

# EARLY INDICATORS OF PROGNOSIS IN SEVERE TRAUMATIC BRAIN INJURY

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# INTRODUCTION

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The uncertainty that exists about the likely outcome after traumatic brain injury (TBI) is

encapsulated in the Hippocratic aphorism: “No head injury is so serious that it should be despaired of nor so trivial that it can be ignored.” Today, physicians’ estimates of prognosis are still often unduly optimistic, unnecessarily pessimistic, or inappropriately ambiguous.<sup>1,4,6,12</sup> It still remains impossible to say with certainty what will be the future course of events in an individual patient, but intensive research in the last two decades has made it possible to be much more confident about what is likely to happen, and to consider prognosis in terms of probabilities rather than prophecies.

Prediction of outcome involves making probability statements that depend on a logical relationship between outcome and features encapsulated in antecedent, early data. The advances in prognosis reflect the establishment of methods for categorizing outcome<sup>9</sup> and early injury severity.<sup>18</sup> These became widely accepted<sup>13</sup> and led to multinational, multicenter studies<sup>14</sup> that identified the features about the patient, the injury, and the early clinical course with a distinctive, consistent relationship to outcome.<sup>10,15</sup> The subsequent chapters consider these various features, first with respect to the existence of a relationship to outcome, then the strength of the effect or interaction with outcome, and finally, the extent to which the effect is unique to the feature in question (almost never so) or how far there is interaction (interdependence) with other prognostic features.

Although clinicians usually attempt to take a wide range of factors into account when making clinical decisions and assessing prognosis, there is probably a redundancy in this effort to be complete. In practice, relatively few features have been found to contain most of the prognostic information,<sup>3,10,17</sup> These include the patient age, clinical indices indicating the severity of brain injury (e.g., the depth and duration of coma and other neurological abnormalities), and the results of investigation and imaging studies, particularly intracranial pressure (ICP) and computed tomography (CT) scanning, which disclose the nature of brain injury and its effects on intracranial dynamics. Even though there is little doubt regarding the importance of these features from clinical experience, there are still debates about the precise nature of their relationships and about exactly how the different features should be assessed, categorized, and—most importantly—utilized.

The identification of powerful, single prognostic factors is only one step toward a useful statement about prognosis. Unique relationships between the findings of a feature and outcome may apply only for the most extreme abnormalities found only in a tiny minority of patients. To be useful, prognostic statements need to be applicable across all severities of injury and capable of being expressed in a way that indicates the likelihood of an individual patient achieving different outcomes at some future time. This depends on combining the information on the different individual prognostic features. Although a wide number of statistical approaches have been described, there is little difference in practice between the results that they produce. Also the details of calculation are much less important than the data that are employed.<sup>17,19</sup> Likewise, the results of prognostic calculations can be expressed in a number of ways that include mathematical probability,<sup>8,10</sup> graphical presentations,<sup>2,5</sup> and the methodology used in this document. The merits of different methods have not been established.

The utility of prognostic probabilities can be assessed by various criteria. One is “separation,” in which a particular outcome is emphasized (e.g., by being assigned a very high probability). Separation has the benefit of conveying discrimination and a high degree of certainty; however, it

runs the risk of being excessively confident and leading to extremes of prognosis—either falsely optimistic or falsely pessimistic. Perhaps a more desirable attribute is “faithfulness,” that is, that the probabilities expressed relate reliably to what is likely to happen. Thus, the figure calculated should reflect the distribution of outcomes that occur in a series of patients allocated the respective probabilities of different outcomes. To do this effectively would require a large data set collected prospectively and with relevant patient follow-up.

Clearly, this type of approach cannot be used when reviewing published reports. The methodology described in the next section has been devised to fit the task of literature review while adhering to clinical epidemiological principles. Information about prognosis and predictive statements can be useful in a number of ways. From the start, concern about outcome is often foremost in the mind of the relative of severely brain-injured victims and realistic counseling is preferable to over pessimism—characterized as “hanging crepe”—or the raising of false hopes. An assessment of prognosis is crucial in research studies, both in determining the appropriate target population and in deciding if a given intervention has produced an outcome different from that which would have been expected. The place of prognosis in making decisions about the management of individual patients remains controversial. While many neurosurgeons acknowledge that it is an important factor in decision making,<sup>2</sup> others relegate prognosis to a minor or even nonexistent role, reflecting a range of attitudes arising from cultural and ethical differences as much as clinical convictions.

Although there are concerns that estimation of prognosis may be used to allocate (and in particular to withdraw) resources, and that this might worsen the outcome in some cases, this was not substantiated in a formal study.<sup>16</sup> In a large prospective trial, doctors, nurses, and other staff providing acute care for severe brain injuries were provided with predictions of the outcome in individual cases. Compared with control periods without predictions, there was no lessening of the use of neither intensive care resources nor an increase in the rate of decisions to limit treatment. Instead, there was a shift in the employment of aspects of intensive care from patients with a calculated high likelihood of poor outcome to those with a greater prospect of recovery, without an adverse affect to outcome in the former group.

The purpose of this exercise is to identify from the published medical literature those early clinical factors that may be prognostic for outcome. This will then suggest which early factors should be focused on in prospective database research in patients with TBI.

An estimate of a patient’s prognosis should never be the only factor, and only rarely the main factor, in influencing clinical decisions. Instead, prognosis is simply one of the many factors that need to be considered in the clinical management of a severely brain-injured patient.

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# Prognostic Parameters

for Traumatic Brain Injury Methodology

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## Introduction

With the publicity of *Guidelines for the Management of Severe Head Injury*, those interested in guideline development were exposed to evidence-based principles for determining therapeutic effectiveness. In this paradigm, study strength in terms of design is related directly to the strength of recommendations. Thus, Class I evidence (randomized controlled trials) gave rise to practice standards, Class II evidence (non-randomized cohort studies, case-control studies) supported weaker recommendations called guidelines, and all other evidence—including expert opinion—was given the designation of Class III and produced practice options. While this classification of evidence suits clinical studies related to therapy, it does not pertain to studies of prognosis, diagnostic tests, or clinical assessment. Therefore, the working group convened by the Brain Trauma Foundation, the American Association of Neurological Surgeons, the Neuro-trauma Committee of the World Health Organization, and the Brain Injury Association to evaluate the literature on prognostic indicators in head injury, had the task of developing a different model for making recommendations, while still adhering to the concepts of evidence-based practice.

Committed to continuing to utilize the principles of clinical epidemiology, the working group produced a model in which pertinent literature was qualitatively evaluated. In developing this model, it was recognized that the literature of interest would pertain to prognosis of treated brain-injured patients. It would, therefore, need to comply with standard measures of quality applicable to prognosis in order to minimize bias or systematic error as much as possible.

In addition, it was recognized that the clinical assessments of interest and their relationships to prognosis could be likened to diagnostic tests. In this scenario, the outcome of mortality or Glasgow Outcome Scale score is similar to the reference measure against which a diagnostic test is evaluated, whereas the prognostic indicator is like a diagnostic test. We might therefore, create a 2 x 2 table as follows:

	DEAD	ALIVE
PROGNOSTIC FACTOR PRESENT		
PROGNOSTIC FACTOR ABSENT		

With the data taken from appropriate articles, characteristics of sensitivity, predictive values, and, where applicable, likelihood ratios can be estimated. An additional aspect of this task that had to be acknowledged was that many of the prognostic indicators, as well as one of the outcome measures (Glasgow Outcome Scale), are clinical assessments, which need to be reliable and valid to be useful.

In summary, the criteria we elected to use for this task combined those for prognosis, diagnosis, and clinical assessment, as described below.

## Methodology

The literature was searched, using the appropriate rubrics, via a computerized link to the National Library of Medicine in Washington, D.C., U.S.A. Additional references were found by examination of reference lists at the end of each journal article and through personal knowledge of the experts participating in the working group. Specific prognostic indicators were then examined separately, as shown in the sections that follow. Each paper was qualitatively evaluated according to criteria intended to establish study strength. These included:

1. Twenty-five or more patients in the series with complete follow-up.
2. Outcomes measured — Glasgow Outcome Scale or Mortality — at six months or more.
3. Data gathered prospectively, although retrospective examination from a database creating an ongoing cohort of patients could be used.
4. Glasgow Coma Scale score measured within 24 hours.
5. Appropriate statistics (e.g., multivariate analysis) used to include adjustment for prognostic variables.

It was then decided by the working group that papers thus evaluated could be classified in a similar fashion as those for therapeutic effectiveness, as indicated below:

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### CLASSIFICATION OF EVIDENCE ON PROGNOSIS

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CLASS I:	Those papers containing all of the above characteristics.
CLASS II:	Those papers containing four out of the five characteristics, including prospectively collected data.
CLASS III:	Those papers containing three or fewer of the above characteristics.

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Further, in order to be able to calculate sensitivity, specificity, positive and negative predictive value, and, where applicable, likelihood ratios, the Bayesian table was constructed:

	DEAD	ALIVE
PROGNOSTIC FACTOR PRESENT	a	b
PROGNOSTIC FACTOR ABSENT	c	d

CLINICAL QUESTION	PROGNOSTIC ATTRIBUTE	CALCULATION
If a trauma patient reaches a certain outcome, how likely is she or he to have had a given prognostic indicator?	<i>Sensitivity</i>	a a + c
If a trauma patient does not reach a certain outcome, how likely is she or he to have not had a given prognostic indicator?	<i>Specificity</i>	d b + d
If a trauma patient has a given prognostic indicator, how likely is she or he to reach a certain outcome?	<i>Positive predictive value</i>	a a + b
If a trauma patient does not have a given prognostic indicator, how likely is she or he to reach a certain outcome?	<i>Negative predictive value</i>	d c + d

# GLASGOW COMA SCALE SCORE

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## I. Conclusions

- A. Which feature of the parameter is supported by Class I evidence and has at least a 70% positive predictive value? There is an increasing probability of poor outcome with a decreasing Glasgow Coma Scale (GCS) score in a continuous, stepwise manner.
- B. Parameter measurements:
  1. How should it be measured?
    - It should be measured in a standardized way.
    - It must be obtained through interaction with the patient (e.g., application of a painful stimulus for patients unable to follow commands).
  2. When should it be measured for prognostic purposes?
    - Only after pulmonary and hemodynamic resuscitation.
    - After pharmacologic sedation or paralytic agents are metabolized.
  3. Who should measure it?
    - The GCS can be fairly reliably measured by trained medical personal.

## II. Overview

The GCS was developed by Teasdale and Jennett in 1974 as an objective measure of the level of consciousness.<sup>31</sup> It has since become the most widely used clinical measure of the severity of injury in patients with severe traumatic brain injuries (TBIs). A number of studies have confirmed a fairly high degree of inter- and intra-rater reliability of the scale across observers with a wide variety of experience.<sup>5,11,24,32</sup>

## III. Search Process

The titles and abstracts of approximately 500 journal articles were retrieved using a computerized search of the National Library of Medicine. The MESH heading “Glasgow Coma Scale” was used to search for articles published since the GCS was developed in 1974. The abstracts of all articles were reviewed and those articles that focused on the correlation between the acute GCS score (obtained within the first 24 hours) and outcome in patients with severe closed head injuries were selected for review of the entire article. This left 20 articles that dealt primarily with correlation of the GCS score and outcome, 8 articles that focused on the use of the initial GCS score to predict outcome, and 6 articles describing the reliability of the GCS score.

## IV. Scientific Foundation

The modern, prehospital treatment of many TBI patients (sedation, pharmacologic paralysis, and/or intubation) complicates the early determination of valid GCS scores in nearly half of the patients admitted to trauma centers. A recent review of patients entered into various drug trials as part of the European Brain Injury Consortium revealed that the motor score was untestable in 28% of the patients at the time of admission to the neurosurgery service, and the full GCS score was untestable in 44% of the patients (Personal communication, A.I.R. Maas). In addition, a survey of major trauma centers in the United States found that there is substantial variability of practice regarding the assignment of the initial GCS score both within the hospital and among different hospitals when patients are admitted following such prehospital treatment.<sup>22</sup> In many cases, patients are assigned a GCS score even though they have received paralytic medication within minutes prior to the

assessment. For those patients who were intubated prior to assessment of the initial GCS score, members of the Traumatic Coma Data Bank (TCDB) arbitrarily decide to assign a GCS verbal score of 1.1. This practice may significantly overestimate the severity of the injury, however. Gale, et al., found that the mortality rate for those with a true (testable) GCS score of 3-5 was 88%, while it was only 65% for those with the same GCS sum score when a verbal score of 1 was used because of endotracheal intubation.<sup>12</sup> Others also have found that prediction of outcome is less accurate if all three components of the GCS, and particularly eye opening, are not assessed.<sup>4,18</sup>

When assessing the motor sub-score, some controversy exists regarding the best location for applying a painful stimulus. Teasdale, et al., recommend stimulation of the nailbed initially, but recording the best response obtained from either arm to any stimulus.<sup>32</sup> In their study of observer variability, they found that, for inexperienced observers, interobserver variability was less when nailbed pressure was used. For those with more experience variability was less when supraorbital pressure was used.

