

Christian Compagnone, M.D.

Intensive Care Unit,
Bufalini Hospital,
Cesena, Italy

Domenico d'Avella, M.D.

Department of Neurosciences,
University of Padua,
Padua, Italy

Franco Servadei, M.D.

Division of Neurosurgery,
Azienda Ospedaliero-Universitaria,
Parma, Italy

Filippo F. Angileri, M.D.

Clinica Neurochirurgica,
University of Messina,
Messina, Italy

Gianluigi Brambilla, M.D.

IRCCS Policlinico S. Matteo,
Pavia, Italy

Carlo Conti, M.D.

Division of Neurosurgery,
Azienda Ospedaliera Mestre,
Mestre, Italy

Luciano Cristofori, M.D.

Department of Neurosurgery
Azienda Ospedaliera Verona,
Verona, Italy

Roberto Delfini, M.D.

Department of Neurosurgery
University of Rome La Sapienza,
Rome, Italy

Luca Denaro, M.D.

Institute of Neurosurgery,
Catholic University of Rome,
Rome, Italy

Alessandro Ducati, M.D.

Clinica Neurochirurgica,
University of Torino,
Turin, Italy

Sergio M. Gaini, M.D.

Clinica Neurochirurgica
Ospedale Policlinico IRCCS,
Milan, Italy

Roberto Stefani, M.D.

Clinica Neurochirurgica,
University of Brescia,
Brescia, Italy

Giustino Tomei, M.D.

Clinica Neurochirurgica,
Università dell'Insubria Varese,
Varese, Italy

Fernanda Tagliaferri, M.D.

Intensive Care Unit,
Bufalini Hospital,
Cesena, Italy

Giuseppe Trincia, M.D.

Division of Neurosurgery,
Azienda Ospedaliera Mestre,
Mestre, Italy

Francesco Tomasello, M.D.

Clinica Neurochirurgica,
University of Messina,
Messina, Italy

Reprint requests:

Domenico d'Avella, M.D.,
Department of Neurosciences,
University of Padova Medical School,
Via Giustiniani 2,
35128 Padova, Italy.
Email: domenico.davella@unipd.it

Received, March 25, 2008.

Accepted, October 27, 2008.

Copyright © 2009 by the
Congress of Neurological Surgeons

PATIENTS WITH MODERATE HEAD INJURY: A PROSPECTIVE MULTICENTER STUDY OF 315 PATIENTS

OBJECTIVE: To analyze the risk factors of worst outcome associated with moderate head injury.

METHODS: Data on patients with moderate head injury were collected prospectively in 11 Italian neurosurgical units over a period of 18 months. Patients older than 18 years with blunt head injury and at least one Glasgow Coma Scale (GCS) score between 9 and 13 were enrolled. The outcome was determined at 6 months using the Glasgow Outcome Scale.

RESULTS: We analyzed 315 patients. Initial computed tomographic scans showed a diffuse injury type I or II in 63%, a mass lesion in 35%, and traumatic subarachnoid hemorrhage in 42% of the patients. The risk of progression toward a mass lesion was 23% when the admission computed tomographic scan showed diffuse injury type I or II. An emergency craniotomy was performed in 22% of the patients, delayed surgery was performed in 14%, and both were performed in 25%. A favorable outcome was obtained in 74% of the patients. When the GCS score was 9 or 10, the predictor of worst outcome was a motor GCS score of 4 or lower (odds ratio [OR], 8.08; 95% confidence interval [CI], 1.22–67.35; $P = 0.008$), but when the GCS score was 11 to 13, the factors associated with worst outcome were neuroworsening (OR, 3.43; 95% CI, 1.45–8.17; $P = 0.002$), seizures (OR, 7.94; 95% CI, 1.18–64.48; $P = 0.02$), and medical complications (OR, 4.24; 95% CI, 1.74–10.33; $P = 0.0006$).

CONCLUSION: There is a high percentage of surgery and worsening on computed tomographic scans in patients with moderate head injury. Neuroworsening, seizures, and medical complications as outcome predictors were more strongly associated with a GCS score of 11 to 13, whereas a low motor GCS score was more outcome-related in patients with GCS scores of 9 and 10.

KEY WORDS: Computed tomographic scan, Moderate head injury, Neuroworsening, Outcome

Neurosurgery 64:690–697, 2009

DOI: 10.1227/01.NEU.0000340796.18738.F7

www.neurosurgery-online.com

In the literature describing clinical research on head trauma, moderate head injury remains a clinicopathological entity that has received relatively little attention. The first definition of moderate head injury was given by Rimel et al. (25) in 1982. Patients with moderate head injury were identified as those presenting with a Glasgow Coma Scale (GCS) score of 9 to 12 at admission and at 6 hours from injury. Because the cases were collected before 1982,

ABBREVIATIONS: CI, confidence interval; CT, computed tomographic; DI, diffuse injury; GCS, Glasgow Coma Scale; ICP, intracranial pressure, OR, odds ratio; tSAH, traumatic subarachnoid hemorrhage

only a minority of patients were studied with computed tomographic (CT) scanning, but as many as 30% required some sort of neurosurgical treatment. A few years later, Miller and Jones (19) showed that only 9% of patients with moderate head injury in their series had intracranial hematomas. The first article containing cases studied with CT scanning was published by Stein et al. (31) in 1993. In a series of 447 patients with a GCS score of 9 to 13, a 30% incidence of intracranial abnormalities and the need for neurosurgical intervention in 8% of the cases were demonstrated. Patients with an admission GCS score of 13 had a similar risk of intracranial hematoma than those patients with a GCS score of 9 to 12 (30). Subsequently, they

were formally included among moderate head injuries (28). Whereas there are guidelines for management of patients with severe head injuries (GCS score of 3–8) (2, 15) and for patients with mild head injuries (GCS score of 14 and 15) (7, 11), no guidelines have been published regarding management of moderate head injuries. This may be because of the lack of good evidence-based data for this group of patients.

