Early Prognosis of Severe Traumatic Brain Injury in an Urban Argentinian Trauma Center

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Background: Previous studies indicate that age, Glasgow Coma Scale score (GCS), arterial hypotension, computed tomography (CT) findings, and pupillary reactivity are strong predictors of outcome for patients with severe traumatic brain injury (TBI). However, the predictive validity of these variables has never been rigorously tested in patients from the developing world. The objective of this study was to evaluate the prognostic value of these variables in a resource-limited setting and to test their predictive power by using them to create an outcome model.

Methods: The study was conducted at Hospital Emergencias "Dr. Clemente Alvarez" in Rosario, Argentina. All patients with severe TBI meeting criteria between August 2000 and February 2003 were included. Outcome at 6 months postinjury was measured by mortality and by the Extended Glasgow Outcome Scale score. Two logistic regression models were created for predicting mortality and outcome.

Results: Outcome measures were acquired for 100% of the sample (N = 148). There was 58% mortality; 30% had moderate to good recovery, and 12% were severely disabled. The model accurately predicted 83.9% of mortality, and 81.1% of outcome. Because of variation in timing of CT scans, the models were recalculated without the CT variable. The accuracy of prediction was 79.7% and 79% for mortality and Extended Glasgow Outcome Scale, respectively.

Conclusions: This study provides rigorous, prospective data that (1) validates the generalizability of the five World Health Organization/Organization Mondiale de la Santé TBI prognostic predictors outside of the developed world, and (2) provides outcome benchmarks for mortality and morbidity from severe TBI in developing countries.

Key Words: Traumatic Brain Injury, Prognosis, Argentina.

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Despite improvements in prevention and treatment, traumatic brain injury (TBI) remains one of the most frequent causes of death and disability worldwide.[1–4] Early estimation of prognosis for the patient with severe TBI is an important factor in making triage and treatment decisions and communicating with family. Rigorously defined and consistently measured prognostic indicators with demonstrated validity and reliability are critical to prognosis estimation, contributing to the internal validity of research investigations and strongly enhancing confidence in their application.[5]

In 1996, at the request of the World Health Organization/Organization Mondiale de la Santé (WHO/OMS), the authors of the Guidelines for the Management of Severe Brain Injury[6] added an evidence report on early predictors of outcome to the publication of the management guidelines. They reported that the available literature supported age, Glasgow Coma Scale (GCS) score, arterial hypotension, computed tomography (CT) findings, and pupillary reactivity as early predictors with a positive predictive value (PPV) for poor outcome of >70%. Although disseminated globally with the Guidelines for the Management of Severe Brain Injury,[6] the validity of these five early variables in predicting outcome has never been rigorously tested outside of the "developed" countries that produced the supporting literature.

Such early variables have been extensively studied (in resource-rich countries),[7–15] but the development of accurate prognostic tools for severe TBI has met with limited success. Reasons for this include (1) incompletely controlled heterogeneity in the underlying pathology and subsequent evolution of the trauma across patients; (2) differences in treatment, including prehospital management, initial resuscitation, criteria for monitoring, and rehabilitation; (3) variations in measurement indices spanning initial assessment through long-term outcomes; and (4) wide variability in the rigor of study design and data collection and analysis.[16–18]

With respect to early prognosis, initial patient assessment is often confounded by early interventions such as sedation, analgesia, neuromuscular blockade, or endotracheal intubation. Furthermore, outcomes across patients with similar initial profiles may vary with different rehabilitation treatments. Finally, decisions not to treat based upon quality of life considerations and the use of advanced directives change the distribution of characteristics of patients used to develop prognostic models in ways that may not be well described or controlled. Taken together, sophisticated analy-

sis may not be sufficient to resolve the variation introduced by such differences.

The objective of this study was to evaluate the prognostic value of the WHO/OMS set of admission variables measured in severe TBI patients in a resource-limited setting where the influence of prehospital and admission confounding factors was minimal, and to test their predictive power by using them to create an outcome model. Our goal was to create an accurate and reliable instrument for predicting outcome from TBI that physicians in Argentina, and perhaps other middle- and low-income countries, can use to make treatment decisions, guide prognosis discussions with patients and families, and conduct research.

