862	1.067
Site of bleeding				
Putamen	0.695	1.536	0.180	13.092
Thalamus	0.810	0.680	0.029	15.939
Ventricular extension				
Severe	0.003	0.001	0.001	0.035
Moderate	0.010	0.001	0.001	0.146
Slight	0.023	0.017	0.001	0.569
Mass effect				
Moderate	0.862	1.315	0.060	28.830
Severe	0.902	1.417	0.106	12.784

CI - confidence interval

GCS for traumatic brain injury (and other disorders), the Hunt-Hess[17] and World Federation of Neurological Surgeons (WFNS)[18] scales for aneurysmal SAH, the National Institutes of Health Stroke Scale (NIHSS)[19] for ischemic stroke, and the Spetzler-Martin scale[20] for arteriovenous malformations. Among the various characteristics, levels of consciousness on hospital admission and hematoma volume have usually been the most robust outcome predictors, with other factors, such as presence and amount of IVH, also associated with outcome in some models and these have led to the use of hematoma volume as enrollment criteria for various studies of intervention in ICH.[19,21,22] In essentially every clinical grading scale there exists a compromise between simplicity and accuracy of outcome prediction.[23]

The predictors of health status and injury outcome are supposed to be easy in assessment and may predict outcome easily. How might the independent predictors be used? Prognosis after ICH or other acute neurological disorder is often a fundamental question, and various scales discussed above are often used to provide initial information regarding this. While prognostication is undoubtedly important to assess treatment benefits and risks and to provide patients and families with information regarding severity of illness, attempts to precisely prognosticate outcome may lead to inappropriate (self-fulfilling prophecies). The independent predictors are most appropriately used to provide a framework for clinical decision making and providing reliable criteria for assessing efficacy for new treatments. For example, the age has been an independent predictor of ICH outcome in some prior prediction models, while age has not been associated with outcome in many studies[19,21,22] as well as in our study. Hence, age cannot be included in those factors on which decision is dependent.

The ICH volume has been used as a strong predictor and often divided into 3 groups representing small, medium, and large hematoma size.[8,15] While the specific volume cut points vary depending on the specific model, small hematomas have often been considered as 30 cm³, and large hematomas as 60 cm³.[15] Its association with outcome was not as strong as some other predictors in our study. In fact, in univariate analysis it was significantly associated ($p<0.05$), but it was not an independent predictor for outcome. This may be because small hemorrhages in the brain stem or cerebellum may have catastrophic consequences, making location, not size, the more important predictor for ICH. Additionally, while larger ICH volumes were associated with increased mortality, the addition of a "large hematoma" group did not improve the model as patients with larger hematomas who died also had other predictors such as low GCS score, advanced age, or IVH that influenced outcome to a greater degree. Importantly, assessment of ICH volume by the ABC/2 method has been shown to be accurate and with good interrater reliability.[9]

The ventricular extensions of hemorrhage and GCS scale were strongly associated (p<0.05) as an independent factor for prediction of 30-day mortality. Undoubtedly, further characterization of the degree of ventricular extension of hemorrhage and IVH-associated hydrocephalus could provide additional prognostic information, but these were not included in this model. Additionally, mass effect was significant (p<0.05) in patients with uni-variable analysis, but this factor was not an independent predictor of mortality. In the simplified model, the effects of GCS score and ventricular extension of hemorrhage might have diminished the strong general effect of mass effect.[21-23]

Since the study was conducted in a main referral center of the North Zone, the sample was representing the whole zone. However, the number of patients might be considered small, and the study needs to be conducted on a larger scale to verify the results. Thus, independent predictors from this study could be used as part of risk stratification for ICH treatment studies. Additionally, factors not represented in this model, such as time of onset, medical co-morbidities, and patient or family treatment preferences, will always play an important role in selection of patients for clinical research or clinical treatment studies.

In conclusion, despite the issues of accuracy and reliability, improved standardization of clinical assessment with the use of GCS score, ICH volume, mass effect, and presence of IVH are likely to provide more consistency in clinical care and clinical research for ICH. Hence, our study's model may aid in making decisions of the appropriate level of care for such patients with ICH.

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