The need for studies in which a larger number of patients are followed and analyzed led us to conduct this study. Eleven Italian neurosurgical units provided clinical, radiological, management, and outcome data on a cohort of 315 patients with moderate head injury. Although this study is not population based, it is the first multicenter prospective study providing information on clinical-radiological presentation and evaluation of prognostic factors. No similarly extensive, contemporaneous study has been published to date.

PATIENTS AND METHODS

Data on patients with moderate head injury were collected prospectively over a period of 18 months in 11 Italian neurosurgical units distributed strategically in the south, center, and north of Italy (i.e., Ancona, Brescia, Cesena, Messina, Milan, Monza, Padova, Pavia, Rome, Mestre, and Verona). The inclusion criteria were the presence of traumatic brain injury with at least one GCS score between 9 and 13 and age older than 18 years. The GCS score was determined at 3 different times: prehospital, at admission to the emergency department, and at admission to the neurosurgical unit. Different from previous studies, we considered patients with a GCS score of 13 as having moderate head injury because their risk of surgical interventions and intracranial hematomas is different from those with a GCS score of 14 or 15 (28, 29). Exclusion criteria were the presence of penetrating injuries and associated spinal cord trauma.

Data were collected either by paper forms sent by fax or mail to the coordinating center (University of Messina, Messina, Italy) or, in the large majority, by online forms. We used a modified version of the data collection form used for European Brain Injury Consortium surveys (4). The retrieved variables were as follows: age, sex, date and hour of trauma, date and hour of admission, type of trauma, use of alcohol or drugs, extracranial trauma, type of extracranial trauma, severity of extracranial trauma, GCS score (prehospital, at admission to the emergency department, and at admission to the neurosurgical unit), pupillary status, presence of hypoxia and/or arterial hypotension, aphasia, initial and worst CT scan (27) classified according to the Marshall scale (18) (type I diffuse injury [DI], intracranial abnormality not visible on CT scan; type II DI, cistern present with shift of 0–5 mm, lesion present, but not high- or mixed-density lesion > 25 cc; type III DI, cistern compressed or absent, shift of 0–5 mm, not high- or mixed-density lesion > 25 cc; type IV DI, shift of > 5 mm, not high- or mixed-density lesion > 25 cc; evacuated mass lesion [any lesion surgically evacuated]; non-evacuated mass lesion [high- or mixed-density lesion > 25 cc, not surgically evacuated]), emergency (within 24 h from injury) surgery, type of neurointensive monitoring (i.e., jugular venous oxygen saturation, arterial pressure, intracranial pressure [ICP], and presence of mechanical ventilation), complications such as meningitis, delayed hematoma evacuated after 24 hours from injury, rate of elevated ICP (elevated pressure was defined as an ICP higher than 20 mm Hg sustained for at least 10 minutes) (15), neuroworsening and presence of medical complications (e.g., respiratory, cardiovascular, and infective), and date and cause of death.

Worst CT scan was defined as that in which the midline shift, the cistern compression, and/or the focal parenchymal lesions were greater than at admission (27). The appearance of a higher Marshall CT category on the follow-up CT scan in comparison with that on the initial CT scan was considered a significant CT progression. The change from DI type I to IV to evacuated mass lesion or nonevacuated mass lesion was considered a progression toward a mass lesion (3). We have considered complete CT scan information, when it was available, the Marshall description of the first and worst CT scans for the same patient. Neuroworsening was defined according to Morris et al. (20) as a reduction in the total GCS score of at least 2 points or more than 1 point in the motor GCS score and alteration of pupil size and/or pupil reaction to light. The outcome was determined at 6 months from injury using the Glasgow Outcome Scale (12). For statistical reasons, the Glasgow Outcome Scale was dichotomized into favorable (moderate disability and good recovery) and unfavorable (dead, persistent vegetative state, severe disability) results.

Statistical Analysis

Categorical data were tabulated and data variables were summarized using median and interquartile range. Continuous variables were summarized using mean and standard deviation. Univariate (χ^2 test or *t* test as appropriate) and stepwise forward multivariate logistic regression analyses were used. The odds ratios (ORs), together with their 95% confidence intervals (CIs), were also derived. Statistical analyses were performed using the SAS statistical package (Version 9.1; SAS Institute, Inc., Cary, NC). *P* values of less than 0.05 were considered statistically significant.

RESULTS

We analyzed 315 patients with moderate head injury (Table 1). The cohort mean age was 46.9 ± 26.7 years (range, 18–91 years). Two hundred nineteen of the patients (72%) were men. The prehospital median GCS score was 12 (interquartile range, 11–13). Thirty-eight patients had a prehospital GCS score of 14 to 15 with subsequent deterioration at hospital arrival. Two hundred sixty-four patients had a first GCS score of 9 to 13 and were stable at hospital arrival. Only one patient with a GCS score of 13 at the scene improved. In 12 patients, the GCS score at the scene was incomplete but the GCS score at arrival to the hospital was 9 to 13. The most frequent cause of trauma was road traffic accident (54%). Drug or alcohol abuse was present in 8% of the patients. Major trauma at 1 or more other body sites was found in 64 of the cases (21%). Initial CT scan (Table 2) showed a type I or II DI in 192 cases (63%) and a mass lesion in 106 cases (35%). Traumatic subarachnoid hemorrhage (tSAH) was present at admission in 41.9% of the patients.