MATERIALS AND METHODS

Setting and Subjects

Hospital Emergencias "Dr. Clemente Alvarez" (HECA) in Rosario, Argentina, is the only Level I trauma center in the State of Santa Fe, serving a population of 1,400,000 people. It has a 12-bed intensive care unit (ICU), 180 beds in the general ward, and 24-hour neurosurgery, laboratory, and radiology. Approximately 25% of the population lives at poverty level, and there is a 5% illiteracy rate. Fifty-five percent of the people are of mixed races, 40% are Caucasian, and 5% other.

Approximately 97% of patients with TBI treated at HECA arrive at the emergency department (ED) shortly after trauma without resuscitation or intubation. Thus, the GCS is assessed at hospital arrival in virtually all patients without the interference of prehospital interventions. ED and ICU treatment is performed using protocols in accordance with the Guidelines for the Management of Severe Brain Injury,[6] providing a tightly controlled research environment. In this population, all patients, except those that are brain dead on arrival, are fully treated, in contrast with other populations in which quality of life considerations may alter treatment decisions. Finally, there is currently no postdischarge TBI rehabilitation for this patient population. These factors minimize variability in the assessment of early prognostic factors for this study.

All patients admitted to the ED between August 2000 and February 2003 with indications of brain trauma were screened for eligibility for this study. Patients were eligible who met the following criteria: admitted to the ED within 24 hours of injury, diagnosis of TBI, GCS score $\leq$8 maintained during the first 24 hours, and age $\geq$12. Patients were excluded if they were sedated or intubated, had a penetrating brain injury, were brain dead on arrival, or if consent was refused.

Measures

Data describing patient characteristics, demographics, and premorbid history were collected consistent with the syllabus of the Traumatic Brain Injury Model System program funded by the National Institute on Disability and Rehabilitation Research. Predictor variables were age, GCS, pupillary response, hypotension and initial CT scan findings. GCS, arterial pressure, and pupil reactivity were obtained from the physical examination by the treating physician at hospital admission. Age was recorded in years and categorized in blocks of 10 years. Pupil reactivity was dichotomized as normal or abnormal. Pupil data were missing if swelling or direct trauma prevented examination (n = 5). Arterial hypotension was defined as the occurrence of systolic blood pressure $<$90 mm Hg on admission and recorded as either present or absent. CT scans, conducted within 24 hours of admission, were classified in two ways: (1) globally, based on the presence or absence of abnormalities, and (2) specifically, according to the presence or absence of compression of the basal cisterns, midline shift ($>$5 mm), extradural hematoma, subdural hematoma, contusion, and traumatic subarachnoid hemorrhage (TSAH). Outcome, measured at 6 months postinjury, was mortality and function using the Extended Glasgow Outcome Scale (GOS-E) score. The GOS-E was dichotomized into favorable (score of 5–8) or unfavorable (score of 1–4) outcomes.

Procedures

When a patient with a suspected TBI was admitted to the ED of HECA, the attending physician contacted the on-call study coordinator, who screened the patient for eligibility and met with family to obtain consent. All patients were treated according to the Guidelines for the Management of Severe Brain Injury.[19] Patients were asked to return to the hospital for follow-up evaluations. Study personnel conducted follow-up evaluations in the homes of patients who could not return to the hospital. All evaluations were performed by physicians who had been trained in the assessment measures specific to this study. The Institutional Review Board of Oregon Health & Science University and the Ethical Committee of HECA approved this study.

Analysis

A likelihood χ^2 test was used to evaluate the predictive power of each variable separately. Sensitivity, Specificity, positive and NPVs were also calculated, with dichotomized forms of the predictors (age $\leq$ or $>$40 years, GCS score of 3 and 4 or 5–8, pupils normal or abnormal, hypotension present or absent, and CT indications present or absent). Two logistic regression models were created, each with the five predictor variables, one predicting mortality and the other predicting 6-month GOS-E scores classified as favorable or unfavorable outcomes. For the logistic regression analyses, age and GCS were continuous variables.