Despite these concerns, the GCS score has been shown to have a significant correlation with outcome following severe TBI, both as the sum score,<sup>7,8</sup> or as just the motor component.<sup>1,3,8,25</sup> In a prospective study by Narayan a positive predictive value of 77% for a poor outcome (dead, vegetative, or severely disabled) was measured for patients with a GCS score of 3-5 and 26% poor predictive value for a GCS score 6-8 (see Evidentiary Table).<sup>27</sup> As is commonly done, this study grouped GCS measurements versus outcome. In a larger study each GCS level would have its own predictive value. For example, in a series of 315 TBI patients from Australia, a significant inverse correlation was demonstrated between the initial GCS score (obtained 6-48 hours after injury) and mortality.<sup>10</sup>

GCS score	Mortality
3	65%
4	45
5	35
6	24
7-13	10-15

In the United States, 746 patients with closed head injuries who were entered into the TCDB were reviewed to determine the relationship of the initial GCS score with outcome.<sup>23</sup> In this study, the interval from injury to outcome assessment was quite variable and ranged from 11 to 1199 days, with a median of 674 days. The mortality rate for those with an initial post-traumatic GCS score of 3 was 78.4%; initial GCS score of 4, 55.9%; and initial GCS score of 5, 40.2%. Of note, however, is that 4.1%, 6.3%, and 12.2% of the three groups, respectively, had a good outcome.

In a large study of 46,977 head-injured patients the relationship between GCS scores 3-15 and mortality was investigated.<sup>13</sup> A sharp progressive increase in mortality was noted in patients who presented to the Emergency Room with a GCS score of 3-8.

In 109 adults with acute subdural hematomas, Phuenpathom also showed a significant inverse relationship with GCS score (best score within 24 hours) and mortality.<sup>28</sup>

GCS score	Mortality	Number of patients
3	100%	(37)
4	90	(9/10)
5	63	(5/8)
6	33	(2/6)
7	22	(2/9)
8-15	0	(39)

In a series of 115 patients with epidural hematomas, Kудay found that the initial GCS score was the single most important factor affecting outcome ( $p < 0.00001$ ).<sup>21</sup>

Because of the strong association with the initial GCS score and outcomes, a number of investigators have studied the predictive value of the initial GCS score using various logistic regression techniques.<sup>2,16,20,30,33</sup> Thatcher, et al., used multimodal statistical models to study the ability of the initial GCS score or the GCS score obtained at a mean of 7.5 days after the injury to predict outcome at one year after injury for 162 patients with TBI.<sup>33</sup> When based on the initial GCS score, only 68.6% of those predicted to have a good outcome and 76.5% of those predicted to have a poor outcome actually had such outcomes at one year. If the later GCS was used for predictions, there was a significant increase in the rate of correct predictions for a good outcome (80.6%), but the rate of correct predictions for a poor outcome remained essentially unchanged (78.6%).

Kaufman described the accuracy of outcome predictions of an experienced neurosurgeon for 100 patients with severe TBI.<sup>20</sup> Outcomes were categorized as dead/vegetative, severely disabled, or capable of independent survival, and were predicted based on the best GCS scores obtained within 24 hours after injury. Age, pupils, blood pressure, heart rate, laboratory values, and initial computed tomography (CT) scans were also considered. Correct prognosis was estimated in only 56% of the cases.

GOS	Predicted/Actual Outcomes
Dead/Vegetative	35/24
Severe Disability	23/11
Independent	42/65

The table reveals that predictions were best for very bad or very good outcomes. In addition, poor outcomes were overestimated by 32%-52%, while good outcomes were underestimated by 35%. In a study of 254 patients with severe TBI, Benzer used logistic regression methods to predict patient outcome based on the immediate post-traumatic GCS score, and made correct predictions 82.68% of the time.<sup>2</sup>

It should be emphasized that most of these studies looked at the least discriminate scenario (e.g., reduction of potential outcomes to two or at most three groups). When attempts were made to predict more precisely into one of the five categories of the Glasgow Outcome Scale (GOS), the predictive accuracy of the initial GCS score was poor.<sup>19</sup>

## V. Summary

When considering the use of the initial GCS score for prognosis, the two most important problems are the reliability of the initial measurement, and its lack of precision for prediction of a good outcome if the initial GCS score is low. If the initial GCS score is reliably obtained and not tainted by prehospital medications or intubation, approximately 20% of the patients with the worst initial GCS score will survive and 8%-10% will have a functional survival (GOS 4-5).

## VI. Key Issues for Further Investigation

- A. The optimal time after injury for determining the initial GCS
- B. When to assess the GCS score for those who have received paralytic or sedative medication
- C. Reliability of the prehospital GCS score

## VII. Evidentiary Table

Fearnside,<sup>10</sup> 1998

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Description of Study: Prospective study of 315 consecutive patients of all ages with severe TBI to identify factors responsible for morbidity and mortality.

Classification: Class II Study

Conclusions:

GCS	GOS
3	65%
4	45
5	35
6	24
7-13	10-15

Marshall,<sup>23</sup> 1991

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Description of Study: Prospective study of 746 consecutive patients with severe TBI to gather demographic and outcome data; adults.

Classification: Class II Study

Conclusions:

GCS	GOS	
	1	4, 5
3	78.4%	7.2%
4	55.9	14.4
5	40.2	29.3
6	21.2	50.5
7	17.6	68.9
8	11.3	77.4

Narayan,<sup>27</sup> 1989

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Description of Study: Prospective study of 133 consecutive patients with severe TBI to identify factors responsible for morbidity and mortality; all ages.

Classification: Class I Study

Conclusions:

GCS	GOS		
	1	2, 3	4, 5
3-5	62%	15%	23% +PPV=77%
6-8	20	74	
9-11	18	76	

Beca,<sup>1</sup> 1995

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Description of Study: Prospective study of 109 children with severe TBI to compare outcome prediction of somatosensory evoked potentials (SEPs) with GCS.

Classification: Class III Study

Conclusions:

GCS Motor	GOS
	4, 5
1	0%
2-3	41-47
4-5	75-78

Braakman,<sup>6</sup> 1980

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Description of Study: Prospective study of 305 consecutive patients with severe TBI studied to identify prognostic indicators; all ages.

Classification: Class I Study

Conclusions:

GCS	GOS
	1
3	100%
4	80
5	68
6	51
7	27
8	22
9-15	15

Phuenpathom,<sup>28</sup> 1993

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Description of Study: Retrospective study of 109 patients with acute subdural hematomas to determine outcome; all ages.

Classification: Class II Study

Conclusions:

GCS	GOS
	1
3	100%
4	90
5	63
6	33
7	22
8-15	

Wilberger,<sup>34</sup> 1990

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Description of Study: Retrospective study of 101 adult patients with severe TBI who also had acute subdural hematomas.

Classification: Class III Study

Conclusions:

GCS	1	GOS	4, 5
3	90%		5%
4	76		10
5	62		18
6-7	51		44

Rivas,<sup>29</sup> 1988

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Description of Study: Retrospective study of 66 patients with severe TBI who also had epidural hematomas; all ages.

Classification: Class III Study

Conclusions:

GCS Motor	1	GOS	4, 5
1	80%		20%
2-3	24		73
4-5	5		90

Colohan,<sup>9</sup> 1989

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Description of Study: Prospective comparison of outcomes for 551 patients from New Delhi and 822 patients from Charlottesville with severe TBI; all ages.

Classification: Class II Study

Conclusions:

New Delhi

GCS Motor	GOS
1	81.3%
2-4	40.9
5	4.8
6	0.2

Charlottesville

GCS Motor	GOS
1	88.9%
2-4	56.2
5	12.5
6	0.4

Miller,<sup>26</sup> 1981

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Description of Study: Prospective study of 225 patients with severe TBI to analyze factors related to outcome; all ages.

Classification: Class II Study

Conclusions:

GCS Motor	1	GOS	4, 5
3-4	71%		16%
5-7	30		59
8-15	13		79

Young,<sup>35</sup> 1981

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Description of Study: Prospective study of outcomes at one year following severe TBI in 94 patients; all ages.

Classification: Class II Study

Conclusions:

GCS Motor	1	GOS	4, 5
3-4	90%		5%
5-7	33		49

Jaggi,<sup>17</sup> 1990

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Description of Study: Prospective study of cerebral blood flow changes following severe TBI in 96 adults.

Classification: Class II Study

Conclusions:

GCS	GOS	
	1, 2	3-5
3-4	78.9%	21.2%
5-6	45.2	54.8
7-9	25.7	74.3

Gale,<sup>12</sup> 1983

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Description of Study: Prospective study of outcomes in 142 adults with severe TBI.

Classification: Class III Study

Conclusions:

GCS	GOS
	1, 2
3-5	65%
6-7	20

Generalli,<sup>14</sup> 1982

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Description of Study: Retrospective multicenter study of 1,107 patients with severe TBI, GCS < 9 for 6 hours or more with onset of coma at any time within the first 48 hours of injury; GOS assessed at 3 months after injury.

Classification: Class III Study

Conclusions:

GCS Motor	GOS	
	1, 2	3-5
3-5	65%	34%
6-8	20	79

The type of intracranial lesion, particularly subdural hematoma, had a significant negative impact on outcomes for those with an initial GCS score of 3-5.

Generalli,<sup>13</sup> 1994

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Description of Study: A multicenter analysis of the Major Trauma Outcome Study database. The relationship between admission GCS score and mortality showed an exponential relationship with a marked increase in mortality in patients with GCS < 9.

Classification: Class III Study

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## VIIa. Description of the Studies According to Classification Criteria

First Author	# Pts	Pro-spective	Time	When was indicator measured	Method	Who did it	Outcome measure	When	Blind Observer	Multi variate statistic	Statistics
Fearnside <sup>10</sup>	315	Y	NR	6-48 mo p injury	GCS	NR	GOS	6mo	NR	Y	Log regression
Marshall <sup>23</sup>	746	Y	1984-1987	< 48 hrs p adm	GCS	NR	GOS	Discharge thru last contact - 32.5-674 days	NR	Y	Cont table, log regression
Narayan <sup>27</sup>	133	N	1976-1979	< 6 hrs p injury	GCS	Neuro-surgeon	GOS	3, 6, 12 mo	NR	Y	Log regression
Beca <sup>1</sup>	109	Y	1991-1992	NR	GCSm	NR	GOS	> 6mo	NR	Y	Log regression
Phuenpathom <sup>28</sup>	109	N	1986-1989	Immediately p admission & best score 1 <sup>st</sup> 24 hours	GCS	NR	GOS Injury	6 mo	NR	Y	Log regression
Wilberger <sup>34</sup>	101	N	1982-1987	NR	GCS	NR	GOS	NR	NR	NR	Chi-square t-test
Rivas <sup>29</sup>	161	N	1977-1986	On arrival	GCS	NR	GOS	> 6 mo p injury	NR	NR	Chi-square
Colohan <sup>9</sup>	551 822	Y	1977-1979	On admission, time from injury variable	GCSm	NR	Death	Within 2 yrs	NR	Y	Conting table, Mann-Whitney
Miller <sup>26</sup>	225	Y	1976-1980	6-24 hrs p admission	GCS	House-staff	GOS	3, 6, 12 mo for 60%, last contact for others	NR	NR	Chi-square
Young <sup>35</sup>	170	Y	NR	During 1 <sup>st</sup> week	GCS	NR	GOS	12 mo	NR	Y	Multiple Log regression
Jaggi <sup>17</sup>	96	Y	NR	< 96 hrs	GCS	NR	GOS	6 mo	Y	Y	2 way ANOVA, Log regression
Gale <sup>12</sup>	451	Y	1980-1981	NR	GCS	NR	Death	NR	NR	NR	NR
Braakman <sup>5</sup>	305	Y	1973-1978	24 hrs	GCS	NR	GOS	1, 3, 6, 12 mo	NR	Y	Stepwise Log regression
Gennarelli <sup>13</sup>	1,107	N	NR	6-48 hrs p injury	GCS	NR	GOS	3 mo	NR	N	NR
Gennarelli <sup>14</sup>	46,977	Y	1982-1989	On admission	GCS	NR	Death	In-hospital	NR	N	Exponential model

Abbreviations:

NR= not recorded

# AGE

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## I. Conclusions

- A. Which feature of the parameter is supported by Class I evidence and has at least a 70% positive predictive value? There is an increasing probability of poor outcome with increasing age, in a stepwise manner.
- B. Parameter measurement for prognosis:  
Age is not subject to observer measurement variability. Age should be obtained on admission, preferably with documentation.