One hundred eighty-two patients (59%) had complete information regarding CT scan time evolution. In this cohort, the risk of progression toward a mass lesion was 30 of 132 (22.7%) in the event of an admission CT scan with type I or II DI.

An emergency craniotomy (within 24 hours of injury) was performed in 68 of 305 patients (22.3%) and delayed surgery was necessary in 44 patients (14.4%) (Table 3). Both procedures were performed in 18 of 68 of the patients (25%). As a sign of trauma severity, we also recorded mechanical ventilation in 59 of 306 patients (19.3%), invasive monitoring of arterial blood

TABLE 1. Demographic data^a

	Value (%)
No. of patients	315
Age ^b	
Mean ± SD (y)	46.9 ± 23.7
Range (y)	1–91
IQR range (y)	25–68
Male	219/305 (71.8)
Prehospital total GCS score	
Median	12
Range	9–15
IQR	11–13
Meningitis	1/305 (0.3)
Type of trauma	305/315
RTA	166 (54.4)
Work	27 (8.8)
Assault	3 (1)
Domestic incident	56 (18.4)
Others	53 (17.3)
Alcohol or drugs	19/260 (7.3)
Associated major trauma	64/315 (21)
Hemiplegia	28/305 (9.2)
Aphasia	15/304 (4.9)
Hypoxia (documented or suspected)	5/305 (1.6)
Hypotension (documented or suspected)	6/304 (2)

^a SD, standard deviation; IQR, interquartile range; GCS, Glasgow Coma Scale; RTA, road traffic accident.

^b Age data were available for 304 of 315 patients.

pressure in 58 of 306 patients (18.9%), and ICP monitoring in 26 of 305 patients (8.5%).

Data regarding 6-month outcome according to the Glasgow Outcome Scale were obtained in 249 patients. A favorable outcome (good recovery and moderate disability) was reached in 73.9% of the cases, and 62% (183/296) of the patients were discharged to home directly from the first hospital. In Table 4, we have compared the initial GCS score and outcome. It is to be noted that the mortality rate does not differ between initial GCS scores but, as expected, the rate of favorable outcome increases sharply from a GCS score of 9 to a GCS score of 13. Of a total of 51 deaths (20.5%), only 16 patients died during the hospital stay. In this subgroup of patients, the mean age was 76.1 ± 8.4 years and the main cause of death was the occurrence of medical complications (9/16).

Age, prehospital motor GCS score less than or equal to 4 (OR, 3.92; 95% CI, 1.01–15.54; *P* = 0.03), tSAH (OR, 1.80; 95% CI, 0.97–3.35; *P* = 0.046), medical complications (OR, 3.16; 95% CI, 1.51–6.63; *P* = 0.0018), neuroworsening (OR, 3.24; 95% CI, 1.65–6.39; *P* = 0.0004), and presence of delayed hematoma (OR, 2.36; 95% CI, 1.11–5.02; *P* = 0.019) were identified as prognostic

TABLE 2. Computed tomographic scan data^a

	No. (%)
Initial CT scans	304/315
Type I DI	56 (18.4)
Type II DI	136 (44.7)
Type III DI	4 (1.3)
Type IV DI	2 (0.6)
EML	39 (12.8)
NEML	67 (22)
Subarachnoid hemorrhage	127/303 (41.9)
Intraventricular hemorrhage	9/305 (2.9)
Fracture	263/315
Linear	75 (28.5)
Basal	41 (15.6)
Depressed	6 (2.3)
Worst CT scans	186/315 (60)
Without changes	74 (39.8)
Type I DI	10 (8.9)
Type II DI	33 (29.5)
Type III DI	1 (0.9)
Type IV DI	4 (3.6)
EML	30 (26.8)
NEML	34 (30.3)

^a CT, computed tomographic; DI, diffuse injury; EML, evacuated mass lesion; NEML, nonevacuated mass lesion.

TABLE 3. Intracranial monitoring, clinical evolution, and type of surgery^a

	No. (%)
ICP	23/305 (7.5)
ICP increased	9/23 (39.1)
Mechanical ventilation	59/306 (19.3)
Invasive arterial pressure	58/306 (18.9)
Jugular venous oxygen saturation	15/306 (4.9)
Extracranial surgery	35/304 (11.5)
Craniotomy within 24 h	68/305 (22.3)
Delayed hematoma	44/306 (14.4)
Neuroworsening	73/261 (28)

^a ICP, intracranial pressure.

factors related to unfavorable outcome (Table 5). Medical complications were, as expected, more frequent in older patients (mean age of patients with medical complications, 64 years; mean age of patients without medical complications, 44 years; *P* = 0.0001). In the multivariate analysis, the only variables with significant statistical association with worst outcome were age

TABLE 4. Initial Glasgow Coma Scale score and outcome^a

	GR (%)	MD (%)	PVS (%)	SD (%)	Dead (%)
GCS score of 9 (20/24)	10/20 (50)	2/20 (10)	1/20 (5)	3/20 (15)	4/20 (20)
GCS score of 10 (36/40)	23/36 (63.9)	2/36 (5.6)	3/36 (8.3)	1/36 (2.8)	7/36 (19.4)
GCS score of 11 (42/58)	30/42 (71.5)	2/42 (4.8)	1/42 (2.4)	1/42 (2.4)	8/42 (19.1)
GCS score of 12 (57/71)	43/57 (75.5)	0/57	1/57 (1.8)	1/57 (1.8)	12/57 (21.1)
GCS score of 13 ^b (82/110)	65/82 (79.3)	1/82 (1.2)	1/82 (1.2)	0/82	15/82 (18.3)

^a GR, good recovery; MD, moderate disability; PVS, persistent vegetative state; SD, severe disability; GCS, Glasgow Coma Scale.

