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Severe head injuries: an outcome prediction and survival analysis

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Abstract *Objective:* To identify the predictors determined early after admission and associated with unfavorable outcome or early (within 48 h) death after severe head injury.
Design: Prospective cohort study.
Setting: A neurosurgical intensive care unit in a university hospital.
Patients: 198 consecutive comatose patients hospitalized from 1989 to 1992.
Results: Logistic regression showed that a combination of age, best motor response score from the Glasgow Coma Scale, and hypoxia provided a good prediction model of unfavorable outcome (sensitivity=0.93). The length of participation of survivors was 6 to 61 months (median 27.1). The Cox model demonstrated age, motor score less than 3, mydriasis, and hypoxia as poor prognosis factors.
Conclusions: Clinicians can determine the odds of a good outcome from the combination of three easily measurable factors using a simple diagram constructed from logistic regression. Survival analysis showed that motor score adjusted values greater than 3 had the same prognosis.

Key words Head injury · Prognosis · Trauma severity · Grading system · Logistic regression model · Cox regression analysis

Introduction

Head injuries continue to be a major health problem in 1995, not only in terms of their frequency but also because of the fatalities and handicaps that result in the population they most often affect. The majority of patients are young victims of motor vehicle, sports, or occupational accidents.

The analysis of prognostic factors in comas resulting from head injury is crucial to the specialized care teams involved in their management. In addition to being helpful in making therapeutic decisions, it provides a basis for objective responses to the legitimate questions asked by families and paramedical care-givers.

Numerous studies have described a statistical relationship between one predictor and either overall outcome or neurological deficits following severe head injury [1–12]. Mortality and the Glasgow Outcome Scale (GOS) [13] have been studied extensively [4–6, 14–21], while predictions combining several indicators are less common. Most prognostic studies of severe head injury use clinical or radiological variables obtained during the first few hours following the accident. The variables most closely linked to overall outcome reported in the literature are depth of coma, age, ocular signs, and the presence of an intracranial lesion exerting a mass effect [4, 5, 15, 17, 18]; however, such univariate studies did not provide any adjusted value of the relative risk of predictors.

A population of 198 consecutive patients with severe head injury was studied to evaluate the clinical predictors easily determined early after admission and associated with a significant increase of unfavorable outcome. It also defined factors associated with early (within 48 h) death. The objective was to find a way of judging prognosis in the clinical setting as easily as possible.

Table 1 Factors noted on admission and clinical outcome in 198 comatose patients following severe head injury. Logistic regression of probability of death or vegetative survival from a sample of 132 randomized patients (*PaO_2* partial pressure of oxygen in arterial blood)

Factors	Favorable outcome n=105 (53%)	Unfavorable outcome n=93 (47%)	Beta	Standard error	Wald statistic	p value
Best motor response			–0.738	0.168	19.364	0.0000
5: localizes	70 (72)	27 (28)				
4: normal flexor	9 (50)	9 (50)				
3: abnormal flexor	14 (56)	11 (44)				
2: extensor	10 (23)	34 (77)				
1: none	2 (14)	12 (86)				
Age (years, mean±SD)	33.7±4.7	44.0±17.0	0.0402	0.0129	9.678	0.0019
PaO_2<8 kPa	7 (22.6)	24 (77.4)	1.532	0.638	5.6767	0.0163
Male	83 (51.6)	78 (48.4)	0.959	0.6029	2.530	0.1117
Systolic blood pressure <90 mmHg	13 (32.5)	27 (67.5)	0.073	0.301	0.059	0.7870
Arterial pH<7.40	14 (38.9)	22 (61.1)	1.464	1.192	1.510	0.2262
Pupil size						
Normal	79 (66.4)	40 (33.6)				
Unilateral mydriasis	22 (40.0)	33 (60.0)	0.087	0.323	0.072	0.7685
Bilateral mydriasis	4 (16.7)	20 (83.3)	0.474	0.685	0.479	0.4911
CT high- or mixed-density lesion < 25 cc						
Absence	42 (58.3)	30 (41.7)				
Single	31 (55.4)	25 (44.6)	1.083	1.012	1.145	0.2981
Multiple	32 (45.7)	38 (54.3)	1.239	1.102	1.263	0.2658
Mass lesion >25 cc:						
Absence	58 (58.6)	41 (41.4)				
Single	43 (47.3)	48 (52.7)	0.000	0.000	0.000	0.9986
Multiple	4 (50.0)	4 (50.0)	0.984	0.997	0.974	0.3211
Midline shift >5 mm	21 (36.2)	37 (63.8)	0.119	0.367	0.105	0.7302
Associated traumatic lesion:						
Absence	41 (54.7)	34 (45.3)				
Single	42 (49.4)	43 (50.6)	0.216	0.479	0.204	0.6418
Multiple	22 (57.9)	16 (42.1)	0.104	0.347	0.090	0.7470
Open head injury	13 (56.5)	10 (43.5)	0.124	0.375	0.109	0.7250
Evacuated mass lesions	47 (54.7)	39 (45.3)	0.7677	0.881	0.760	0.3809