The models were re-estimated removing the CT scan variables because the time at which the initial CT scan occurred was different across patients (although all within 24 hours of admission), which introduced error variance to the data. A cut-point of 0.5 was established for classification. Finally, to facilitate practical application of the model, we developed tables and a computer-based calculator that might be used to predict mortality and outcome based upon individual patient measures on the predictor variables.

RESULTS

During the study period 386 patients treated in the ED of HECA were screened for eligibility. Of those, 238 were

excluded: 177 had a GCS score of >8, 2 were brain dead on arrival, 45 had penetrating head injuries, 6 arrived more than 24 hours postinjury, 2 were not traumatic injuries, 4 recovered to a GCS score of >8 within the first 24 hours, and for 2, consent was not acquired. The entire group of excluded patients was 89% male, with an average age of 34.3 years (16.18 standard deviation [SD]).

Of the 150 patients who met the inclusion criteria, 50 died within the first 24 hours and 98 were consented and included in the study. We received permission from the Ethical Committee to include public registry data from the 50 patients who died within the first 24 hours after injury so that a total of 148 patients were included in the study. Mortality and 6-month GOS-E data were acquired for 100% of the patients involved in the study. Table 1 illustrates patient characteristics and outcomes. More than 58% of the patients died, 33.8% within the first 24 hours and 19.6% during acute care. Thirty percent achieved a relatively good recovery (GOS-E score of 5–8), and 12% remained seriously disabled at 6 months postinjury.

Table 2 shows the results of the χ^2 tests. All predictors were significantly associated with mortality and 6-month GOS-E except CT scan indications of contusion, epidural hematoma, and subarachnoid hemorrhage.

Table 3 illustrates sensitivity, specificity, PPV, and negative predictive value (NPV) for each variable. For mortality as well as unfavorable outcomes, the only variable with low predictive value was epidural hematoma CT scan findings (N = 11). The predictive value of all variables is approximately 10% stronger when predicting unfavorable outcomes than when predicting mortality.

Mortality

A multiple logistic regression model was created that correctly estimated mortality status for 85.7% of patients and that correctly estimated survival status for 81.4% (overall correct prediction of 83.9%). The five cases with missing pupil data were excluded from the analysis. The goodness of fit adjustment was not rejected (Hosmer-Lemeshow $\chi^2 = 2.563$, $p = 0.959$). Details of the regression are shown in Table 4. The variables with the strongest adjusted predictive value are age, GCS, pupillary response, hypotension, and the presence of compression or midline shift on CT findings. The estimated odds ratio shows significant increases in risk of death for each unitary change in these variables.

GOS-E

To evaluate the value of all variables for predicting 6-month GOS-E, a multiple regression model was estimated using GOS-E as a dichotomous variable (Table 5). It accurately predicted 88% of cases with unfavorable outcomes and 65.1% of cases with favorable outcomes (overall correct prediction of 81.1%). The goodness of fit adjustment was not rejected (Hosmer-Lemeshow $\chi^2 = 9.834$, $p = 0.277$). The variables with the highest predictive values are GCS, pupillary response, hypotension, and the presence of compression or contusion on CT findings. The highest risk of bad outcome is the presence of hypotension.

TABLE 1. Patient Characteristics and Outcome

Average age	34 yr [16.2 SD, 14–77 yr range]	
Male (%)	81.1	
Mechanism	Motorcycle	39.8%
	Automobile	18.4%
	Bicycle	15.3%
	Pedestrian	13.3%
	Violence	9.2%
	Falls	4.1%
GCS	3	23.6%
	4	14.9%
	5	8.8%
	6	10.8%
	7	26.4%
	8	15.5%
Pupillary response	Normal 41.9%, abnormal 54.7%, unmeasurable 3.4%	
Hypotension	19.6%	
ct scan	Cisternal compression	56.8%
	Contusion	44.6%
	Midline shift (>5 mm)	41.9%
	Epidural Hem	7.4%
	Subdural Hem	35.8%
	TSAH	64.9%
Mortality	58.8%—total	
		33.8% within first 24 h
		19.6% >24 h, during acute care
		5.4%—Postacute care, during first 6 mo
6-mo GOS-E	16.2% good recovery	
	6.8% lower good recovery	
	6.8% upper moderate disability	
	0.7% lower moderate disability	
	4.0% upper severe disability	
	6.0% lower severe disability	
	0.7% vegetative state	
	58.8% dead	
Neurosurgery (among the 98 cases surviving at least 24 h)	Removal of mass lesion only	15.3%
	Removal of mass lesion with craniectomy	18.3%
	Craniectomy only	0%
	Other neurosurgery	2%
	No neurosurgery	64.2%