^b Patients with GCS scores of 14 or 15 at admission and subsequent neuroworsening (38/110 [34%]) are included in this category. Outcome for patients with a GCS score of 14 or 15: GR, 28; dead, 4; missing, 6.

TABLE 5. Prognostic factors related to outcome^a

	Poor (%)	Good (%)	Univariate <i>P</i> value	OR (95% CI)	Multivariate <i>P</i> value
Age ^b	58.2 ± 24.7	43.9 ± 22.5	≤0.0001		0.0069
Male sex	39/61 (63.9)	127/178 (71.3)	0.33	0.71 (0.37–1.38)	
Alcohol	2/47 (4.26)	11/178 (6.18)	1.00	0.67 (0.10–3.4)	
Associated major trauma	15/61 (24.6)	38/178 (21.3)	0.59	1.20 (0.57–2.50)	
Prehospital motor GCS score ≤ 4 ^b	6/59 (11.2)	5/178 (2.8)	0.03	3.92 (1.01–15.54)	0.041
Nonreactive pupils	4/61 (6.6)	12/178 (6.7)	1.00	0.97 (0.25–3.42)	
At least 1 nonreactive pupil	6/60 (10)	20/178 (11.2)	0.79	0.88 (0.30–2.47)	
Hypoxia	1/61 (1.64)	3/178 (1.69)	1.00	0.97 (0.18–35)	
Arterial hypotension	2/61 (3.28)	2/178 (1.18)	0.27	2.98 (0.29–30.42)	
tSAH ^b	35/63 (55.6)	73/178 (40.8)	0.046	1.80 (0.97–3.35)	
Intraventricular hemorrhage	2/61 (3.28)	5/178 (2.81)	1.00	1.17 (0.15–7.07)	
Fracture	24/47 (51.1)	82/178 (46.1)	0.68	1.15 (0.57–2.29)	
Extracranial surgery	7/59 (11.9)	20/177 (11.3)	0.90	1.06 (0.38–2.83)	
Medical secondary events ^b	20/64 (31.3)	23/183 (12.6)	0.0018	3.16 (1.51–6.63)	
Neuroworsening ^b	29/53 (54.7)	50/184 (27.2)	0.0004	3.24 (1.65–6.39)	
Seizures	5/64 (7.81)	6/184 (3.26)	0.15	2.51 (0.64–9.75)	
Delayed hematoma ^b	17/65 (26.2)	24/184 (13)	0.0193	2.36 (1.11–5.02)	0.034
Significant progression	12/43 (27.9)	17/110 (15.5)	0.11	2.12 (0.84–5.33)	
Prehospital neuroworsening	13/58 (22.4)	50/178 (28.1)	0.49	0.74 (0.35–1.56)	

^a OR, odds ratio; CI, confidence interval; GCS, Glasgow Coma Scale; tSAH, traumatic subarachnoid hemorrhage.

^b Prognostic factors related to unfavorable outcome.

(*P* = 0.0069), prehospital motor GCS score of 4 or less (*P* = 0.04), and the presence of delayed hematoma (*P* = 0.034).

Identification of 2 Different Groups

For the purpose of data analysis, patients were divided into 2 groups according to their level of consciousness at admission. All the patients with a prehospital GCS score of 9 or 10 were included in the first group, and those patients with a prehospital GCS score between 11 and 13 were included in the second group. Significant differences were found in the rate of associated major trauma (31.2% in those with a GCS score of 9 or 10 versus 18.4% in those with a GCS score of 11–13; *P* = 0.037) and

the presence of prehospital neuroworsening (7.8% versus 29.2%; *P* = 0.0002). If all patients who died are excluded from the analysis, the incidence of unfavorable outcome is higher in the first group (17.8% versus 3.4%; *P* = 0.002). Older age was a predictor of worst outcome in both groups (poor outcome, 54.9 ± 27.3 versus good outcome, 40.4 ± 22.1, *P* ≤ 0.025; and poor outcome, 59.8 ± 23.6 versus good outcome, 45.1 ± 22.7, *P* = 0.0004, respectively, for the first and second groups). However, although in the first group of patients (GCS score of 9 or 10) the motor GCS score less than or equal to 4 (OR, 8.08; 95% CI, 1.22–67.35; *P* = 0.008) was a predictive factor of worst outcome, in the second group (GCS score of 11–13), the pres-

ence of neuroworsening (OR, 3.43; 95% CI, 1.45–8.17; $P = 0.002$), seizures (OR, 7.94; 95% CI, 1.18–64.48; $P = 0.02$), and medical complications (OR, 4.24; 95% CI, 1.74–10.33; $P = 0.0006$) were associated with worst outcome. The presence of tSAH was associated with bad outcome (OR, 3.81; 95% CI, 0.98–15.64; $P = 0.055$) in the group with lower GCS scores.

DISCUSSION

Data on patients with moderate head injury were usually reported together with data on patients with severe head injury (34). In a European Brain Injury Consortium report (21), the overlap between these two categories was such that it was necessary to create an intermediate category that contained patients with 2 different GCS recordings at 2 different times: one between 3 and 8 and another between 9 and 12. This category represented as much as 18% of all the cases, and it was larger than the category of pure moderate head injury (16%). In other reports (10, 17), this group of patients was not identified, raising the doubt that whenever we incorporate data on severe and moderate head injury, there are intermediate patients who are assigned randomly to 1 of the 2 categories. The key point is when to assign a patient to a given severity category. For years, we have classified the patient's severity based on the poststabilization GCS score at admission. With the improvement of prehospital care, an accurate GCS assessment on arrival is not always possible. It has been shown recently that whereas the correlation between age and prognosis remains stable, the correlation between GCS score at admission and outcome was lost in recent years (1); this was probably attributable to a too-severe evaluation of traumatic brain injury patients, who are often sedated at the scene (32). Therefore, clinical researchers have used a combination of prehospital and admission assessments to include patients in clinical trials (16, 27). We have also used the same criterion, but this may affect the comparison with previous studies where only GCS score at admission was used (5).