Totals: good outcome (n=73) and moderately disabled (n=32), severely disabled (n=32), severely disabled (n=24), vegetative state (n=6), and death (n=63)

Materials and methods

Patients

This work concerned patients hospitalized at the Centre Hospitalo-Universitaire Grenoble, France, from 1989 to 1992. The population consisted of 198 consecutive, comatose patients (no eye-opening, not speaking, and not obeying commands) due to severe head injury. The mean age was 38.5±17.8 years; 81.3% were male. This clinical setting represents the World Health Organization's definition of coma and corresponds to a score of ≤8 on the Glasgow severity scale [22]. Victims of craniocerebral wounds by firearms or presenting with clinical criteria of brain death on admission were not included in this study. Table 1 describes the prognostic factors noted at admission. High- or mixed-density lesions shown on computed tomography (CT) were graded in three categories (absence, unique, and multiple) in the analysis.

Best motor response was used in place of the Glasgow Coma Score. Since in these cases verbal response cannot be tested owing to the presence of an endotracheal tube, the large majority of these patients were under general anesthesia to assure optimal hemodynamic stability and ventilator adaptation. Under these conditions, patients showed a pharmacologically induced myosis which made inaccurate the assement of the pupil light reflex, therefore measuring pupil size was preferred.

Treatment protocol

Fifty-one percent of patients were admitted directly to the hospital as opposed to being referred from outlying hospitals. The mean length of time (±SE) between trauma and arrival at the hospital was 7±0.5 h. All patients were admitted directly to the emergency department and were examined by a neurosurgeon. CT of the head was carried out unless it had already been done by another hospital. Patients presenting with intracranial mass lesions larger than 25 cc, or causing a midline shift greater than 5 mm, underwent immediate surgery. Patients were than admitted to the neurosurgery intensive care unit (ICU). The same physicians worked in this unit throughout the entire study. All patients were mechanically ventilated. Moderate passive hyperventilation was routinely given in order to maintain a partial pressure of carbon dioxide in arterial blood of between 3.5 and 4.5 kPa. Intracranial pressure (ICP) was monitored when the clinical picture and/or the results of CT of the head suggested high ICP. A pressure greater than 20 mmHg was treated with mannitol 20% and barbiturate sedation (sodium thiopental by IV drip) alone or in combination with i.v. xylocaine. The infusion rates of these drugs were adjusted to maintain an ICP of ≤15 mmHg. Volume expansion was provided to maintain a central venous pressure close to 10 cmH_2O. Mean arterial pressure was maintained at over 80 mmHg, using inotropic drugs when needed. Benzodiazepine and opiate administration were titrated to patient discomfort. Sedation was routinely interrupted on day 10 in order to evaluate neurological status and was reinstated whenever necessary. As long as the patient was comatose, a neurologic examination evaluating GOS, pupil size, and light reflex was done every hour by the patient's primary nurse. A neurologic exam was performed at least twice a day by an intensive care physician. Follow-up CT was routinely done between the 2nd and 4th day after trauma and on an urgent basis whenever the patient presented worsening neurological signs.

Statistical analysis

A logistic regression was carried out to test the predictive value of a combination of 12 categorical variables and age; however, the motor score had been treated as a continuous variable providing the simplest model (Table 1). This was made using the SPSS forward selection procedure using the likelihood ratio, a p in of 0.05 and a p out of 0.10 as statistical criteria. In order to reduce the bias of classification inherent in the use of an entire sample [23], the model was constructed on two-thirds of the patients designated at random and was validated on the remaining third.

Data permitting analysis of factors influencing survival were studied using the Cox semiparametric model. The hypothesis of proportionality was verified in a graphic manner for each categorical variable by the graphic log-minus-log method.

Recording of data and statistical analysis were carried out by two entirely different teams.