## II. Overview

The prognosis for recovery from trauma as one ages is a function not only of the aged brain, but the type of injury that occurs frequently in each age group. In addition, a decline in health as one ages may predispose the aged to systemic complications after head injury.

An examination of injury type with respect to age demonstrates an increasing proportion of injuries secondary to falls and pedestrian accidents with advancing age<sup>2, 20, 24, 34, 42</sup>. In this prospective study of the Traumatic Coma Data Bank (TCDB), motor-vehicle crashes were the cause of injury in 55% of patients ages 15–25, whereas only about 5% suffered falls. However, in the age range above 55, 45% suffered falls and only about 15% were in motor-vehicle crashes. However, falls as a mode of injury did not appear as an independent predictor of poor outcome. Old patients had a poor outcome compared to younger patients, regardless of the cause of injury.

In the TCDB study, a marked increase in pre-existing systemic disease was found with increasing age. There were a significantly increased percentage of poor outcomes (death and vegetative) in those patients with prior systemic disease in ages above 56 (86% vs 50%); however, this correlation was not found in younger age groups. In addition, multiple systemic injuries were less likely in the older age group thus emphasizing the role of the severity of brain injury in determining outcome.

The reaction of the aged brain to trauma may be apparent in the head computed tomography (CT) scans of patients. In the above TCDB study there was an age-related trend toward increasing intracranial hematomas with the largest intracerebral hematomas observed in the oldest groups. The chances of survival in patients with intracranial hematomas decrease with advancing age<sup>2, 4, 9, 15, 29, 34, 39, 42, 43</sup>. A significant correlation was noted in the TCDB study between a poor outcome and those patients who had intracerebral or extracerebral hematomas greater than 15 cc, subarachnoid hemorrhage, midline shift, compressed cisterns, or shift, which all increased with age (except for compressed cisterns). Unfortunately there were too few older patients without mass lesion to critically evaluate the effect independent of age.

A multivariate logistic regression analysis was done of the TCDB to evaluate the independent effect of age on outcome from severe head injury. Age was found to be an independent predictor after other factors were excluded. One explanation for this is that the brain has a decreased capacity for repair as it ages. This has some support in that the proportion of survivors in Glasgow Outcome Scale scores of good recovery (GCS scores 5, 4, and 3) all declined with age.

### III. Process

A MEDLINE search was performed between 1966 and 1995 exploring the following subjects: 1) age, 2) human head injury, and 3) prognosis. The search resulted in 44 references that were individually reviewed and classified.

### IV. Scientific Foundation

In the last few decades, several authors have identified age as a strong prognostic indicator following injury to the brain<sup>6, 14, 20, 22, 31, 41</sup>. Most investigations have stressed that younger individuals do better than adults. A remarkably low mortality rate among children was noted as early as 1973.<sup>20</sup> Later studies described similar results, and revealed that a higher proportion of children achieved a lower incidence of mortality and better outcomes than adults.<sup>1, 3, 5, 8, 17, 26</sup>

There are discrepancies in the literature when defining the age point where prognosis significantly worsens. For example, there has been disagreement regarding the pediatric age group. One group of reports has indicated that outcome tends to be better in children under ten years of age<sup>9, 13, 28, 44</sup>, while others report that children under five have a higher mortality rate<sup>6, 18, 22, 25, 27, 32, 35, 36</sup>. Several large pediatric head injury series have reported that children have a lower mortality than adults, while others report that the primary mortality rate does not differ between children and adults. Additionally, some investigations reported better outcomes below the age range of 40-50 years<sup>6, 7, 12, 16, 19, 21, 36</sup>, while other studies reported outcome as a continuous function of age without threshold values<sup>4, 10, 11, 17, 22, 26, 30, 31, 32, 37, 40</sup>. These discrepancies appear to be related to variations in the definitions of age groups.

A prospective investigation of 372 TBI patients in the UK with a GCS score less than 13 or ISS greater than 16 and age above 14 years showed no prognostic effect of age to 50 years.<sup>38</sup> At this point, age became an independent predictor of mortality, and GCS and ISS added high mortality significance when individually added to this model.

A prospective study of age and outcome from the TCDB revealed that patients older than 60 had a significantly worse outcome. Six months after severe head injury, 92% were dead, vegetative, or severely disabled. Four Class I studies demonstrated a mortality of greater than 75% in severely brain injured patients older than 60.<sup>5, 25, 31, 33</sup> The critical age threshold for worsening prognosis appears to be above 60 in a review of Class I and II studies. However, this may be an artifact of the age grouping used by various authors in converting continuous data into categorical data.

The following chart summarizes the Class I papers with regard to age threshold and poor outcome:

First Author	Age Threshold	Poor Outcome	Age Range	Poor Outcome
Vollmer, <sup>42</sup> 1991	> 55	92% (GOS 1, 2, 3) 80% (GOS 1)	46-55	78% (GOS 1, 2, 3) 49% (GOS 1)
Braakman, <sup>6</sup> 1980	> 51 > 61	75% (GOS 1) 77% (GOS 1)	41-50	49% (GOS 1)
Teasdale, <sup>40</sup> 1979	> 60	87% (GOS 1, 2)	40-60	56% (GOS 1)
Narayan, <sup>31</sup> 1981	> 60	78%	41-60	57% (GOS 1, 2, 3) 46% (GOS 1)
Signorini, <sup>38</sup> 1999	≥ 50	Linear decline in probability of survival	14-49	No significant effect

## V. Summary

Age is a strong factor influencing both mortality and morbidity. Despite some contradictions, most literature supports children faring better than adults who have severe brain injury. The significant influence of age on outcome is not explained by the increased frequency of systemic complications or intracerebral hematomas with age. Increasing age is a strong independent factor in prognosis with a significant increase in poor outcome above 60 years of age.

## VI. Key Issues for Future Investigation

Future studies should record age as a continuous variable in their study designs. Furthermore, potentially confounding variables such as pre-existing medical conditions should be recorded and analyzed. The biology of the aging brain and its vulnerability to injury should be investigated.

## VII. Evidentiary Table for Age and Outcome

Alberico,<sup>1</sup> 1987

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Description of Study: Prospective analysis of a consecutive series of 330 severely head-injured pediatric and adult patients treated with the same protocol, by the same physicians and staff in the Intensive Care Unit. The pediatric patients had a significantly higher percentage of good outcomes than the adult patients. They also had a significantly lower mortality rate than the adult patients.

Classification: Class II Study

Conclusions:

Age	GOS	
	1	5
1-4 (N=6)	17%	17%
5-9 (N=18)	22	61
10-14 (N=20)	20	40
15-19 (N=56)	25	40
21-40	35	33
41-60	55	15
61-80	80	5

Amacher,<sup>2</sup> 1987

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Description of Study: Retrospective analysis of 56 patients 80 or more years of age. Even if a significant proportion (60%) of old people may make a full recovery from head injury, the mortality rate is high even in those with good admissions.

Classification: Class III Study

Conclusions:

Age	GOS			
	1	2	3	4 5
≥ 80 (N=10)	80%	0%	10%	10%

Description of Study: Retrospective analysis of a consecutive series of 37 children with severe head injury. The data confirm that morbidity and mortality are lower in children than in adults: 51% of these young patients had a good recovery or moderate disability after 6 months. The mortality rate of 33% is higher than in some reports but probably more closely approximates the death rate from these injuries.

Classification: Class II Study

Conclusions:

Age	GOS				
	1	2	3	4	5
0-5 (N=16)	26%	0%	12%	12%	50%
6-10 (N=7)	43	0	0	14	43
11-17 (N=14)	36	7	21	29	7

Description of Study: Retrospective analysis of 305 consecutive head-injured Dutch patients. The relationship between age and mortality after 6 months shows an increasing mortality rate with increasing age.

Classification: Class I Study

Conclusions:

Age	GOS
0-10 (N=40)	1
11-20 (N=85)	35%
21-30 (N=46)	33
31-40 (N=38)	37
41-50 (N=29)	44
51-60 (N=20)	55
61-70 (N=26)	75
≥ 70 (N=21)	77
	100

Description of Study: Retrospective analysis of 800 patients with severe head injuries with and without decerebrate rigidity. In patients of all ages without decerebrate rigidity, the mortality rate progressively increases with age whereas the mortality rate in decerebrate patients is constant and independent of age. Of the survivors, three-fourths of those with good recovery were under 40 years of age.

Classification: Class III Study

Conclusions:

Age (N=800)	GOS
5	1
10	1%
20	4
30	8
40	15
50	22
60	29
70	35
80	45
	55

Description of Study: Retrospective analysis of the outcome in 53 children following severe head injury. 90% of the patients made a good recovery or were moderately disabled, and 8% died or were left vegetative.

Classification: Class III Study

Conclusions:

Age	GOS		
	1	2-3	4-5
0-5 (N=21)	5%	5%	90%
6-10 (N=19)	5	5	90
10-17 (N=13)	8	0	92

Description of Study: Retrospective analysis of 264 patients with severe head injury. A combination of the Glasgow Coma Scale score, oculocephalic response, and age can provide a simple but reliable prediction of outcome in severe head injury.

Classification: Class II Study

Conclusions: Age not assessed as an independent predictor of outcome.

Edna,<sup>14</sup> 1983

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Description of Study: Prospective analysis including 1,120 head-injured patients between 1979 and 1980. In addition to the level of unconsciousness at admission, age, pupillary light reactions, intracranial hematoma, associated extracranial injuries, and skull fractures seem to be important for predicting the outcome.

Classification: Class III Study

Conclusions:

Age	GOS
0-39 (N=38)	24%
≥ 40 (N=18)	33

Gordon,<sup>16</sup> 1995

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Description of Study: Retrospective analysis of 2,298 head-injured patients. Outcome significantly correlates to age and type and severity of lesion. No table of age versus outcome in GCS less than or equal to 8.

Classification: Class II Study

Heiskanen,<sup>19</sup> 1970

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Description of Study: Retrospective analysis of 204 patients with severe head injury. In patients over 60, no special or heroic methods of treatment are indicated, but in children and adolescents every effort should be made as long as there has not been respiratory arrest and cerebral death.

Classification: Class III Study

Conclusions:

Age	GOS
0-20 (N=62)	32%
21-40 (N=62)	48
41-60 (N=53)	59
≥ 60 (N=27)	78

Description of Study: Retrospective analysis of the relationship between clinical features of brain dysfunction in the first week after severe head injury and outcome 6 months later for 1,000 patients. Depth of coma, pupil reactions, eye movements, motor response pattern, and patient's age proved to be the most reliable predictors of outcome.

Classification: Class II Study

Conclusions:

Age	GOS 1-2
< 20 (N=320)	33%
20-39 (N=284)	47
40-59 (N=245)	56
> 60 (N=151)	87

Description of Study: Prospective analysis of a series of 8,814 head-injured patients admitted to 41 hospitals in three separate metropolitan areas. The pediatric patients exhibited a significantly lower mortality rate compared to the adults indicating that age itself, even within the pediatric age range, is a major independent factor affecting the mortality rate in head-injured patients.

Classification: Class III Study

Conclusions:

Age	GOS 1
0-14 (N=95)	28%
≥ 15 (N=681)	48

Description of Study: Prospective analysis of 225 patients with severe head injury who were managed in a uniform way and analyzed to relate outcome to several clinical variables. Factors important in predicting a poor outcome include the presence of an intracranial hematoma, increasing age, abnormal motor responses, impaired or absent eye movements or pupillary reflexes, early hypotension, hypoxemia, or hypercarbia, and elevation of intracranial pressure over 20 mm Hg, despite artificial ventilation.

Classification: Class II Study

Conclusions:

Age	GOS		
	1	2-3	4-5
0-20	19%	11%	70%
21-40	34	10	56
41-60	44	12	44
61-90	71	23	6

(N<sub>T</sub> = 225)

Narayan,<sup>31</sup> 1981

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Description of Study: Prospective analysis of 133 severely head-injured patients in predicting outcome. A combination of clinical data including age, GCS score, pupillary response, presence of surgical mass lesions, extra-ocular motility, and motor posturing predicts outcome with 82% accuracy, 43% with over 90% confidence.

Classification: Class I Study

Conclusions:

Age	GOS		
	1	2, 3	4, 5
0-20 (N=46)	17%	11%	72%
21-40 (N=50)	28	6	66
41-60 (N=28)	46	11	43
≥ 61 (N=9)	78	0	23

Overgaard,<sup>32</sup> 1973

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Description of Study: Prospective analysis of 201 patients injured in road-traffic accidents in an attempt to ascertain clinical factors of prognostic significance after traumatic head injury. Increasing age and post-traumatic hypotension were both related to poor recovery, while major intracranial and extracranial surgical complications were associated with poor functional recovery and increased mortality, respectively.