Other significant clinical and epidemiological differences between our patients and those from previously published studies were older age (mean age, 47 years compared with a mean age never exceeding 39 years) (5, 25, 35, 36), a lower percentage of patients admitted under the influence of alcohol (7% versus 34% or even 67%) (25, 35), and a higher proportion of patients with a mass lesion on admission CT scan (35% versus 14%) as reported by Fearnside and McDougall (5). This could be attributable to a policy of centralizing patients with abnormal CT scans to neurosurgical centers (26). Therefore, it is not surprising that the mortality observed in this study (at 6 months) is 20.5%, which is higher than other published series, where the mortality range was between 15% and 20% (21, 24, 35). The in-hospital mortality in our study is relatively low. Of 51 deaths, only 16 occurred during the hospital stay.

Another difference with previous published studies on moderate head injury is the lower percentage in our cohort of mechanically ventilated patients (19.3% versus 96%), as reported by Vitaz et al. (36). These data do not contradict the

previously cited observation about the severity level of the studied population but merely represents a different policy of emergency medical service personnel to routinely intubate patients with GCS scores less than 8.

High Risk of Evolution from the Initial CT Scan

We have learned in recent years that a significant proportion of patients with moderate, severe, and even mild head injuries can exhibit a clinical-radiological evolving course (up to 50% in the first posttraumatic hours according to Oertel et al. [23]). Data based on severe and moderate patients collected by the European Brain Injury Consortium show an evolution from a type I and type II DI to a mass lesion in 13% of cases (27).

In recent series of tSAH patients, the highest percentage of significant lesion evolution (44%) was observed in patients with moderate head injury (3). In unselected (tSAH and non-tSAH) multicenter series of patients with moderate head injury, 1 patient of 4.5 presented a CT scan evolution from a diffuse injury to mass lesion, confirming the high risk of lesion progression in this population (4). These findings are also confirmed by the high rate (almost 15%) of delayed surgical intervention based on the increasing number of lesions judged as "not surgical" at admission and also on the occurrence of neuroworsening in 73 patients (28%).

Our data are in favor of moderate traumatic brain injury centralization, with the unique exception of patients with a normal CT scan at admission in whom the risk of development of intracranial lesions is extremely low (14, 27). Clinical and radiological worsening can then be detected in units where the surgical treatment can be promptly organized.

Identification of the 2 Subpopulations

As already reported, there is scarce evidence that patients with moderate head injury can be considered as a homogeneous group. It seems that they are identified as "the patients between severe and mild head injuries." According to the determinants of outcome (9), we arbitrarily divided our patients into 2 groups: moderate to severe injury (GCS score of 9–10) and the moderate to mild injury (GCS score of 11–13). Older age, a known factor for worst outcome (6, 33), was related to bad outcome in both groups. In patients with moderate to severe injury, the outcome prediction was based on the motor GCS score (Table 6). The motor component of the GCS has proved to be even superior to the entire GCS for outcome prediction only in severe and lower moderate injury patients where the verbal component of the GCS is not testable (8).

In patients with mild to moderate injury (GCS score of 11–13), the outcome was related to the presence of clinical deterioration (neuroworsening), seizures, and medical complications. The occurrence of clinical deterioration (neuroworsening) was strongly related to bad outcome (20). In our cohort, 73 patients (28%) presented a clinical deterioration during their hospital stay. The presence of this neuroworsening was extremely important for surgical indications. In fact, almost all patients with an evacuated delayed hematoma also presented a neuroworsening (42/44 [95%]). This again reinforces the con-

TABLE 6. Significant factors predicting outcomes in patients admitted with Glasgow Coma Scale scores of 9 to 10 and 11 to 13^a

	Unfavorable outcome (%)	Favorable outcome (%)	P value	OR (95% CI)
GCS 9–10				
tSAH	13/18 (72.2)	15/37 (40.5)	0.055	3.81 (0.98–15.64)
Motor prehospital GCS score < 5	6/19 (31.6)	2/37 (5.4)	0.008	8.08 (1.22–67.35)
Age (y)	54.9 ± 27.3	40.4 ± 22.1	0.025	
GCS 11–13				
Seizures	4/39 (10.3)	2/141 (2.1)	0.02	7.94 (1.18–65.48)
Neuroworsening	17/32 (53.1)	35/141 (24.8)	0.002	3.43 (1.45–8.17)
Secondary medical events	15/39 (38.5)	18/140 (12.9)	0.0006	4.24 (1.74–10.33)
Age (y)	59.8 ± 23.6	45.1 ± 22.7	0.0004	

^a OR, odds ratio; CI, confidence interval; GCS, Glasgow Coma Scale; tSAH, traumatic subarachnoid hemorrhage.

cept of the current practice of “waiting for clinical deterioration” before operating on patients not in a comatose state. A recently published article (4) reached the same conclusion: particularly in brain contusions, the presence of clinical and/or radiological deterioration plays an important role in deciding in favor of surgical evacuation. The delayed surgery group had a 41% rate of unfavorable outcome and the immediate surgery group had a 31% rate without significant differences in age, motor GCS score, or pupils. The design of our study does not allow us to determine whether early surgical evacuation before neuroworsening could lead to a better outcome.