Model Reestimation Without CT Scan Results

The initial CT scan was obtained at different times within the first 24 hours for different patients, which introduced measurement error to the model. In addition, early CT

TABLE 2. The Association of Individual Indicators With Mortality and 6-mo GOS-E

	Mortality			GOS-E*		
Predictive Variables	**Yes (n = 87)**	**No (n = 61)**	***P* Value†**	**Bad (n = 103)**	**Good (n = 45)**	***p* Value†**
Age by groups						
13–19	14	10	0.006	16	8	0.011
20–29	26	28		32	22	
30–39	12	9		17	4	
40–49	10	11		12	9	
50–59	10	1		10	1	
60+	15	2		16	1	
GCS						
3	33	2	0.000	33	2	0.000
4	16	6		19	3	
5	5	8		8	5	
6	8	8		10	6	
7	17	22		21	18	
8	8	15		12	11	
Initial pupil response						
Normal	20	42	0.000	30	32	0.000
Unilat.	29	17		35	11	
Bilater.	35	0		35	0	
Hypotension	26	3	0.000	28	1	0.000
CT scan abnormal	87	55	0.001	102	40	0.006
Compression	65	19	0.000	71	13	0.000
Contusion	42	24	0.282	51	15	0.066
CT scan findings						
Midline shift	50	12	0.000	53	9	0.000
Epidural H.	4	7	0.120	5	6	0.083
Subdural H.	39	14	0.006	43	10	0.020
TSAH	58	38	0.584	69	27	0.415

*Glasgow Outcome Scale Extended (GOS-E) was dichotomized as "Good Outcome" = scores 5–8, or "Bad Outcome" = scores 1–4.
†χ^2 Likelihood ratio test.

imaging is not uniformly available in developing countries. In response to these issues, two final models were estimated without CT scan indicators (Tables 6 and 7). Both maintain strong capacity for prediction. For mortality the model has an overall correct prediction of 79.7% (82.1% for death and 76.3% for survival). For GOS-E the model has an overall correct prediction of 79% (88% for bad outcomes and 58.1% for good outcomes). The tests of goodness of fit were not rejected (Homer-Lemeshow $p = 0.293$ for mortality and 0.581 for GOS-E).

DISCUSSION

This article examines the power of accepted early prognostic indicators to predict outcome in a patient population that reflects TBI in low- and middle-income countries. The majority of trauma patients in such regions arrive at hospital without field interventions. They are treated by well-informed and dedicated physicians under conditions of often severely restricted logistic and management resources. Nursing is often limited in education and relegated to performing only basic care tasks rather than acting as a part of the medical team. Ancillary support (such as respiratory and physical therapy) is marginally available, floor care is managed under crowded and understaffed conditions, and postdischarge rehabilitation is extremely rare.

These conditions differ markedly from those in developed countries. Although they are strong sources of potential confounding interaction with treatment and outcome, the status of such variables are very rarely mentioned in the Materials and Methods sections of similar articles from developed countries; the assumption being that they are comparable across all trauma centers. Without the ability to quantify and control for such influences, the generalizability (external validity) of many treatment and prognosis studies from United States and European trauma centers is unclear and, therefore, suspect. For this reason, the operational relevance of many published TBI studies from United States and European trauma centers to developing world hospitals remains questionable.

When the first set of the Guidelines for the Management of Severe Brain Injury[6] were reviewed by the WHO/OMS, they requested the addition of a section on prognosis to the text before granting their imprimatur to the document. The process of writing this evidence-based prognosis section generated a list of five variables that were found to be associated with a PPV >70% for poor outcome. This list, based on developed world literature, was then distributed globally with the Guidelines for the Management of Severe Brain Injury.[6] To date, however, there have been no rigorous, prospective outcome studies on the applicability and accuracy of these predictors to TBI occurring in low- and middle-income countries. As such, their validity for the majority of patients with TBI served by the WHO/OMS remains unclear. Addressing this validity issue with a high degree of rigor[20] is the focus of this article.