Classification: Class II Study

Ruff,<sup>36</sup> 1993

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Description of Study: Retrospective analysis of 335 severely head-injured patients with respect to outcome as a function of employment status or return to school. The three most potent predictors for returning to work or school are intactness of the patient's verbal intellectual power, speed of information processing, and age.

Classification: Class III Study

Signorini,<sup>38</sup> 1999

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Description of Study: Prospective analysis of 372 consecutive TBI patients with a GCS score less than 13 or ISS greater than 16 and age greater than 14 years. Multiple logistic regression resulted in a predictive survival model using mortality at one year with 98% follow-up. No effect of age to 50 years, then age was significantly correlated to higher mortality, particularly if associated with a lower GCS score and higher ISS score.

Classification: Class I Study

Teasdale,<sup>40</sup> 1979

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Description of Study: Retrospective analysis of 1,000 severely head-injured patients with respect to age and outcome. Age has an important influence on outcome after severe head injury and this is not explained solely by the increased frequency of intracranial complications in older

patients. It is necessary to take age into account when considering the prognosis of an individual patient and also when comparing series of patients managed in different centers or treated in different ways.

Classification: Class I Study

Conclusions:

Age	GOS 1
11-20	35%
21-30	39
31-40	45
41-50	55
51-60	66
61-70	77
71-80	85
81-90	95

Vollmer,<sup>42</sup> 1991

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Description of Study: Prospective analysis of age and clinical outcome following traumatic coma, age 15 years or older. The effect of age and outcome following head injury is dependent on an alteration in the pathophysiological response of the aging central nervous system to severe trauma and not on an increased incidence of non-neurological complications or other clinical parameters.

Classification: Class II Study

Conclusions:

Age	GOS				
	1	2	3	4	5
15-25 (N=311)	31%	4%	16%	16%	33%
26-35 (N=151)	29	7	16	21	28
36-45 (N=83)	41	7	18	17	17
46-55 (N=45)	49	9	20	11	11
≥ 56 (N=71)	80	3	9	9	0

## Evidentiary Table for Age and Outcome

First Author	# Pts	Pro-spective	Time	When was indicator measured	Method	Who did it	Outcome measure	When	Blind Observer	Multi variate statistic	Statistics
Alberico <sup>1</sup>	330	Y	1976-1984	On admission	Age	Neuro-surgeon	GOS	3 mo-8 yrs	NR	ND	Descriptive
Amacher <sup>2</sup>	56	N	1981-1985	On admission	Age	NR	Excellent-poor grading	NR	NR	ND	Descriptive
Becker <sup>4</sup>	160	N	1972-1976	On admission	Age	Neuro-surgeon	GOS	> 3 mo	NR	ND	Chi-square
Berger <sup>5</sup>	37	Y	1972-1982	On admission	Age	NR	GOS	> 6 mo	NR	ND	Descriptive
Braakman <sup>6</sup>	305	Y	1972-1978	On admission	Age	NR	GOS	6 mo	NR	Y	Multi-variant
Bricolo <sup>7</sup>	800	N	1973-1975	On admission	Age	Neuro-surgeon	Motor pattern	< 48 mo	NR	ND	Descriptive
Bruce <sup>8</sup>	53	N	1975-1977	On admission	Age	NR	GOS	6 mo	NR	ND	Descriptive
Choi <sup>11</sup>	264	N	1976-1981	On admission	Age	NR	GOS	6 mo	NR	Y	Log regression
Edna <sup>14</sup>	1,120	Y	1979-1988	On admission	Age	NR	GOS	At discharge	NR	ND	Chi-square
Gordon <sup>16</sup>	2,298	N	1968-1988	On admission	Age	NR	GOS	3, 6, 12 mo	NR	ND	Chi-square
Heiskanen <sup>19</sup>	204	N	1962-1965	On admission	Age	NR	Death	3-5 yrs	NR	ND	Student's t-test
Jennett <sup>22</sup>	1,000	N	1968-1976	On admission	Age	NR	GOS	6 mo	NR	ND	Descriptive
Luerssen <sup>26</sup>	8,814	N	1980-1981	On admission	Age	NR	Death	NR	NR	Y	Chi-square, Log regression
Miller <sup>30</sup>	225	Y	1976-1980	On admission	Age	NR	GOS	3, 6, 12 mo	NR	ND	Chi-square
Narayan <sup>31</sup>	133	Y	1976-1979	On admission	Age	NR	GOS	3, 6, 12 mo	NR	Y	Log regression
Overgaard <sup>32</sup>	201	Y	1968-1969	On admission	Age	NR	Neuro function exam	24, 36 mo	NR	ND	Chi-square
Ruffi <sup>36</sup>	93	N	4 yrs	On admission	Age	NR	Employment, return to school	6, 12 mo	NR	Y	Log regression
Signorini <sup>38</sup>	372	Y	1989-1991	On admission	Age	NR	Death	12 mo	NR	Y	Log regression
Teasdale <sup>40</sup>	1,000	Y	1968-1976	On admission	Age	NR	GOS	6 mo	NR	ND	Descriptive
Vollmer <sup>42</sup>	661	Y	1984-1987	On admission	Age	NR	GOS	6 mo	NR	Y	Chi-square, Log regression

**Abbreviations:**

NR= not recorded; ND= not done

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# PUPILLARY DIAMETER AND LIGHT REFLEX

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## I. Conclusions

- A. Which feature of the parameter is supported by Class I evidence and has at least a 70% positive predictive value? Bilaterally absent pupillary light reflex.
- B. Recommendations for parameter measurement for prognosis:
  1. How should it be measured?
    - A measurement difference of 1mm or more is defined as asymmetry.
    - A **fixed** pupil shows no response (< 1mm) to bright light.
    - A pupillary size of > 4mm is recommended as the measure for a **dilated** pupil.
    - The duration of pupillary dilation and fixation should be recorded.

The following pupillary exam should be noted with L (left) or R (right) distinction and duration:

- Evidence of direct orbital trauma
  - Asymmetrical response to light
  - Asymmetry at rest
  - Fixed pupil (one or both)
  - Dilated pupil (one or both)
  - Fixed and dilated pupils (one or both)
2. When should it be measured?
    - After pulmonary and hemodynamic resuscitation
  3. Who should measure it?
    - Trained medical personnel

## II. Overview

The parasympathetic, pupilloconstrictor, light reflex pathway mediated by the third cranial nerve is anatomically adjacent to brainstem areas controlling consciousness and the medial temporal lobe. Therefore, damage to the midbrain third nucleus or the efferent third nerve by temporal lobe compression produces dilation of the pupil. If the damage or compression is significant, the pupil will be unresponsive (fixed) to a light stimulus. This pupillary light reflex and the size of the pupil has traditionally been used as a clinical parameter in assessing transtentorial herniation and as a prognostic indicator. The pupillary light reflex and size equality of pupils has a high interobserver reliability.<sup>21</sup> The use of the pupillary size and light reflex are, therefore, indirect measures of dysfunction to pathways subserving consciousness and, thus, an important clinical parameter in assessing outcome from traumatic coma. Direct orbital trauma can damage the third nerve leading to a dilated and/or a fixed pupil and be independent of intracranial hypertension. Direct oculomotor trauma should be excluded before pupillary reactivity or size is used as a prognostic indicator.

## III. Search Process

A MEDLINE search for the period 1980-1995 was done using the key words “pupils,” “pupils and prognosis,” and “pupils and trauma.” This resulted in the critical review of 19 articles.

## IV. Scientific Foundation

The pupillary light reflex pathways are adjacent to brain structures essential for cognitive function and the temporal lobe. Increased intracranial pressure resulting in uncal herniation compresses the third cranial nerve resulting in a reduction in parasympathetic tone to the pupillary constrictor fibers and therefore results in a dilated pupil. Similarly, destruction of the third nerve parasympathetic brainstem pathway also results in a dilated and fixed to light pupil. Therefore, the pupillary light reflex is an indirect measure of herniation and brainstem injury. Generally, dilation and fixation of one pupil signifies herniation, whereas the appearance of bilaterally dilated and fixed pupils is consistent with irreversible brainstem injury in a fully resuscitated patient. A limitation in terms of prognosis is a dilated and nonreactive pupil due to direct orbital trauma without brainstem or intracranial third nerve compression. The “blown pupil” is important in the context of a decreased level of consciousness. This measurement of pupil function must be assessed for outcome with the level of consciousness or intracranial pathology.

Clinical studies investigating the prognostic weight of the pupillary light reflex have examined this parameter in a variety of methodologies. Few studies have rigorously measured the size and reaction of the pupil to light.<sup>18</sup> The vast majority label pupils as dilated without giving the size and do not state whether the pupils are fixed to light even though it is implied.

The incidence of pupillary abnormalities (%) within 24 hours, post-resuscitation, in patients with severe head injury is shown in the following table:

First Author	Both Reactive	One Reactive	One or Both Unreactive	Both Unreactive
Jennett, <sup>8</sup> 1976	78%	—%	—%	22% <sup>†</sup>
Jennett, <sup>9</sup> 1979	—	—	—	19*, 29, 32
Braakman, <sup>4</sup> 1980	62	12	—	26
Miller, <sup>13</sup> 1981	77	—	—	23
Narayan, <sup>14</sup> 1981	65	—	—	35
Heiden, <sup>7</sup> 1983	68	—	—	32
Van Dongen, <sup>22</sup> 1983	47	—	53	—
Levin, <sup>10</sup> 1990 <sup>††</sup>	64	—	36	—
Marshall, <sup>12</sup> 1991	56	11	—	33
Average	65	12	—	28

\*Represents % from Glasgow, Netherlands, and Los Angeles, respectively.

<sup>†</sup>Earlier series from Glasgow and Netherlands

<sup>††</sup>Traumatic Coma Data Bank (TCDB) study

On average 65% of patients with severe head injury have normally reactive pupils after resuscitation, 12% have one abnormal pupil, and 28% have bilateral pupillary nonreactivity.

There is significant interaction between pupillary reactivity and other early indicators of prognosis; Glasgow Coma Scale (GCS) score,<sup>4</sup> hypotension,<sup>1</sup> and CT basal cisterns,<sup>22</sup> as seen in the following table:

	GCS 3-5	GCS 6-7	SBP < 60	SBP 60-90	Cisterns Partly Open	Cisterns Closed
Unreactive Pupils (%)	56	20	65	53	15*	38*

\*Includes bilateral and unilateral unreactive pupils

In reviewing large studies (> 200 patients), there was a strong association between bilaterally unreactive pupils and poor outcome as shown in the following table:

% Vegetative/Dead (Glasgow Outcome Scale Score [GOS] 1, 2)

First Author	# of Patients	Bilateral Reactive Pupils	Unilateral Unreactive	Bilateral Unreactive
Jennett, <sup>8</sup> 1976	600	42%	—%	95%
Braakman, <sup>4</sup> 1980	305	29	54	90
Heiden, <sup>7</sup> 1983	213	36	—	91
Marshall, <sup>12</sup> 1991	746	32	34	74
	<b>Average</b>	<b>35</b>	<b>44</b>	<b>88</b>

In two Class I studies, bilaterally absent pupil reaction had a greater than 70% positive predictive value for a poor outcome. In a prospective study of 133 patients with severe head injury, bilaterally absent pupillary light reflex was noted in 35%; a poor outcome (dead, vegetative, or severely disabled) was found in 70% of these patients.<sup>14</sup> Similarly, in a larger study of 305 patients with regard to prognostic features, bilaterally absent pupillary light reflex was associated with a 90% mortality (see Evidentiary Table).<sup>4</sup>

In large series, patients who had bilaterally reactive pupils made a significantly better outcome as seen below:

% Good Recovery/Moderate Disability (GOS 4, 5)

First Author	# of Patients	Bilateral Reactive Pupils	Unilateral Reactive	Bilateral Unreactive
Jennett, <sup>8</sup> 1976	600	50%	—%	5%
Heiden, <sup>7</sup> 1983	213	49	—	3
Levin, <sup>10</sup> 1990	259	53	17*	—
	<b>Average</b>	<b>51</b>		<b>4</b>

\*One or both pupils unreactive.

The outcome from bilaterally unreactive pupils is influenced by the underlying pathology and timing of surgical evaluation of significant hematomas. In patients who are comatose from epidural hematomas, the mortality with bilateral fixed pupils is only 56% compared to an average of 88% in patients with subdural hematomas.<sup>15, 16</sup> In another study of patients who were operated on for epidural hematomas, with bilaterally fixed pupils, only 18% had a poor outcome (GOS 1-2) compared to 64% poor outcome in those patients who were operated on for subdural hematomas and had bilaterally fixed pupils.<sup>17, 18</sup> In this same study a delay of greater than three hours in evacuating a traumatic intracranial hematoma increased the chance of a poor outcome with bilateral fixed pupils from 40% to 63%.