CONCLUSION

This study reveals a high percentage of surgery and worsening of the CT scan in patients with moderate head injury, highlighting the need for strict clinical-radiological monitoring in these types of patients. In this cohort, neuroworsening, seizures, and medical complications as outcome predictors were more strongly associated with GCS scores of 11 to 13, whereas low motor GCS score was more outcome-related in patients with GCS scores of 9 and 10.

Study Limitation

We had a 21% rate of missing data for the outcome at 6 months. This rate is not different from the data of other multicenter studies (between 9% and 18%) (13, 22). Whereas the rate of missing data was 4% for the first CT scan, the rate for the worst CT scan (follow-up CT scan) was higher (40%). However, these data were used only to show the risk of evolution from type I and type II DI to a mass lesion in the subset of patients for whom we had the information.

Disclosures

This work was supported in part by grant PRIN1999 from the Italian Ministry of University and Research to Francesco Tomasello, M.D. The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

- Balestreri M, Czosnyka M, Chatfield DA, Steiner LA, Schmidt EA, Smielewski P, Matta B, Pickard JD: Predictive value of Glasgow Coma Scale after brain trauma: change in trend over the past ten years. *J Neurol Neurosurg Psychiatry* 75:161–162, 2004.
- Bullock R, Chesnut RM, Clifton G, Ghajar J, Marion DW, Narayan RK, Newell DW, Pitts LH, Rosner MJ, Wilberger JW: Guidelines for the management of severe head injury. Brain Trauma Foundation. *Eur J Emerg Med* 3:109–127, 1996.
- Chieregato A, Fainardi E, Morselli-Labate AM, Antonelli V, Compagnone C, Targa L, Kraus J, Servadei F: Factors associated with neurological outcome and lesion progression in traumatic subarachnoid hemorrhage patients. *Neurosurgery* 56:671–680, 2005.
- Compagnone C, Murray GD, Teasdale GM, Maas AI, Esposito D, Princi P, D’Avella D, Servadei F: The management of patients with intradural post-traumatic mass lesions: a multicenter survey of current approaches to surgical management in 729 patients coordinated by the European Brain Injury Consortium. *Neurosurgery* 57:1183–1192, 2005.
- Fearnside M, McDougall P: Moderate head injury: A system of neurotrauma care. *Aust N Z J Surg* 68:58–64, 1998.
- Flaada JT, Leibson CL, Mandrekar JN, Diehl N, Perkins PK, Brown AW, Malec JF: Relative risk of mortality after traumatic brain injury: a population-based study of the role of age and injury severity. *J Neurotrauma* 24:435–445, 2007.
- Gómez PA, Lobato RD, Ortega JM, De La Cruz J: Mild head injury: differences in prognosis among patients with a Glasgow Coma Scale score of 13 to 15 and analysis of factors associated with abnormal CT findings. *Br J Neurosurg* 10:453–460, 1996.
- Healey C, Osler TM, Rogers FB, Healey MA, Glance LG, Kilgo PD, Shackford SR, Meredith JW: Improving the Glasgow Coma Scale score: motor score alone is a better predictor. *J Trauma* 54:671–680, 2003.
- Hukkelhoven CW, Steyerberg EW, Habbema JD, Farace E, Marmarou A, Murray GD, Marshall LF, Maas AI: Predicting outcome after traumatic brain injury: Development and validation of a prognostic score based on admission characteristics. *J Neurotrauma* 22:1025–1039, 2005.
- Hukkelhoven CW, Steyerberg EW, Habbema JD, Maas AI: Admission of patients with severe and moderate traumatic brain injury to specialized ICU facilities: A search for triage criteria. *Intensive Care Med* 31:799–806, 2005.
- Ingebrigtsen T, Romner B, Kock-Jensen C: Scandinavian guidelines for initial management of minimal, mild, and moderate head injuries. The Scandinavian Neurotrauma Committee. *J Trauma* 48:760–766, 2000.
- Jennett B, Bond M: Assessment of outcome after severe brain damage. *Lancet* 1:480–484, 1975.
- Livingston DH, Lavery RF, Mosenthal AC, Knudson MM, Lee S, Morabito D, Manley GT, Nathens A, Jurkovich G, Hoyt DB, Coimbra R: Recovery at one