Results

Logistic regression: According to the GOS, the outcome was defined as favorable (good outcome and moderate disability) or unfavorable (severe disability, vegetative state and death). Table 1 shows the log of the odds ratio of being classified an unfavorable outcome and the statistics associated with the covariates initially included in the model. Motor score, age, and hypoxia were the best predictive factors obtained on the training randomized sample (n=132). No interaction of clinical relevance was revealed in the model and it fitted the data correctly (X^2=134.8, 129 df, p=0.3456). The three variables provided an overall rate of correct classification, estimated from the validation sample (n=66) X^2=81.1, 63 df, p=0.0621), of 73%, sensitivity of 93%, and specificity of 57%. This was established with the rule being a threshold greater than 0.50 in order to identify the outcome for each patient; this rule corresponded to the highest Youden index [24]. This gives a high sensitivity model, capable of defining poor prognosis, but with weaker specificity; however, the area under the receiver operating characteristic ROC curve, drawn from the validation sample, was equal to 0.87, which conferred good predictive value to the model [25]. The confusion matrix improved with the population size and the number of variables included in the model [23]. Considering the 198 patients and the 13 variables, the rate of correct classification was 80.81% and only 76.26% with the three variables described above. In these conditions, mydriasis on arrival at the scene was a statistically significant poor prognostic factor. The motor score evaluated on day

Table 2 Relative riks *RR* and 95% confidence interval *CI* according to Cox model

Variable	Coefficient	RR	95% CI
Age	0.035	1.04*	
Motor score[a]			
1	1.560	4.80	3.80 to 5.90
2	1.169	3.22	2.59 to 4.00
3	0.779	2.18	1.76 to 2.71
4	0.385	1.47	1.19 to 1.82
5	0	1	
Unilateral mydriasis	0.4278	1.54	0.76 to 3.11
Bilateral mydriasis	1.1028	3.01	1.42 to 6.39
Hypoxia	0.8861	2.43	1.38 to 4.28
ATL 1	–0.3566	0.70	0.41 to 1.19
ATL 2	–1.1235	0.33	0.13 to 0.80
Emergency surgery	–0.6552	0.52	0.31 to 0.81

* p<0.0001
[a] Best motor response in the emergency room (*ATL* associated traumatic lesion, *1* unique, *2* multiple)

10 did not improve the prediction. The logit of the probability of having an unfavorable outcome on the basis of motor score, age, and hypoxia was equal to:

$$\text{logit}\ (p) = 0.0327 – 0.7382 \cdot \text{motS} + 0.0402 \cdot \text{age} + 1.5319 \cdot \text{hypoxia}$$

Cox regression model: Sixty-three patients died. The survivors were in the study from 6 to 61 months (median 27.1). The cox model, calculated on all 198 patients, defined, age, a motor score of less than 3, mydriasis, and hypoxia as poor prognosis factors. On the other hand, lesions accessible to surgery were associated with a better survival and the presence of associated traumatic lesions did not worsen it (Table 2). Median survival were 2 days (95% CI 0 to 66) and 111 days (95% CI to 782) for motor scores 1 and 2, respectively.

Discussion

The predictive variables considered here were essentially clinical variables available at the time of the accident or in the emergency room once cardiopulmonary conditions were stabilized. Brain-stem evoked potentials and ICP measurements were not included in this model. Although these variables are very good prognostic indicators [19], they are not always practicable in extreme emergencies; furthermore, systematic ICP monitoring immediately after admission had not been the object of a consensual practice [16, 19]. In this series, ICP was monitored in 66 patients (33%) and was inversely related to outcome. Among these patients, 46 (70%) had an unfavorable outcome and 20 (30%) a favorable one. Mean ICP was higher in the first group (26.2±8.2 mmHg vs 21.0±5.9 mmHg, p=0.0137).

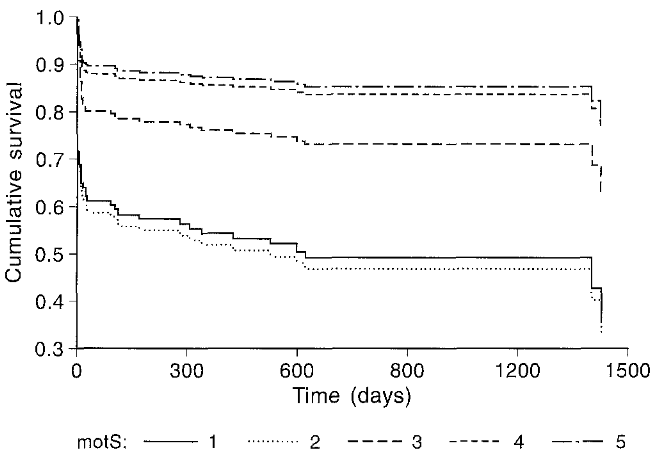

Fig. 1 Adjusted survival curves for motor score. motS is the best motor response noted in the emergency room