In conclusion, pupil reactivity to light can prognosticate outcome. However, direct orbital trauma should be excluded as a causative agent, hypotension should be reversed prior to assessment of pupils, and repeat examination after evacuation of intracranial hematomas should be performed.

## V. Summary

The pupillary diameter and the pupilloconstrictor light reflex are the two parameters that have been studied extensively in relation to prognosis. Accurate measurement of pupil diameter or the constrictor response or the duration of the response has not been performed in studies on traumatic brain-injured individuals—for lack of a standardized measuring procedure. The following is recommended:

1. Pupillary light reflex for each eye should be used as a prognostic parameter.
2. The duration of pupillary dilation and fixation should be documented.
3. A pupillary size greater than 4 mm is recommended as the measure for a dilated pupil.<sup>17</sup>
4. A fixed pupil should be defined as no constrictor response to bright light.
5. Right or left distinction should be made when the pupils are asymmetric.
6. Hypotension and hypoxia should be corrected before assessing pupils for prognosis.
7. Direct orbital trauma should be excluded.
8. Pupils should be reassessed after surgical evacuation of intracranial hematomas.

## VI. Key Issues for Further Investigation

Future studies should dissect the prognostic value of each of the recommended measurements to discern the least number of pupillary size and light reflex measurements necessary to reliably prognosticate outcome. Also, a standardized method of measuring pupil size and reactivity to light would decrease interobserver variability.

## VII. Evidentiary Table

Andrews and Pitts,<sup>2</sup> 1991

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Description of Study: Retrospective study of 153 consecutive patients presenting with transtentorial herniation—altered level of consciousness, anisocoria or pupillary unresponsiveness, and abnormal motor findings; age range 2-83 years.

Classification: Class III Study

Conclusions:

	GOS		
	1-3	4	5
One Pupil Fixed	72%	13%	15%
Both Pupils Fixed	96	4	0

Braakman,<sup>4</sup> 1980

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Description of Study: Review of the International Databank with reference to 305 comatose head-injured patients' prognostic parameters measured with 24 hours of admission and (GOS) evaluated at 6 months.

Classification: Class I Study

Conclusions:	GOS
	1
Both Pupils Reactive	29%
One Pupil Fixed	54
Both Pupils Fixed	91 + PPV = 91%

Choi,<sup>5</sup> 1988

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Description of Study: A review of 523 severely head-injured patients analyzing significant prognostic parameters to predict outcome into four GOS categories.

Classification: Class III Study

Conclusions: Pupillary response to light was a significant ( $p < .001$ ) factor in determining outcome.

Cordobes,<sup>6</sup> 1981

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Description of Study: Retrospective analysis of 82 patients with regard to mortality before and after instituting a computed tomography (CT) scanner.

Classification: Class III Study

Conclusions:	GOS
	1
One Pupil Fixed	18%
Both Pupils Fixed	100

Heiden,<sup>7</sup> 1983

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Description of Study: Prospective study of 213 patients of all ages with severe head injury to identify favorable and unfavorable clinical factors.

Classification: Class II Study

Conclusions:	GOS		
	1, 2	3	4, 5
Both Pupils Reactive	36%	15%	49%
Both Pupils Fixed	91	6	3

Jennett,<sup>8</sup> 1976

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Description of Study: Prospective study in 600 severe head injury patients from Glasgow and the Netherlands.

Classification: Class II Study

Conclusions:

	GOS	
	1, 2	4, 5
Both Pupils Reactive	42%	50%
Both Pupils Fixed	95	5

Jennett,<sup>9</sup> 1979

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Description of Study: Expanded patient enrollment from 1976 publication with 1,000 patients from Glasgow, Netherlands, and Los Angeles.

Classification: Class I Study

Conclusions:

	GOS	
	1, 2	4, 5
Both Pupils Reactive	39%	50%
Both Pupils Fixed	91	4

Levin,<sup>10</sup> 1990

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Description of Study: Review of 300 survivors in the Traumatic Coma Data Bank prognostic factors in evaluating GOS at 1 year after injury; age range 16-70.

Classification: Class I Study

Conclusions:

	GOS			
	2	3	4	5
Both Pupils Reactive	4 %	14%	21%	61%
One or Both Fixed	15	38	20	27

Lobato,<sup>11</sup> 1988

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Description of Study: Review of 64 consecutive comatose patients who were operated on for epidural hematomas; age range 1-72 years.

Classification: Class III Study

Conclusions:

	GOS			
	1	3	4	5
Both Pupils Reactive	13%	4%	39%	43%
One Pupil Fixed	11	4	44	41
Both Pupils Fixed	82	0	9	9

Marshall,<sup>12</sup> 1991

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Description of Study: Prospective analysis of 746 patients in the Traumatic Coma Data Bank. Pupil status unknown in 106 of these patients.

Classification: Class II Study

Conclusions:

	GOS	
	1, 2	
Both Pupils Reactive At All Times	10%	
One Pupil Fixed	47	
Both Pupils Fixed	82	

Miller,<sup>13</sup> 1981

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Description of Study: A prospective study of 225 consecutive severe head injury patients in regard to outcome. 41% and 10% of the surgical and nonsurgical cases, respectively, had bilateral fixed pupils; age range 2-89.

Classification: Class III Study

Conclusions:

	GOS		
	1	2, 3	4, 5
Surgical: Both Pupils Fixed	77%	12%	11%
Nonsurgical: Both Pupils Fixed	71	11	18

Narayan,<sup>14</sup> 1981

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Description of Study: A study of 133 consecutive patients with severe head injury; age range 0-61+ years.

Classification: Class I Study

Conclusions:

	GOS		
	1	2-3	4-5
Both Pupils Reactive	16%	8%	76%
Both Pupils Unreactive	61	9	30

positive productive value (PPV) = 70%

Phonprasert,<sup>15</sup> 1980

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Description of Study: An analysis of 138 consecutive patients who were operated on for epidural hematomas with regard to factors influencing mortality; age range 3 to 71 years.

Classification: Class III Study

Conclusions:

	GOS
	1
One Pupil Fixed	15%
Both Pupils Fixed	56

Phuenpathom,<sup>16</sup> 1993

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Description of Study: A retrospective outcome prediction study of 109 consecutive with a GCS score of 3-15 who presented with an acute subdural hematoma. 83 patients had clot removal. Age range was 6 months to 79 years old.

Classification: Class III Study

Conclusions:

	GOS
	1
Both Pupils Reactive	16%
One Pupil Fixed	48
Both Pupils Fixed	88

Rivas,<sup>17</sup> 1988

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Description of Study: A series of 161 consecutive patients with a GCS score of 3-15 were operated on for epidural hematomas with regard to prognostic factors; age range 3 days to 78 years old.

Classification: Class II Study

Conclusions:

	GOS			
	1	3	4	5
One Pupil Fixed	14%	4%	43%	39%
Both Pupils Fixed	82	0	9	9

Sakas,<sup>18</sup> 1995

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Description of Study: One-year outcome analysis of 40 consecutive patients who underwent craniotomy for traumatic hematoma at various times after developing bilaterally fixed and dilated pupils (> 4 mm); age range 6-75 years old.

Classification: Class II Study

Conclusions:

	GOS		
	1, 2	3	4, 5
Patients Operated On Within Three Hours of Both Pupils Fixed	40%	30%	30%
Patients Operated On After Three Hours of Both Pupils Fixed	63	12	25
Patients Operated On for Epidural Hematomas and Both Pupils Fixed	18	27	55
Patients Operated On for Subdural Hematomas and Both Pupils Fixed	64	23	13

Stone,<sup>19</sup> 1983

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Description of Study: Review of 206 patients who were operated on for acute subdural hematomas; age range 3-88 years old.

Classification: Class III Study

Conclusions:

	GOS
	4, 5
One Pupil Fixed	25%
Both Pupils Fixed	25

Suddaby,<sup>20</sup> 1987

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Description of Study: Review of 49 cases of civilian gunshot wounds to the brain with a GCS score of 3-15; age range 8-92 years old.

Classification: Class III Study

Conclusions:

	GOS	
	1-3	4, 5
Both Pupils Reactive	28%	72%
Both Pupils Fixed	100	0

Wilberger,<sup>23</sup> 1991

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Description of Study: Review of 115 severely head injured patients (GCS  $\leq$  7) with subdural hematoma analyzing morbidity, mortality, and operative timing.

Classification: Class III Study

Conclusions:

	GOS
	1
Both Pupils Fixed	88%

## VIIa Description of Studies According to the Classification Criteria

First Author	# Pts	Pro-spective	Time	When was indicator measured	Method	Who did it	Outcome measure	When	Blind Observer	Multi variate observer	Statistics
Andrews	153	N	1981-1988	Admission	PE	NR	GOS	1-37 mo	N	N	Chi-square
Braakman	305	N	1973-1978	Best pupillary response within 24 hrs of admission	PE	NR	GOS	6 mo	NR	Y	Independence model
Choi	523	N	1976-1986	ER	PE	ER staff	GOS	6 mo	NR	Y	Location model discriminate analysis
Cordobes	82	N	1973-1980	Just before operation	PE	NR	GOS	NR	NR	N	Chi-square
Heiden	213	Y	NR	24 hrs p injury	PE	NR	GOS	12 mo	N	N	Mantel-Haenzel
Jennett	600	Y	1968-1976	Within 24hrs	PE	NR	GOS	6 mo	N	N	Chi-square
Jennett	1,000	Y	1968-1976	Within 24hrs	PE	NR	GOS	6 mo	N	N	Chi-square
Levin	300	Y	1984-1987	1 <sup>st</sup> post resuscitation pupillary activity & lowest post resuscitation pupillary activity	PE	Neurosurgeon	GOS (263 points) & complete neuro-psych eval (127 points)	12 mo	NR	Y	Log & linear regression
Lobato	64	N	1977-1986	At operation	PE	NR	GOS	6 mo	NR	N	Chi-square
Marshall	640	Y	1984-1987	Post resuscitation	PE	NR	GOS	Last contact	NR	Y	Chi-square
Miller	225	Y	1976-1980	Admission, mean delay 3 hrs p injury or time of deterioration	PE	Authors	GOS	3, 6, 12 mo	NR	N	Chi-square
Narayan	133	Y	1976-1979	Admission	PE	NR	GOS	3, 6, 12 mo	NR	Y	Log regression
Phonprasert	138	Y	1971-1978	NR	NR	NR	Mortality	NR	NR	N	Chi-square
Phuenpathom	109	N	1/86-12/89	Admission & 24hrs p admission	Referral notes/patient records	NR	GOS	6 mo	N	Y	Log regression
Rivas	161	N	1977-1986	Admission	PE	NR	GOS-Good recovery	6 mo	N	N	Chi-square
Sakas	40	B	1985-1988	Admission	PE, CT & chart review	Authors, residents, nurses	GOS	6 & 12 mo post op	NR	N	Chi-square
Stone	206	N	1/69-6/81	Pre-op	PE/chart review	NR	GOS-functional recovery	6 mo	N	N	Chi-square
Suddaby	49	N	1975-1985	Admission	Chart review	Authors	GOS	Discharge	N	NR	NR
Wilberger	101	N	1982-1987	Early operative, at time of operation/intervention < 4 hrs	NR	NR	GOS-functional recovery	18 mo	N	N	Chi-square, student's paired or pooled t-test p trauma

Abbreviations:

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NR= not recorded; ND= not done; PE= physical exam; B= retrospective & prospective

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# HYPOTENSION

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## I. Conclusions

- A. Which feature of the parameter is supported by Class I evidence and has at least a 70% positive predictive value (PPV)? A systolic blood pressure less than 90 mm Hg was found to have a 67% PPV for poor outcome and, when combined with hypoxia, a 79% PPV.
- B. Parameter measurement:
  1. How should it be measured?

Systolic and diastolic blood pressure should be measured using the most accurate system available under the circumstances. Monitoring by arterial line, when free of signal artifact, provides data that is both accurate and continuous and is the method of choice. Methods that do not determine the mean arterial pressure are less valuable.
  2. When should it be measured?

Blood pressures should be measured as frequently as possible. The incidence and duration of hypotension (systolic blood pressure < 90 mm Hg) should be documented by direct blood pressure values.
  3. Who should measure it?

Blood pressure should be measured by trained medical personnel.