- year following isolated traumatic brain injury: A Western Trauma Association prospective multicenter trial. *J Trauma* 59:1298–1304, 2005.
14. Lobato RD, Sarabia R, Rivas JJ, Cordobes F, Castro S, Muñoz MJ, Cabrera A, Barcena A, Lamas E: Normal computerized tomography scans in severe head injury. Prognostic and clinical management implications. *J Neurosurg* 65:784–789, 1986.
 15. Maas AI, Dearden M, Teasdale GM, Braakman R, Cohadon F, Iannotti F, Karimi A, Lapiere F, Murray G, Ohman J, Persson L, Servadei F, Stocchetti N, Unterberg A: EBIC-guidelines for management of severe head injury in adults. European Brain Injury Consortium. *Acta Neurochir (Wien)* 139:286–294, 1997.
 16. Maas AI, Murray G, Henney H 3rd, Kassem N, Legrand V, Mangelus M, Muizelaar JP, Stocchetti N, Knoller N: Efficacy and safety of dexanabol in severe traumatic brain injury: results of a phase III randomised, placebo-controlled, clinical trial. *Lancet Neurol* 5:38–45, 2006.
 17. Marshall LF, Maas AI, Marshall SB, Bricolo A, Fearnside M, Iannotti F, Klauber MR, Lagarrigue J, Lobato R, Persson L, Pickard JD, Piek J, Servadei F, Wellis GN, Morris GF, Means ED, Musch B: A multicenter trial on the efficacy of using tirilazad mesylate in cases of head injury. *J Neurosurg* 89:519–525, 1998.
 18. Marshall LF, Marshall SB, Klauber MR, Van Berkum Clark M, Eisenberg H, Jane JA, Luerssen TG, Marmarou A, Foulkes MA: A new classification of head injury based on computerized tomography. *J Neurosurg* 75 [Suppl]:S14–S22, 1991.
 19. Miller JD, Jones PA: The work of a regional head injury service. *Lancet* 1:1141–1144, 1985.
 20. Morris GF, Juul N, Marshall SB, Benedict B, Marshall LF: Neurological deterioration as a potential alternative endpoint in human clinical trials of experimental pharmacological agents for treatment of severe traumatic brain injuries. Executive Committee of the International Selfotel Trial. *Neurosurgery* 43:1369–1374, 1998.
 21. Murray GD, Teasdale GM, Braakman R, Cohadon F, Dearden M, Iannotti F, Karimi A, Lapiere F, Maas A, Ohman J, Persson L, Servadei F, Stocchetti N, Trojanowski T, Unterberg A: The European Brain Injury Consortium survey of head injuries. *Acta Neurochir (Wien)* 141:223–236, 1999.
 22. Myburgh J, Cooper DJ, Finfer S, Bellomo R, Norton R, Bishop N, Kai Lo S, Vallance S: Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med* 357:874–884, 2007.
 23. Oertel M, Kelly DF, McArthur D, Boscardin WJ, Glenn TC, Lee JH, Gravori T, Obukhov D, McBride DQ, Martin NA: Progressive hemorrhage after head trauma: predictors and consequences of the evolving injury. *J Neurosurg* 96:109–116, 2002.
 24. Pentland B, Hutton LS, Jones PA: Late mortality after head injury. *J Neurol Neurosurg Psychiatry* 76:395–400, 2005.
 25. Rimel RW, Giordani B, Barth JT, Jane JA: Moderate head injury: completing the clinical spectrum of brain trauma. *Neurosurgery* 11:344–351, 1982.
 26. Servadei F, Antonelli V, Mastrilli A, Cultrera F, Giuffrida M, Staffa G: Integration of image transmission into a protocol for head injury management: a preliminary report. *Br J Neurosurg* 16:36–42, 2002.
 27. Servadei F, Murray GD, Penny K, Teasdale GM, Dearden M, Iannotti F, Lapiere F, Maas AJ, Karimi A, Ohman J, Persson L, Stocchetti N, Trojanowski T, Unterberg A: The value of the “worst” computed tomographic scan in clinical studies of moderate and severe head injury. European Brain Injury Consortium. *Neurosurgery* 46:70–77, 2000.
 28. Servadei F, Teasdale G, Merry G: Defining acute mild head injury in adults: a proposal based on prognostic factors, diagnosis, and management. *J Neurotrauma* 18:657–664, 2001.
 29. Stein SC, Ross SE: Moderate head injury: a guide to initial management. *J Neurosurg* 77:562–564, 1992.
 30. Stein SC, Spettell C, Young G, Ross SE: Delayed and progressive brain injury in closed-head trauma: radiological demonstration. *Neurosurgery* 32:25–31, 1993.
 31. Stein SC, Spettell C, Young G, Ross SE: Limitations of neurological assessment in mild head injury. *Brain Inj* 7:425–430, 1993.
 32. Stocchetti N, Pagan F, Calappi E, Canavesi K, Beretta L, Citerio G, Cormio M, Colombo A: Inaccurate early assessment of neurological severity in head injury. *J Neurotrauma* 21:1131–1140, 2004.
 33. Susman M, DiRusso SM, Sullivan T, Risucci D, Nealon P, Cuff S, Haider A, Benzil D: Traumatic brain injury in the elderly: Increased mortality and worse functional outcome at discharge despite lower injury severity. *J Trauma* 53:219–224, 2002.
 34. Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus J: A systematic review of brain injury epidemiology in Europe. *Acta Neurochir (Wien)* 148:255–268, 2006.
 35. Thornhill S, Teasdale GM, Murray GD, McEwen J, Roy CW, Penny KI: Disability in young people and adults one year after head injury: prospective cohort study. *BMJ* 320:1631–1635, 2000.
 36. Vitaz TW, Jenks J, Raque GH, Shields CB: Outcome following moderate traumatic brain injury. *Surg Neurol* 60:285–291, 2003.

Acknowledgment

We thank Valerio Gerunda for excellent technical support.

COMMENTS

Moderate traumatic brain injury (TBI) has not received the clinical or basic research attention that severe TBI and, more recently, minor TBI have generated. This study is thus an important contribution by a respected group of TBI investigators.

That almost 25% of these patients required surgery is important to know in guiding the need for appropriate neurological monitoring and setting a lower threshold for repeat computed tomographic (CT) scanning. Additionally, the identification of specific risk factors in patients with Glasgow Coma Scale (GCS) scores of 9 or 10 versus 11 to 13 may allow us to more intensively monitor such patients prospectively.

Although the authors acknowledge the limitations caused by missing data in this study, one must maintain some degree of caution about the generalizability of these findings when full CT data to access evolutionary changes were unavailable in 40% of the patients and outcome data were missing in 20%.