Another attractive and relevant aspect of this patient population is the absence of factors that highly confound TBI outcome studies from developed world trauma centers. Patients arrive at HECA without having been sedated, pharmacologically relaxed, or intubated. Although this is likely to contribute to the detrimental influence on outcome of secondary insults such as hypoxia and hypotension, it also allows an unimpeded initial examination of the nervous system (e.g. GCS). Additionally, ethical constraints in this population preclude decisions not to treat or to withdraw care, which eliminates the confounding influence of such decisions on outcome. As well, the absence of postdischarge rehabilitation removes the influence of another source of variability. Finally, these populations are much less mobile, which facilitated our accomplishing 100% 6-month follow-up. In aggregate, these patient and system attributes, unique to less developed countries, optimize gathering relatively uncounfounded data on outcome from TBI and increase the generalizability of our findings to other counties with limited resources.

One striking finding is the high mortality rate among those over 50 years of age. Almost 90% of patients in this age group died. Although most studies have found increased

TABLE 3. Prognostic Attributes of Predictive Variables for Mortality and 6-mo GOS-E

Mortality					Poor Outcome on GOS-E				
Variable	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**n**
Age >40 yr	0.402	0.770	0.714	0.474	0.369	0.756	0.776	0.343	148
GCS score <4	0.563	0.869	0.860	0.582	0.505	0.889	0.912	0.449	148
Pupils Abn	0.762	0.712	0.790	0.677	0.700	0.744	0.864	0.516	143
Hypotension	0.299	0.951	0.897	0.487	0.272	0.977	0.966	0.370	148
CT									
Abnormal	1.000	0.098	0.613	1.000	0.990	0.111	0.718	0.833	148
Compress	0.747	0.689	0.740	0.656	0.689	0.711	0.845	0.500	84
Contusion	0.483	0.607	0.636	0.451	0.495	0.667	0.773	0.366	66
Mid Shift	0.575	0.803	0.806	0.570	0.514	0.800	0.855	0.419	62
Epidural	0.046	0.885	0.364	0.394	0.049	0.867	0.455	0.284	11
Subdural	0.448	0.770	0.736	0.495	0.417	0.778	0.811	0.368	53
TSAH	0.667	0.377	0.604	0.442	0.670	0.400	0.712	0.346	96

TABLE 4. Logistic Regression for Mortality

					95% CI	
Predictor	**Coefficient**	**SE Coef.**	***p* Value**	**Odds Ratio**	**Lower**	**Upper**
Age	0.055	0.019	0.003	1.06	1.02	1.10
GCS	−0.383	0.162	0.018	0.68	0.50	0.94
Pupils abnormal	1.281	0.573	0.025	3.60	1.17	11.08
Hypotension	1.827	0.867	0.035	6.21	1.14	33.98
CT: compression	1.826	0.606	0.003	6.21	1.89	20.38
CT: contusion	0.841	0.541	0.120	2.32	0.80	6.70
CT: midline shift	1.819	0.723	0.012	6.17	1.50	25.42
CT: epidural H.	−0.760	0.960	0.428	0.47	0.07	3.07
CT: Subdural H.	−0.478	0.650	0.462	0.62	0.17	2.21
CT: TSAH	0.005	0.575	0.993	1.00	0.33	3.10
Constant	−2.077	1.336	0.120	—	—	—

TABLE 5. Logistic Regression for GOS-E at 6 mo

					95% CI	
Predictor	**Coefficient**	**SE Coef.**	***p* Value**	**Odds Ratio**	**Lower**	**Upper**
Age	0.038	0.018	0.037	1.04	1.00	1.08
GCS	−0.342	0.166	0.040	0.71	0.51	0.98
Pupils abnormal	1.133	0.574	0.049	3.10	1.01	9.57
Hypotension	2.400	1.155	0.038	11.03	1.15	106.07
CT: compression	1.186	0.556	0.033	3.27	1.10	9.74
CT: contusion	1.202	0.534	0.024	3.33	1.17	9.48
CT: midline shift	1.293	0.754	0.086	3.64	0.83	15.97
CT: epidural H.	−0.945	0.951	0.319	0.39	0.06	2.50
CT: Subdural H.	−0.504	0.666	0.449	0.60	0.16	2.23
CT: Subarachnoid H.	0.185	0.557	0.740	1.20	0.40	3.58
Constant	−0.594	1.31	0.649	—	—	—