## II. Overview

Secondary brain insults are defined as post-traumatic insults to the brain arising from extracranial sources and intracranial hypertension. They are generally ischemic and include hypotension, hypoxia, anemia, infection, etc. There is a growing body of evidence that secondary insults to the injured brain are common and can powerfully influence recovery. The most detrimental and best studied of these is hypotension. Because hypotension is amenable to therapeutic manipulation, an understanding of its influence on prognosis is useful for both prediction of outcome at present and optimization of recovery in the future.

## III. Process

A MEDLINE search back to 1966 was undertaken using the following key words: “head injury or brain injury” and “secondary insult or hypotension” and “outcome or prognosis” and “human subject.” This produced 70 references that were individually reviewed for design, content, and relevance. The results of this review were then incorporated into analysis presented here.

## IV. Scientific Foundation

In the scientific literature published to date, the definition of hypotension has been accepted from the literature on systemic insults. Despite the necessity for redefining this term in the brain injury literature, for the purposes of clarity in the following discussion, this entity is defined as:

- Hypotension = Systolic blood pressure < 90 mm Hg

The major secondary brain insults that have been studied with respect to their influence on outcome from severe brain injury are hypotension and hypoxia. Seminal studies by Miller, et al., established the importance of these secondary insults as outcome determinants, but did not study their independence with respect to other predictive factors.<sup>6,7</sup>

The largest and most definitive study of the influence of secondary brain insults on outcome comes from a Class I analysis of a large (717 patients), prospectively collected data set from the Traumatic Coma Data Bank (TCDB).<sup>2</sup> Hypotension was defined as a single measurement of a systolic blood pressure less than 90 mm Hg. The occurrence of one or more episodes of hypotension during the period from injury through resuscitation or during the shorter period of resuscitation only was associated with a doubling of mortality and a marked increase in morbidity (see Evidentiary Table).<sup>2</sup> Hypotension was found to be a statistically significant predictor of outcome and statistically independent of other major predictors of outcome, including age, hypoxia, and the presence or absence of severe trauma to one or more extracranial organ systems. When the influence of hypotension on outcome was controlled separately, the statistical significance of severe trauma to one or more extracranial organ systems as a predictor of outcome was eliminated, suggesting that the influence of systemic multiple trauma on the outcome of severe head injury patients is primarily mediated through hypotension.

The analysis of outcome from severe head injury in the TCDB revealed that the five most powerful predictors occurring from injury through resuscitation were age, intracranial (computed tomographic) diagnosis, pupillary reactivity, post-resuscitation Glasgow Coma Scale (GCS) score, and presence or absence of hypotension. Notably, of these five major predictors, only the occurrence and severity of hypotension is amenable to medical manipulation.

The analysis of a smaller, prospectively collected database from Australia corroborated the above findings.<sup>4</sup> This study found early and late hypotension to be statistically significant, independent predictors of outcome, both for mortality and for dichotomized quality of outcome (good or moderate-to-severe deficits versus vegetative survival or death). In this study, hypotension was again the only predictor amenable to medical modification.

Further support of the strong association between early hypotension and outcome comes from a study of the influence of various resuscitation fluids on the outcome of hypotensive multiple system trauma patients.<sup>12</sup> The subgroup of patients with severe head injuries had an overall mortality of 74%, with those being treated using conventional means of resuscitation having an 88% mortality rate.

A Class II report has recently extended the above findings to the pediatric population (age less than 17 years).<sup>10</sup> In this study, both hypoxia and hypotension had deleterious influences on outcome with hypotension being significantly more powerful in independently determining recovery. In this study, an episode of hypotension appeared to eliminate the generally more favorable outcome afforded by youth.

Although the above studies firmly establish an association between secondary brain insults (particularly hypotension) and outcome, they do not address the issue of whether preventing or treating such insults during this period improves recovery. With respect to secondary insults in general (hypotension, hypoxia, hypercapnia, and anemia), a recent Class III study addressed the ability of on-site, physician-directed resuscitation to decrease the incidence of secondary brain insults and improve outcome.<sup>1</sup> Patients whose secondary brain insults were reversed in the field had a 42% decrease in the frequency of poor outcomes (death, vegetative survival, or severe deficits) at three-month follow-up. Unfortunately, this study did not control for many confounding factors.

Nevertheless, it does suggest that patients with secondary brain insults that respond to treatment have improved outcome when compared to those that are refractory to correction.

With respect to hypotension in particular, Class II results from a recent Class I study strongly suggest that reversing or preventing hypotension in the field improves outcome. A recent prospective, randomized, placebo-controlled, multicenter trial examined the efficacy of administering 250 cc's of hypertonic (7.5%) saline versus normal saline as the initial resuscitation fluid in hypotensive, multiple-trauma patients. For the group as a whole, there was no statistically significant difference in outcome between the two groups. The hypertonic saline group did have improved blood pressure responses, decreased overall fluid requirements, and a trend toward improvement in survival. A retrospective, subgroup analysis of those patients with severe head injury, however, revealed that those patients in this group that received hypertonic saline as their initial bolus had a statistically significant improvement in survival measured at the time of discharge.<sup>12</sup> Although such a retrospective, subgroup analysis renders this a Class II result from a Class I study, it strongly suggests that the correction of hypotension in the field improves outcome from severe head injury.

The occurrence of early secondary brain insults also appears to be correlated with the subsequent appearance of other factors that are strongly associated with prognosis. In particular, early systemic hypotension appears to exacerbate the subsequent development of intracranial hypertension in terms of both frequency of occurrence and magnitude.<sup>5,8,11</sup> Unfortunately, at present, data regarding the strength of these associations and their independent utility as prognostic indicators are unavailable.

The improvement in outcome from severe head injury that would result if hypotension was eliminated as a secondary insult has been modelled.<sup>3</sup> The interaction of secondary brain insults occurring during the early (injury through resuscitation) and late (intensive care unit) periods was evaluated in 493 patients from the TCDB who survived at least nine hours in the intensive care unit. Although the definitions of early and late insults used in this study were somewhat different from previous TCDB investigations, the frequency of secondary insults remained high, with early hypotension occurring in 14% of patients and late hypotension in 32%. Of note, late hypotension was the only hypotensive insult in 24%. The percent outcome of vegetative survival or death was 17% for patients without hypotensive episodes, 47% for those with early hypotension, 66% for those with late hypotension, and 77% for those with both insults. Both early and late hypotension were significant, independent predictors of outcome in these patients, controlling for age, sex, mechanism of injury, GCS score, and intracranial diagnosis. Logistic regression modeling revealed that early hypotension was responsible for a 15-fold excess mortality and late hypotension for an 11-fold excess mortality, these two factors individually being the two most responsible for excess risk of any analyzed variables.

The influence on outcome of iatrogenic hypotensive episodes was reported in a Class III study that examined the influence of intraoperative hypotension on outcome in patients with severe head injury who had not otherwise been hypotensive.<sup>9</sup> All procedures were performed within 72 hours of admission. Patients with intraoperative hypotension had significantly worse neurologic outcomes than those without. Additionally, outcome was inversely correlated with duration of intraoperative hypotension. This study suggests that the potential benefits of therapeutic procedures can be reversed if there is concomitant hypotension. Therefore, the performance of these procedures either has to be predicated on strict avoidance of hypotensive episodes or consideration be given to delaying them.

## V. Summary

Hypotension, occurring at any time from injury through the acute intensive care course, has been found to be a primary predictor of outcome from severe head injury for the health care delivery systems within which prognostic variables have been best studied. Hypotension is repeatedly found to be one of the five most powerful predictors of outcome and is generally the only one of these five that is amenable to therapeutic modification. A single recording of a hypotensive episode is generally associated with a doubling of mortality and a marked increase in morbidity from a given head injury. The estimated reduction in unfavorable outcome that would result from the elimination of hypotensive secondary brain insults is profound.

## VI. Key Issues for Future Investigation

Although the impact on outcome of hypotension as a secondary brain insult is well established, there are only very preliminary studies on how it can be eliminated or minimized, on what the effective mechanisms are for doing so, and on what the specific influences are on outcome of such protocols. There is also little known as to the “critical values” of magnitude and duration for hypotension following brain injury. Future investigations must prospectively collect accurate and frequent physiologic data on the occurrence of hypotension (systolic blood pressure < 90 mm Hg) as well as the actual blood pressure values throughout resuscitation. Critical physiologic threshold values and the efficacy of various therapeutic manipulations in decreasing secondary brain insults and improving outcome must be derived from such data using statistical methods that control for factor-factor interactions as well as the magnitude of effect attributable to individual factors. Given the magnitude of influence on outcome attributed to secondary insults in predictive models, investigations into their prevention or elimination might well represent the area of early brain injury treatment with the greatest potential for improving outcome.

## VII. Evidentiary Table for Resuscitation of Blood Pressure and Oxygenation

Carrel,<sup>1</sup> 1994

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Description of Study: Retrospective study of 51 consecutive patients with non-penetrating severe head injury treated with physician-directed aggressive advanced traumatic life support in the field. They assessed the effect of secondary insults on 3-month outcome. The secondary insults studied were anemia (hematocrit  $\leq$  30%), hypotension (systolic arterial pressure  $\leq$  95 mm Hg), hypercapnia (PaCO<sub>2</sub>  $\geq$  45 mm Hg), and hypoxemia (PaO<sub>2</sub>  $\leq$  65 mm Hg).

Classification: Class III Study

Conclusions:

	GOS 1, 2, 3	GOS 4, 5
No Secondary Insults	42%	58%
Secondary Insults	72	28

Chesnut,<sup>2</sup> 1993

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Description of Study: A prospective study of 717 severe head injury patients admitted consecutively to four centers investigated the effect on outcome of hypotension (systolic blood pressure [SBP] < 90 mm Hg) occurring from injury through resuscitation.

Classification: Class I Study

Conclusions:

	GOS 1	GOS 2, 3	GOS 4, 5
Neither	27%	19%	54%
Hypoxia	28	22	50
Hypotension	50% + PPV=67%	17	33
Both	57% + PPV=79%	22	20

Chesnut,<sup>3</sup> 1993

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Description of Study: A prospective study of 717 severe head injury patients admitted consecutively to four centers investigated the effect on outcome of hypotension (SBP < 90 mm Hg) occurring from injury through resuscitation (early hypotension; N = 717) or in the Intensive Care Unit (ICU) (late hypotension; N = 493).

Classification: Class I Study

Conclusions:

	GOS 1, 2	Relative Risk of Mortality
No Hypotension	17%	
Early Hypotension	47	15-fold (p < 0.001)
Late Hypotension	66	11-fold (p < 0.001)
Early & Late Hypotension	77	

Fearnside,<sup>4</sup> 1993

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Description of Study: A prospective study of 315 severe head injury patients admitted consecutively to a single center investigated prehospital and in-hospital predictors of outcome.

Classification: Class I Study

Conclusions:

	GOS 1
No Hypotension	27%
Hypotension	42

Miller,<sup>6</sup> 1982

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Description of Study: 225 severe head injury patients were prospectively studied with respect to the influence of secondary insults on outcome. The predictive independence of hypotension in comparison to other associated factors, however, was not investigated.

Classification: Class II Study

Conclusions:

	GOS 1	GOS 2, 3	GOS 4, 5
Neither	24%	12%	64%
Hypoxia*	50	9	41
Hypotension*†	53	12	35
Anaemia*	52	9	38

\*Secondary insults not mutually exclusive.

†Hypotension = systolic blood pressure < 95 mm Hg

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Miller,<sup>7</sup> 1978

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Description of Study: 100 consecutive severe head injury patients were prospectively studied with respect to the influence of secondary insults on outcome (report of first 100 patients in subsequent report of 225 patients [*vide supra*]). Hypotension (SBP < 95 mm Hg) associated with a trend (not statistically significant) toward worse outcome in entire cohort; trend met statistical significance for patients without mass lesions. Influence of hypotension on outcome not analyzed independently from other associated factors.

Classification: Class III Study

Conclusions:

	GOS 1, 3	GOS 4, 5
Patients with Mass Lesions		
No Insults	50%	50%
Systemic Insults*	75	25
Patients without Mass Lesions†		
No Insults	12	88
Systemic Insults*	36	64

\*Systemic insults = hypoxia, hypotension, anemia, hypercarbia

†Statistically significant

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Pietropaoli,<sup>9</sup> 1992

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Description of Study: Retrospective review of the impact of intraoperative hypotension (SBP < 90 mm Hg) on 53 otherwise normotensive severe head injury patients who required early surgery (within 72 hours of injury).

Classification: Class III Study

Conclusions:

Intraoperative			
Hypotension	GOS 1	GOS 2, 3	GOS 4, 5
No	25%	17%	58%
Yes	82	2	6

The inverse correlation of intraoperative hypotension with outcome was duration dependent.