Jack E. Wilberger
Pittsburgh, Pennsylvania

Compagnone et al. report their experience with 315 patients with moderate TBI collected prospectively at 11 Italian centers over an 18-month period. This is a group that, to my knowledge, has not been the focus of other reports, and therefore, this study has value. The authors emphasize that this is a group that requires rigorous management and in whom the outcome is not always favorable. Thirty-five percent of these patients had mass lesions greater than 25 mL, 22% required emergency surgical operations, and 20% died, although most of the deaths were after the period of acute hospitalization and resulted from medical causes. This was in spite of including patients with GCS scores of 13, according to the recommendations of Stein and Ross (1), although these guidelines are not universally followed. Also, the outcomes in this cohort may have been affected by patient age (mean, 47 years), which was much higher than in most TBI studies.

Howard M. Eisenberg
Baltimore, Maryland

-
1. Stein SC, Ross SE: Moderate head injury: A guide to initial management. *J Neurosurg* 77:562–564, 1992.

Compagnone et al. have presented a very important article on moderate head injury. One has to recognize that neurosurgical units in Italy serve as referral sources and usually review the scans of patients who are going to be transferred by teleradiology. Therefore, the num-

ber of patients who required a craniotomy is substantially higher than one might see in a similar study in the United States, where patients tend to be taken to a hospital with neurosurgeons, particularly in urban areas, rather than to a "district hospital." Nevertheless, the data are important and of substantial interest. The demonstration that poor outcomes in the group with higher GCS scores (11–13) were attributable to neuroworsening is not surprising, but it indicates that patients—particularly those with contusions or intracerebral hemorrhage on the initial scan—need to be carefully watched for blossoming; the same is true for patients with epidural hemorrhages.

The article is also important in that it outlines a substantial need for a high level of vigilance in this group of patients. These patients are often older than the usual cohort with severe head injuries and, in the United States, these cases are often associated with falls, which in turn have a much higher incidence of intracranial hemorrhages than do motor vehicle accidents.

Of considerable interest also is the fact that the authors have included patients with a GCS score of 13 in the moderately injured category. This change is, in my view, completely appropriate, because these patients do not behave like patients with a GCS score of 14 or 15 with regard to their clinical course and, from a structural basis, their condition often deteriorates from what is seen on the initial CT scan.

What is also of interest in this study is the fact that we have the inclusion of the initial CT scan and the subsequent CT scan, which has not previously been reported in this cohort of patients. Not surprisingly, of the 16 patients who died during their hospital stay, the mean age was 76 years; the majority died of medical complications.

It is particularly important for neurosurgeons to note that deterioration was the most powerful predictor of poor outcome. This means, therefore, that patients should be managed in a unit with a high degree of vigilance and that orders should be written that the pupils be checked at a minimum of once per hour. In addition, the study strongly suggests that rescanning orders should be written in each case, even if the first scan is quite benign. This will avoid having patients deteriorate to a point where their neurological function cannot be restored because of the blossoming of the hematoma or the occasional development of diffuse brain swelling. In summary, this is an important comprehensive review of a prospectively collected series of moderate head injury that provides very useful information to neurosurgeons involved in the care of the head-injured patient.

Lawrence F. Marshall
San Diego, California

This is an extremely important addition to the literature on the moderately head-injured patient. The study includes 315 patients from 11 different neurosurgical centers and was analyzed according to patient age, GCS score, and radiological findings at the time of admission and subsequent studies. Although guidelines exist for the management of the severely head-injured patient and also for the mildly head-injured patient, the moderately head-injured patient has not been studied in depth until now.

Several important conclusions can be drawn from this study, including the need for close monitoring of the moderately head-injured

patient. In the era of regionalization of neurotrauma care, the transport of patients with severe TBI to regionalized trauma centers is well accepted. This article shows us that moderately injured patients also have a fairly high incidence of progression both clinically and radiologically. The fact that approximately 37% of the patients required a surgical procedure indicates that the moderate head injury also should be considered for transfer to regional trauma care centers with neurosurgical capabilities and such patients also should be monitored in critical care areas familiar with the management of head-injured patients.

Several interesting divisions and observations have been made in this study, including the breakdown of moderately injured patients into the moderate/severe group (GCS score, 9 or 10) and the moderate/mild group (GCS score, 11–13). In the first group, older age and the motor component of the GCS seemed to be the most important predictive factors, whereas in the second group, the outcome was related to the presence of clinical deterioration, seizures, and medical complications.

This report reinforces the findings of a recently published article that states that in patients, particularly those with brain contusions, the presence of clinical and/or radiological deterioration plays an important role in deciding issues concerning surgical intervention. An extremely interesting finding from this study is the fact that only 8% of the patients had drugs or alcohol as contributing factors to their traumatic injury. This is obviously in contradistinction to studies done in the United States in which the incidence of alcohol-related severe and moderate TBI is much higher.

In conclusion, this is an excellent article, and it adds to a very scarce amount of literature on the moderately head-injured patient. It will be used and quoted by many institutions in the management of this subset of patients with TBI. These data are also extremely important for determining the disposition and transfer of this subset of patients.

Domenic P. Esposito
Jackson, Mississippi

The neurosurgical literature is replete with studies on the management and outcome of patients with severe head injury; hence, this study by Compagnone et al., which addresses moderate head injury in a relatively large cohort of patients (315 cases) is welcome. The study provides valuable data, including the 23% risk of progression to a mass lesion in patients with diffuse injury types I and II, emphasizing the need for these patients to be transferred to specialized centers that provide 24-hour access to cranial surgery and high-quality neurointensive care. The overall outcome expressed as favorable on the GCS (good recovery/moderate disability) was 74%. It is a pity that more refined measures of outcome, such as quality of life, are not available. The major limitation of this study, a rate of missing outcome of 21%, is recognized by the authors. This must be borne in mind when interpreting the results but should not detract from this valuable contribution to the literature.

Peter J. Hutchinson
Cambridge, England