TABLE 6. Logistic Regression for Mortality Without CT Findings

					95% CI	
Predictor	**Coefficient**	**SE Coef.**	***p* Value**	**Odds Ratio**	**Lower**	**Upper**
Age	0.058	0.016	0.000	1.06	1.03	1.09
GCS	−0.524	0.135	0.000	0.59	0.45	0.77
Pupils abnormal	1.796	0.476	0.000	6.02	2.37	15.30
Hypotension	1.354	0.706	0.055	3.87	0.97	15.47
Constant	0.210	0.928	0.821	—	—	—

TABLE 7. Logistic Regression for GOS-E Without CT Findings

					95% CI	
Predictor	**Coefficient**	**SE Coef.**	***p* Value**	**Odds Ratio**	**Lower**	**Upper**
Age	0.047	0.016	0.004	1.05	1.02	1.08
GCS	−0.437	0.139	0.002	0.65	0.49	0.85
Pupils abnormal	1.472	0.473	0.002	4.36	1.72	11.02
Hypotension	1.977	1.074	0.066	7.22	0.88	59.20
Constant	0.956	0.985	0.332	—	—	—

mortality in older adults, the rate here is substantially higher than reported from the developed countries. It would be interesting to see whether more severe early secondary insults play a role in the high mortality. At present, the salvageability of older patients with a severe TBI in this population appears extremely limited.

The PPV for mortality of 86% and for poor outcome of 91% for GCS score of ≤4 makes the model a valuable tool for early prognosis. This is in contrast to the situation in resource-rich countries where the inability to obtain a reliable, complete admission GCS measurement because of prehospital interventions may approach 50%,[6] which significantly diminishes the prognostic value of this scale.[21] As such, a full GCS score should be obtained in a standard fashion by trained personnel in all patients with TBI on admission in developing countries.

As is almost universally found in studies of early prognostic variables in TBI, hypotension exerts a strong influence on outcome.[15,22] What is remarkable here is the magnitude of this effect. An admission systolic blood pressure of <90 mm Hg had a 90% associated mortality and a 96% association with poor outcome. For mortality, the PPV

was 90%, with a specificity of 95%; for poor outcome, these figures were 98% and 97%, respectively. In our regression model, the odds ratio for mortality was 6.21, and for poor outcome was 11.03. As such, hypotension was the strongest determinant of outcome. Notably, it is the most amenable of these variables to treatment and the only one potentially open to prevention. In light of the glaring paucity of uniform prehospital resuscitation efforts available to these patients, these data suggest that improving care during this period should probably be the primary focus of attempts to improve outcome from TBI in this population.

Recalculating the regression model without CT data served two purposes. Although the other variables were obtained upon admission, the initial CT was performed within 24 hours, which added a measurement error to the model. Calculated without the CT data, the model more accurately reflects the time of admission. Second, although HECA has 24-hour CT availability, it is more common in many Latin American and other resource-poor countries to not have a functioning CT scanner available for immediate use at many centers that regularly receive TBI patients. Even in relatively high resource regions, there may be no scanner in house or it may regularly be nonfunctional. As such, prognostic decisions will need to be considered in the absence of such data and we considered it useful to estimate the confidence associated with a model lacking CT information. The major impact of this modification was a decrease in the power of the model to predict survival (vs. mortality) and favorable outcome (for GOS-E) without much decrement in its ability to predict death or unfavorable outcome. As such, these data should still be useful for early treatment decision-making.

This study provides rigorous, prospective data that (1) validates the generalizability of the five WHO/OMS TBI prognostic predictors outside of the developed world, and (2) provides outcome benchmarks for mortality and morbidity from severe TBI in developing countries. With respect to the former, the remarkably high correlations between these variables and outcome suggest that these five predictors not only hold under such conditions but are actually quite powerful tools for early prognosis. Even without immediate CT information, the ability to predict death or poor outcome remains quite strong.