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Pigula,<sup>10</sup> 1993

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Description of Study: 58 children (< 17 years old) with severe head injuries were prospectively studied for the effect of hypotension (SBP < 90 mm Hg) on outcome.

Classification: Class II Study

Conclusions:

	Mortality	
	Children	Adults
No Hypotension or Hypoxia	16%	42%
Hypotension or Hypoxia	67	66

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Vassar,<sup>12</sup> 1993

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Description of Study: Prospective, randomized, controlled, multicenter trial comparing the efficacy of administering 250 ml of hypertonic saline with or without dextran 70 vs normal saline as the initial resuscitation fluid in facilitating the resuscitation and improving the outcome of hypotensive trauma patients. In this trial, the hypertonic saline group had significantly improved blood pressure responses and decreased overall fluid requirements. Although there was an associated improvement in survival for the overall group, it did not reach statistical significance. Post-hoc analysis of the severe head injury group (Class II analysis) revealed that the hypertonic saline group had a statistically significant improvement in survival-to-discharge vs that predicted by the Major Trauma Outcome Study (MTOS).\*

Classification: Class II Study

Conclusions:

	LR	HS	HS-6%	HS-12%
Predicted GOS 1 (MTOS)	86%	87%	84%	86%
Actual GOS 1	88	66	73	70
P (Actual vs Predicted)	NS	< .001	< .05	< .005

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Abbreviations:

LR=Lactated Ringer's

HS=Hypertonic (7.5%) saline

HS-6%=Hypertonic saline with 6% dextran 70

HS-12%=Hypertonic saline with 12% dextran 70

NS=Not significant

- This study was a prospective, randomized, placebo-controlled trial for hypotensive trauma victims in general. The analysis with respect to severe head injury patients was post-hoc so that, although data collection was prospective, randomization of the subgroup was not in a strict sense. Therefore, with respect to the group of severe head injury patients, this is a Class II study. See text for details.

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# CT SCAN FEATURES

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## I. Conclusions

- A. Which feature of the parameter is supported by Class I and strong Class II evidence and has at least a 70% positive predictive value (PPV) in severe head injury?
  - a. Presence of abnormalities on initial computed tomography (CT) examination
  - b. CT classification
  - c. Compressed or absent basal cisterns
  - d. Traumatic subarachnoid hemorrhage (tSAH):
    - Blood in the basal cisterns
    - Extensive tSAH
- B. Parameter measurement:
  - 1. How should it be measured?
    - Compressed or absent basal cisterns measured at the midbrain level.
    - tSAH should be noted in the basal cisterns or over the convexity.
    - Midline shift should be measured at the level of the septum pellucidum.
  - 2. When should it be measured?
    - Within 12 hours of injury
    - The full extent of intracranial pathology, however, may not be disclosed on early CT examination.
  - 3. Who should measure it?
    - A neuroradiologist or other qualified physician, experienced in reading CT-scans of the brain

## II. Overview

The classical clinical features with prognostic significance in patients with severe traumatic brain injury (TBI) include age, Glasgow Coma Scale (GCS) score, pupil reactivity, brainstem reflexes, and the presence of post-traumatic hypotension. Many patients today arrive in the hospital already intubated, paralyzed, and ventilated. An accurate estimation of the GCS score and changes in the GCS score in the initial hours after trauma are therefore often difficult to obtain. In a recent survey on patients with severe and moderate head injury, conducted by the European Brain Injury Consortium, the full GCS score was only testable in 56% of patients on admission to neurosurgery (Murray, et al.,<sup>2</sup> 1998). Prognostic features based on the results of technical examinations are therefore needed. CT scanning is routinely performed in all patients with severe TBI and provides information with important therapeutic implications for operative intervention or indications for intracranial pressure (ICP) monitoring, and may provide information concerning prognostic significance.

## III. Search Process

A MEDLINE search from 1976 through mid-1998 was undertaken using the following key words: “head injury,” “computerized tomography,” “prognosis,” and “outcome”. A search on “head injury,” “CT scan,” and “prognosis” resulted in 27 articles, and a search on “head injury,” “CT scan,” and “outcome” in 55 articles. Only English-language literature and papers reporting on adult head injury were reviewed. In total, 31 manuscripts relevant to the prognostic value of the CT scan in the acute stage of adult head injury were identified.

Individual CT characteristics found to be particularly relevant in terms of prognosis were:

- a. Status of basal cisterns
- b. tSAH
- c. Presence and degree of midline shift
- d. Presence and type of intracranial lesions

These subheadings, including “intraventricular hemorrhage,” “intracranial lesions,” “normal CT,” “epidural hematoma,” and “subdural hematoma” were then subjected to a second search, combining these with “head injury,” “brain injury,” “prognosis,” and “outcome.” This search yielded an additional 18 manuscripts. Cross referencing and expertise available amongst authors added an additional 14 manuscripts.

#### IV. Scientific Foundation

Topics analyzed for prognostic significance were:

- A. Abnormalities on CT
- B. CT classification
- C. Individual CT characteristics:
  - Status of basal cisterns
  - tSAH
  - Midline shift
  - Presence or absence of intracranial mass lesions

If data permitted, the prognostic value of each feature was analyzed with respect to the Glasgow Outcome Scale (GOS)<sup>1</sup>, dichotomized into unfavorable (dead, vegetative, severe, disabled) and favorable outcome (moderate disability/good recovery). If such analysis was not possible on data reported, features were related to mortality.

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##### **A. Abnormal CT Scan**

Description of parameter: Any abnormality noted on CT examination, consistent with TBI.

##### Reliability of Scoring

No reports concerning the intraobserver reliability in scoring presence or absence of abnormalities on CT examination after head injury are reported. The incidence of occurrence of abnormalities on CT varies in two reports of the Traumatic Coma Data Bank (TCDB). In the initial report by Eisenberg, et al. (1990), describing the CT scan in 753 patients, a normal CT was observed in 45 patients<sup>2</sup>; in the subsequent report by Marshall, et al. (1991), despite a slightly lower number of patients reported in the study (746) an incidence of 52 cases is described. Whether this discrepancy is caused by observer variation or due to methodological inconsistencies is unclear.

### Incidence of Abnormal CT

The reported incidence of abnormalities on CT scan in patients with severe traumatic brain injury (TBI) varies between 68%-94%. Data are summarized in Table 1.

Table 1 — Incidence of Abnormal CT Scans in Severe TBI Patients

First Author	Study Population	Incidence of Abnormal CT	
Sweet, <sup>10</sup> 1978	140 patients GCS $\leq$ 8	114/140	81.5%
Narayan, <sup>8</sup> 1981	133 severely head-injured patients	91/133	68.5
Holliday, <sup>4</sup> 1982	160 patients with closed head injury who had a CT scan within 24 hours of admission, in whom ICP was monitored	143/160	89
Van Dongen, <sup>11</sup> 1983	GCS $\leq$ 8	102/116	88
Lobato, <sup>5</sup> 1986	GCS $\leq$ 8	402/448	90
Eisenberg, <sup>2</sup> 1990	GCS $\leq$ 8 within 48 hours	708/753	94
Marshall, <sup>6</sup> 1991	GCS $\leq$ 8 Traumatic Coma Data Bank	694/746	93
Selladurai, <sup>9</sup> 1992	GCS $\leq$ 8	101/109	93
Fearnside, <sup>3</sup> 1993	GCS $\leq$ 8	275/315	87
European			
Nimodipine trial, <sup>1</sup> 1994	GCS $\leq$ 8	754/819	92
EBIC survey, <sup>7</sup> 1998	GCS $\leq$ 12	862/983	87

### Prognostic Value

Class I and Class II studies show presence of abnormalities on CT to have a positive predictive value of 77%-78% with respect to unfavorable outcome in series of patients with severe head injury as defined by a GCS score of 8 or less. However, both studies already have an incidence just over 70% of unfavorable outcome in the overall population. The predictive value of presence of abnormalities on initial CT examination is therefore limited. The negative predictive value, that is, the relation between absence of abnormalities and favorable outcome, is of much greater importance and significance. Prognosis in patients without abnormalities on initial CT examination is better than in the overall population of patients with severe head injury. Favorable outcomes are reported by Narayan, et al. (1981), Van Dongen, et al. (1983), Holliday, et al. (1982), and Lobato, et al. (1986), in 76%-83% of patients with a normal CT scan on admission.<sup>4, 5, 6, 11</sup> Marshall, et al. (1991), in the report on the TCDB find 62% favorable outcome in patients with a normal CT scan on admission (diffuse injury I).<sup>6</sup> This lower percentage with respect to the other series reported is probably caused by the earlier determination of outcome (e.g., on discharge). Lobato, et al. (1986), however, showed that in approximately one-third of the patients with an initial normal CT scan new lesions may develop on subsequent CT examination. In these patients, ICP can be raised in up to 75% of cases. Patients developing such new lesions had a slightly less favorable outcome than when CT scan remained normal (65% vs 76%). Admission GCS score was not related to outcome in patients without abnormalities.<sup>5</sup> Holliday, et al. (1982), show the occurrence of raised ICP requiring treatment in 41% of patients with a normal CT scan on admission. In 85% of these patients there was severe concomitant pulmonary injury and/or post-traumatic hypotension.<sup>4</sup>

## Conclusions

- Initial CT examination demonstrates abnormalities in approximately 90% of patients with severe head injury.
- Prognosis in patients with severe head injury with demonstrable pathology on initial CT examination is less favorable than when CT is normal.
- In patients with a normal CT on admission, outcome is primarily related to concomitant extracranial injuries.
- The absence of abnormalities on CT at admission does not preclude the occurrence of raised ICP, and significant new lesions may develop in 40% of patients.

## Evidentiary Table — Abnormal CT and Outcome Holliday,<sup>4</sup> 1982

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Years of Study: 1976-1980

Description of Study: Study on predictive value of normal CT scan in head injury. Seventeen patients out of a series of 160 with severe head injury (GCS < 9) and ICP monitoring showing a normal CT.

Classification: Class III Study

Conclusions: Seven of 17 patients with a normal CT scan showed elevated ICP over 25 mm Hg. Six of these patients had major pulmonary injury. Overall outcome was good. In only 3 patients was the outcome unfavorable and this was due to extracranial pathology.

## Van Dongen,<sup>11</sup> 1983

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Years of Study: 1977-1979

Description of Study: Prospective, consecutive series examining prognostic value of CT in 121 patients with severe head injury.

Classification: Class I Study

Conclusions: Normal CT scan was noted in 14 patients (12%). Outcome in this small group was favorable (78.5%).

Outcome at 1 Year:	GOS 1, 2, 3	GOS 4, 5
Normal Scan	3%	11%
Abnormal Scan	76	1
PPV*: 78%		

\*Positive predictive value

## Lobato,<sup>5</sup> 1986

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Years of Study: 1977-1985

Description of Study: Forty-six patients out of a total series of 448 severe head injury with GCS score of 8 or less for at least 6 hours after injury showing no abnormalities on CT.

Classification: Class II Study

Conclusions: No abnormalities were noted in 10.2% of patients with severe head injury. Absence of abnormalities showed a PPV of 76% to favorable outcome. Twenty-four of the 46 patients with a normal CT scan on admission developed new lesions on subsequent examinations. 71% of these patients had a raised ICP. A moderate degree of raised ICP was only seen in 4 patients (8.5%) when the CT remained normal. Outcome was more unfavorable when new lesions developed.

Outcome at 6 Months:	Unfavorable	Favorable
GCS 3-4	4	11
GCS 5-8	7	24

#### Marshall,<sup>6</sup> 1991

Years of Study: 1984-1987

Description of Study: Prospective study of 746 patients with severe head injury.

Classification: Class II Study

Conclusions: Incidence of normal CT scan in this prospective series was 6.9%. There was favorable outcome on discharge in 61% of these patients.

Outcome at Discharge:	Unfavorable	Favorable
Normal CT Scan	20	32
(Diffuse Injury I Abnormal CT Scan	522	155

PPV: 77%

#### Evidence for Classification

First Author	>25	GOS 6 Months	Prospective	Indicator 24 hours	Statistics	Class
Lobato <sup>5</sup>	+	+	+	+	-	II
Holliday <sup>4</sup>	-	-	-	+	-	III
Van Dongen <sup>11</sup>	+	+	+	+	+	I
Marshall <sup>6</sup>	+	-	+	+	-	II

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## **B. CT Classification of Head Injury and Its Prognostic Significance**

Conventional classification of CT findings in severely head-injured patients differentiates between focal (extradural and subdural hematomas, as well as intracerebral hematomas and space occupying contusions) and diffuse head injuries (Gennarelli, et al., 1982).<sup>3</sup> Diffuse injuries according to this classification are defined by the absence of mass lesions, although small contusions without mass effect may be present. In terms of outcome, patients with diffuse injuries were found to have an intermediate prognosis when compared to patients with epidural or subdural hematomas. While acute subdural hematomas with low GCS scores had a high mortality, diffuse injuries with higher GCS scores showed a low mortality and a high incidence of good recovery.