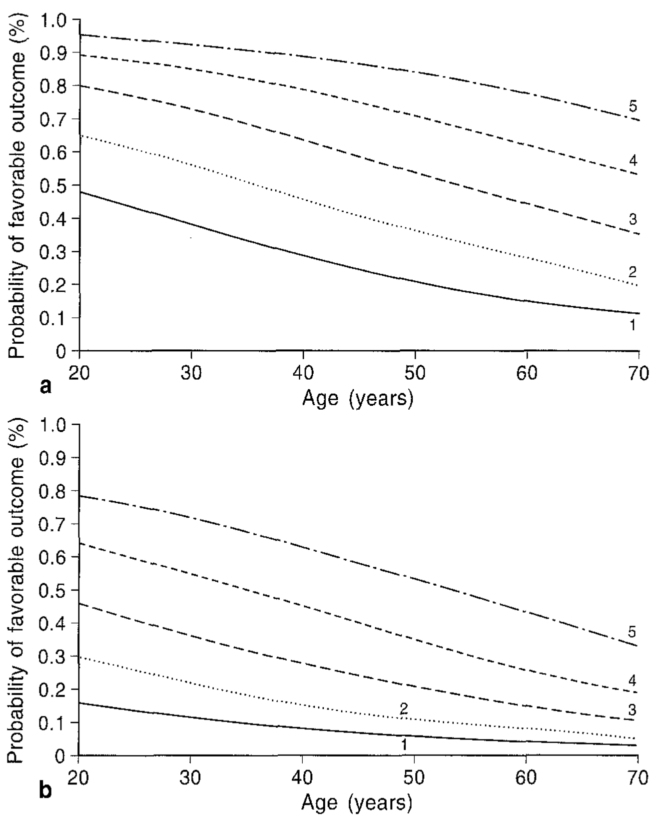

Fig. 2 Probability of favorable outcome based on best motor response on Glasgow Coma Scale, age, and **a** absence, **b** presence of hypoxia

The results of this study are similar to those in another report [19]. A combination of best motor response, age, and the presence of hypoxia determined the prognosis in head injury patients with fairly high accuracy. Taking sampling fluctuations into account, if a more rigorous decision rule is imposed, the model conserved good sensitivity. For example, if the probability of belonging to the poor prognosis group is 0.6, then the sensitivity is 0.79; conversely, if the decision threshold for attribution to the good prognosis group is 0.6, then the specificity would only be 0.49. The total reliability (0.73) in this study is less than that described by Choi et al. (0.79) [16]. This could be explained by the lack of power and the use of pupillary light reflex as a prognostic factor in place of pupillary size [16]. On the other hand, in these 198 patients, the association of a low motor score on arrival and a dilated pupil size was highly significant ($p<0.0001$) and induced a high degree of collinearity in the logistic regression model. The presence of bilateral mydriasis is a factor of poor prognosis multiplying the risk of death by 3, according to the survival analysis.

Hypoxia is an adverse risk factor well recognized in the literature [26]. Arterial oxygen pressure was measured in patients mechanically ventilated with fractional inspired oxygen ≥ 0.4. Hypoxia reflecting multiple organ failure which accompanied severe trauma was highly associated with a poor prognosis. Nevertheless, in that series, we did not attribute any death to hypoxia alone. Finally, age is a universally recognized factor which reflects the pejorative role of other underlying medical conditions.

Analysis of survival data suggested that patients presenting an isolated severe coma had a significantly higher risk of instantaneous death. Figure 1 shows that a shorter survival can easily be predicted only from motor scores of 1 or 2. A motor score of 3 is at the same level as scores 4 and 5. This intermediate level did not allow the clinicians to obtain an accurate calculation of prognosis. This suggests that criteria present upon arrival in the emergency room are not sufficient to get an accurate prognosis and this reflects not only the weaknesses of the model, but also the improvement due to treatment.

In daily clinical practice, use of Fig. 2a and b allows clinicians to determine patient prognosis easily. The main advantage of these multivariate analyses is the adjusted values of factor coefficients to other variables. This is the simplest way to illustrate the modelled results and can be used prospectively for the determination of prognosis in a heterogeneous population of patients.