Regarding the provision of benchmark data, it should be noted that HECA is relatively sophisticated compared with many trauma centers in resource-limited countries, with good ICU facilities, intensivists with specific interest in TBI, and hospital-wide dedication to the care of trauma. Nevertheless, the overall mortality from severe TBI in this population treated at HECA is 58.8%, which is 22% higher than similar outcomes reported from the United States in the Traumatic Coma Data Bank for patients studied between 1984 and 1987.[23] It is 16% higher than the 6-month mortality from the placebo arm of the CRASH trial which combined severe TBI patients from countries of widely varied resource availability.[24] The establishment of such baseline data from a developing country per se highlights the differences between resource-rich and resource-limited systems and suggests that studies specific to the latter population are needed to facilitate the interpretation of the TBI literature by physicians outside of the United States and Europe. It also strongly implies that solutions to problems with TBI care must ultimately be derived from data generated within the system being addressed.

Important questions remain regarding the implications of these data, including their generalizability, and the interactions of early prognostic indicators with subsequent physiologic and therapeutic variables (and how these are influenced by resource availability). The NIH has recently funded this research group, in cooperation with the Latin American Brain Injury Consortium (LABIC), to perform a prospective outcome study at seven centers in five Latin American countries (in conjunction with an RCT on ICP monitoring in 3 of those centers). It is expected that this expanded data set will facilitate the rigorous investigation of many important unanswered questions. It is already apparent that the reality of TBI care is sufficiently different in resource-limited countries to render studies from resource-rich countries minimally relevant. It is hoped that gathering data under their practicing conditions (as well as building research capacity within their medical community) will provide a framework of understanding that will facilitate efficient and effective improvement in TBI care relevant to the developing world.

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EDITORIAL COMMENT

In 1991, Marshall et al.[1] reported a mortality figure of 22% in severe traumatic brain injury (TBI) from the North American Traumatic Coma Data Bank. Severe Brain Injury Guidelines were published 5 years later.[2] Included with those guidelines were five principal predictive markers of outcome: age, Glasgow Coma Scale, arterial hypotension, pupillary reactivity, and computed tomographic findings. The developed world has accepted these predictors essentially on faith and/or experience. Ironically, their first rigorous validation actually comes from a different world. Petroni and coworkers recognizing the novelty of a nonexistent in-field trauma competence cheek-by-jowl with a first rate Trauma Center captured the perfect opportunity to prospectively validate those five outcome predictors enumerated over a decade ago. Although the Argentine trauma center is represented as equal to that of the developed countries, its in-field services are still third world.

For 3 years, although the "confounding" effects of pre- and posthospital intervention are absent, the classic TBI outcome markers were meticulously screened and tabulated with a 100% rate of follow-up. In summary, the powerful effect of age and perfusion pressure on outcome has been soberingly reconfirmed. The likelihood of a good outcome in a patient older than 40 years with severe head trauma and shocky is close to nil by the Argentine experience. The other markers are dwarfed in importance: the Glasgow Coma Scale, and pupils only identify the group in question, but computed tomography is a management tool. A study of the impact of raised intracranial pressure and the treatment effect of same is anticipated.

It is an incidental irony that the city realities of Rosario, Argentina, actually made feasible the validation of our outcome predictors. And that the striking difference in the Argentine mortality of 59% versus that of North America is consequent to the quality difference in on-scene care that would seem inescapable.

The practical implications of the grimmest predictor combination need a societal discussion beyond that of the medical community. Although the promise of quality post-trauma rehabilitation cannot be overstated, that of severe TBI is only relative and with many provisos: one can dwell on the value of "rehab" in TBI to an excess. The personal and familial anguish of chronic severe brain impairment is uniquely awful. Early "treatment" in hopes of mitigating this anguish may only beget it. The facility of aggressive, modern trauma management and the callous political facilitation of defensive medicine conspire and leave severe TBI outcome predictors at the emergency room door. There must be a place for considering "Slow Medicine"[3] for those with the worst TBI prognosis.

The importance of living wills is now generally appreciated. The debate over the place for immediate hospice-type management for any but the young having dismal TBI predictive markers is long overdue.

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