References

1. Alberico AM, Ward JD, Choi SC, Marmarou A, Young HF (1987) Outcome after severe head injury. J Neurosurg 67:648–656
2. Dikmen S, Temkin N, McLean A, Wyler A, Machamer J (1987) Memory and head injury. J Neurosurg Psychiatry 50:1613–1618
3. Greenberg RP, Newlon PG, Hyatt MS, Narayan RK, Becker DP (1981) Prognostic implications of early multimodality evoked potentials in severely head-injured patients. A prospective study. J Neurosurg 55:227–236
4. Jennett B, Teasdale G, Braakman R, Minderhoud J, Knill-Jones R (1976) Predicting outcome in individual patients after severe head injury. Lancet I:1031–1034
5. Jennett B, Teasdale G, Braakman R, Minderkhoud J, Heiden J, Kurze T (1979) Prognosis of patients with severe head injury. Neurosurgery 4:283–289
6. Levin HS, Gary HE, Eisenberg HM, Ruff RM, Barth JT, Kreutzer J, High WM, Portman S, Foulkes MA, Jane JA, Marmarou A, Marshall LF (1990) Neurobehavioral outcome 1 year after severe head injury. Experience of the Traumatic Coma Data Bank. J Neurosurg 73:699–709
7. Levin HS, Grafman J (1987) Neurobehavioral recovery from head injury. In: Eisenberg HM (ed). Oxford University Press, New York
8. Levin HS, Williams D, Crofford MJ, High WM Jr, Eisenberg HM, Amparo EG, Guinto FC Jr, Kalisky Z, Handel SF, Godman AM (1988) Relationship of depth of brain lesions to consciousness and outcome after closed head injury. J Neurosurg 69:861–866
9. Luerssen TG, Klauber MR, Marshall LF (1988) Outcome from head injury related to patient's age. A longitudinal prospective study of adult and pediatric head injury. J Neurosurg 68:409–416
10. McLean A Jr, Dirkmen SS, Temkin NR (1993) Psychosocial recovery after head injury. Arch Phys Med Rehabil 74:1041–1046
11. Oddy M, Humphrey M, Uttley D (1978) Subjective impairment and social recovery after closed head injury. J Neurol Neurosurg Psychiatry 41:611–616
12. Van Zomeren AH, Van Den Burg W (1985) Residual complaints of patients two years after severe head injury. J Neurol Neurosurg Psychiatry 48:21–28
13. Jennett B, Bond M (1975) Assessment of outcome after severe brain damage. A practical scale. Lancet I:480–484
14. Braakman R, Gelpke GJ, Habbema JD, Mass AI, Minderhoud JM (1980) Systematic selection of prognostic features in patients with severe head injury. Neurosurgery 6:362–370
15. Choi SC, Muizelaar JP, Barnes TY, Marmarou A, Brooks DM, Young HF (1991) Prediction tree for severely head injured patients. J Neurosurg 75:251–255
16. Choi SC, Ward JD, Becker DP (1983) Chart for outcome prediction in severe head injury. J Neurosurg 59:294–297
17. Gennarilli TA, Spielman GM, Langfitt TW, Gildenberg PL, Harrington T, Jane JA, Marshall LF, Miller JD, Pitts LH (1982) Influence of the type of intracranial lesion on outcome from severe head injury: a multicenter study using a new classification system. J Neurosurg 56:26–32
18. Marshall LF, Gautille T, Klauber MR, Eisenberg HM, Jane JA, Luerssen TG, Marmarou A, Foulkes MA (1991) The outcome of severe closed head injury. J Neurosurg [Suppl] 75:28–36
19. Narayan RK, Greenberg RP, Miller JD, Enas GG, Choi SC, Kishore PR, Selhorst JB, Lutz HA, Becker DP (1981) Improved confidence of outcome prediction in severe head injury. A comparative analysis of the clinical examination, multimodality evoked potentials, CT scanning and intracranial pressure. J Neurosurg 54:751–762
20. Volmer DG, Torner JC, Jane JA, Sadovnic B, Charlebois D, Eisenberg H, Foulkes MA, Marmarou A, Marshall LF (1991) Age and outcome following traumatic coma: why do older patients fare worse? J Neurosurg 75 [Suppl]:37–49
21. Waxman K, Sundine MJ, Young RF (1991) Is early prediction of outcome in severe head injury possible? Arch Surg 126:1237–1242
22. Teasdale G, Jennett B (1974) Assessment of coma and impaired consciousness. A practical scale. Lancet II:81–84
23. Choi SC (ed) (1986) Statistical methods of discrimination and classification. Advances in theory and applications. Pergamon Press, Oxford
24. Youden WJ (1950) Index for rating diagnostic tests. Cancer 3:32–35
25. Swets JA (1988) Measuring the accuracy of diagnostic systems. Science 240: 1285–1292
26. Miller JD, Butterworth JF, Gudeman SK, Faulkner JE, Choi SC, Selhorst JB, Harbison JW, Lutz HA, Young HF, Becker DP (1981) Further experience in the management of severe head injury. J Neurosurg 54:289–299