In practice, some confusion exists between this category of patients with diffuse lesions and the more neuropathologically oriented entity of diffuse axonal injury (DAI). DAI is based primarily on neuropathological hallmarks, characterized by wide-spread tearing of axones and/or small blood vessels. Radiologic criteria for diagnosis of DAI are small hemorrhagic lesions at the cortico-medullary junction, in the corpus collosum, in the midbrain, and in the brain stem, sometimes in conjunction with some intraventricular bleeding. DAI can sometimes be superimposed by generalized brain swelling (Adams, et al., 1982; Zimmerman, et al., 1978).

Lobato, et al. (1983), have expanded on the anatomical patterns of the conventional CT classification, outlining eight categories of injury, mainly subdividing patients with focal lesions (Table 1). This classification was shown to have a stronger predictive value than the conventional categorization. Outcome was significantly better in extradural hematoma without concomitant brain swelling, simple brain contusion, generalized swelling, and in the absence of lesions.

Table 1  
Classification of CT Lesions and Outcome (Lobato,<sup>4</sup> 1983)

CT Findings	Number of Patients	Unfavorable Outcome (%)
No Lesions	28	32%
Extracerebral Hematoma	19	15
Extracerebral Hematoma and Swelling	27	100
Bilateral Swelling	42	12
Single Brain Contusion	45	22
Multiple Unilateral Contusion	32	84
Multiple Bilateral Contusion	42	54
Diffuse Axonal Injury	43	86

Marshall, et al. (1991), in the publication on the Traumatic Coma Data Bank, propose a new classification in which the category of diffuse injury is further expanded, taking into account signs of raised ICP (i.e., compressed or absent basal cisterns), midline shift, and the presence of mass lesions (Table 2).

Table 2  
CT Classification TCDB

Category	Definition
Diffuse Injury I (no visible pathology)	No visible intracranial pathology seen on CT scan.
Diffuse Injury II	Cisterns are present with midline shift 0-5 mm and/or lesions densities present, no high or mixed density lesion > 25 cc, may include bone fragments and foreign bodies.
Diffuse Injury III (swelling)	Cisterns compressed or absent with midline shift 0-5 mm, no high or mixed density lesion > 25 cc.
Diffuse Injury IV (shift)	Midline shift > 5 mm, no 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.

The frequency of occurrence of the various CT categories according to this classification in three large series of head injury patients is shown in Table 3.

Table 3  
Incidence of CT Categories in Head Injury (Marshall,<sup>5</sup> 1991)

	TCDB n = 746		European Nimodipine Trial n = 819		EBIC Survey n = 983	
Diffuse Injury I	52	7%	69	8.4%	121	12%
Diffuse Injury II	177	23.7	270	32.9	273	28
Diffuse Injury III (swelling)	153	20.5	89	10.9	101	10
Diffuse Injury IV (shift)	32	4.2	31	3.8	21	2
Evacuated Mass Lesion	276	37	314	38.3	467	48
Non-Evacuated Mass Lesion	36	4.8	36	4.4		

A clear correlation between CT classification and outcome was shown on analysis of the TCDB (Table 4).

Table 4  
CT Classification and Outcome on Discharge (Marshall,<sup>5</sup> 1991)

	Number of Patients	Unfavorable Outcome (D, VS, SD)	Favorable Outcome (MD + GR)
Diffuse Injury I	52	38%	62%
Diffuse Injury II	177	65	35
Diffuse Injury III	153	84	16
Diffuse Injury IV	32	94	6
Evacuated Mass Lesion	276	77	23
Non-Evacuated Mass Lesion	36	89	11

Walder, et al. (1995), have compared the predictive value of the TCDB classification to the worst applicable severity code from the Abbreviated Injury Score (AIS). A high correlation was found between AIS and outcome at six months, the TCDB classification and outcome as well as between GCS score and outcome. The predictive power for favorable outcome was shown to be greater for the AIS score than for the TCDB classification (Table 5), with a PPV of 95% toward favorable outcome in the AIS scores 0-3. Conversely an AIS score of 5 was shown to have a PPV of 71% toward the outcome categories dead or vegetative.

Table 5  
 Predictive Power of AIS, TCDB, CT Classification, and GCS score (Walder<sup>7</sup>, 1995)

	Statistical Value of Prediction			Likelihood Ratio	Percentage Correct Predictions
	Sensitivity	Specificity	Positive Predictive Value		
AIS 0-3	40%	98%	95%	25:1	73%
TCDB					
Classification I-IV	51	86	75	3:6:1	66
GCS score 6-8	57	69	59	1:9:1	64

#### Conclusions

- A strong correlation exists between the worst intracranial AIS severity code of the initial CT in severe head injury and outcome at six months.
- The TCDB CT classification is strongly correlated to outcome.

#### Recommendations for Further Research

- Investigation of interobserver reliability in classifying severe head injury according to CT scan.
- There should be further investigation concerning predictive power of the intracranial AIS severity code of the initial CT.

#### Evidentiary Table — CT Classification and Outcome Gennarelli,<sup>3</sup> 1982

Description: Retrospective analysis of 1,107 patients with severe head injury from seven centers analyzing outcome and type of CT lesion.

Classification: Class III Study

Conclusions: Differentiation of focal versus diffuse injuries being split into two categories of severity: marked heterogeneity of outcome; type of lesion as important on outcome as GCS score. Rank order of prognosis: subdural hematoma < diffuse injuries < extradural hematoma.

#### Lobato,<sup>4</sup> 1983

Years of Study: 1977-1982

Description: Study of a consecutive series of 277 severely head-injured patients.

Classification: Class II/III Study

Conclusions: Patients with pure extracerebral hematoma, single brain contusion, generalized brain swelling, and normal CT scans had a significantly better outcome than patients developing acute hemispheric swelling after operation for a large extracerebral hematoma or patients with multiple brain contusion, either unilateral or bilateral, and patients with DAI.

## Marshall,<sup>5</sup> 1991

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Years of Study: 1984-1987

Description: Prospective study of a consecutive series of 746 severely head-injured patients in four centers (TCDB).

Classification: Class II Study

Conclusions: CT classification has clear prognostic value.

## Walder,<sup>7</sup> 1995

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Years of Study: 1986-1988

Description: Prospective series of 109 severely head-injured patients ( $GCS \leq 8$ ) evaluating predictive value of worst applicable intracranial severity score from the AIS and CT classification according to the TCDB.

Classification: Class I Study

Conclusions: The AIS based on initial CT scan provides useful prognostic information in patients with severe head injury. The predictive value of an AIS 0-3 for favorable outcome is higher than the TCDB classification.

## Evidence for Classification

Author	> 25 patients	GOS/ mortality 6 months	Prospective	Indicator within 24 hours	Statistics	Class
Gennarelli <sup>3</sup>	+	-	-	-	-	III
Lobato <sup>4</sup>	+	+	+	-	-	II/III
Marshall <sup>5</sup>	+	-	+	+	-	II
Walder <sup>7</sup>	+	+	+	+	+	I

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### C. Individual CT Scan Characteristics

Definition of parameter: Although the status of the basal cisterns is one of the best studied CT parameters of prognostic significance, it remains ill defined. Most studies concerning the state of the basal cisterns focus on the perimesencephalic cisterns. Authors describe absent, compressed, or open cisterns. Only two authors give definitions of the parameter studied.<sup>11, 15</sup>

- Partial obliteration: Cisterns visible as hypodense slits, usually in one hemisphere.
- Complete obliteration: Cisterns no longer visible as CSF (cerebrospinal fluid) spaces.

Liu, et al. (1995), suggest adding aspects concerning density and deformation of the brain stem in a grading system to the basal cisterns. They describe a good correlation between their proposed grading scale (Grades 0-5) and outcome.<sup>9</sup>

#### Reliability of Scoring Basal Cisterns

No interobserver variation studies have been reported concerning the reliability of scoring of the basal cisterns.

#### Incidence

An overview of the incidence of compressed or absent basal cisterns in reported series of patients with severe head injury is shown in Table 1.

Table 1  
Incidence of Compressed or Absent Basal Cisterns

First Author	Patient Population	Incidence
Van Dongen, <sup>15</sup> 1983	GCS $\leq$ 8	80/116 68.9%
Teasdale, <sup>12</sup> 1984	diffuse head injury in coma	19/37 51
Toutant, <sup>14</sup> 1984	GCS $\leq$ 8	118/218 54
Cordobes, <sup>4</sup> 1986	78 patients with diffuse axonal injury	59/78 76
Colquhoun, <sup>3</sup> 1989	comatose head injury	49/60 81.6
Eisenberg, <sup>5</sup> 1990	GCS $\leq$ 8 within 48 hours	413/753 58
Selladurai, <sup>11</sup> 1992	GCS $\leq$ 8	74/109 67.8
European Nimodipine Trial <sup>1</sup>	GCS $\leq$ 8	472/819 57.6

#### Association with Other Prognostic Indicators

Two studies describe a strong association between status of the basal cisterns and pupil reactivity.<sup>12, 15</sup> Other authors report an association with the GCS score<sup>2, 14</sup> and with the presence of focal lesions<sup>2</sup> or with a history of early hypoxic or hypotensive insults.<sup>5</sup>

Table 2  
Pupil Reactivity and Status of Basal Cisterns

Status of Cisterns	Pupil Reactivity	
	One or Both Reacting	Neither Reacting
Cisterns Present	17%	1%
Cisterns Absent	12	7

(Teasdale, <sup>12</sup> 1984)

Status of Cisterns	Pupil Reactivity	
	Both Reacting	One or None
Partially or Completely Open	40%	17%
Completely Obliterated	14	44

(Van Dongen, <sup>15</sup> 1983)

#### Status of Basal Cisterns and Other CT Indicators of Raised ICP

Compression or absence of the basal cisterns on CT scan is considered one of the indicators of raised intracranial pressure (ICP).<sup>7, 10, 13</sup> Other signs of raised ICP include obliteration of the third ventricle and the presence of small ventricles, often considered indicative of diffuse brain swelling in the absence of midline shift. Some authors combine the status of the third ventricle and that of the basal cisterns in evaluating prognostic significance. Teasdale, et al. report that the third ventricle usually becomes obliterated before the basal cisterns.<sup>13</sup> In the study by Lang, et al. (1994), on 118 patients with diffuse traumatic brain swelling, however, no direct relation was seen between the status of the third ventricle and that of the basal cisterns. When the third ventricle was not visible the basal cisterns remained present in more than half of the patients.<sup>8</sup>

The assessment of the lateral ventricles as being “slitlike” is debatable and in the absence of knowledge of the pretraumatic size of the ventricles it is difficult to attach too much importance to the size of the ventricles. Especially in children the size of the lateral ventricles may normally be small.<sup>15</sup> The main CT parameters indicating raised ICP, therefore, are the status of the third ventricle and that of the basal cisterns. This is confirmed by two Class II studies<sup>5, 12</sup> and one Class III study.<sup>3</sup>

#### Prognostic Value

One Class I,<sup>15</sup> four Class II,<sup>4, 5, 11, 12</sup> and various Class III studies<sup>2, 3, 14, 16</sup> describe an association between compression or absence of basal cisterns and unfavorable outcome. Van Dongen, et al. (1983), in a series of 116 comatose head injured patients in whom CT was performed, showed a 97% positive predictive value for unfavorable outcome when the cisterns were completely obliterated.<sup>15</sup> In a stepwise forward selection of features using the multinomial independence model, the state of the basal cisterns together with lesions of the brain parenchyma emerge as a powerful combination of predictors. Sharp predictions based on these two variables could be made in 30% of cases, all predictions related to the probability of death. The predictive performance of a set of four common CT combinations, using the state of the basal cisterns as the basic discriminative feature was remarkable, allowing predictions in 63% of cases of which 93% were accurate. However, when combining a set of CT features with clinical features including pupil reactivity, best motor response, and age, the state of the basal cisterns was not selected as a discriminating parameter. This was caused by overlap in prognostic information in relation to the pupil reactivity.

In the preliminary report on CT features in the national pilot TCDB, the ominous value of compressed or absent basal cisterns in severe head injury was further demonstrated.<sup>14</sup> Mortality rate when cisterns were absent was 77%; 39% when cisterns were compressed; and only 22% when cisterns were open. A relatively greater importance of cisterns in the risk of poor outcome was shown among patients with a GCS score of 6 to 8. These data were confirmed in the report by Eisenberg, et al. (1990), on the initial CT findings from the NIH TCDB.<sup>5</sup> In this study the risk of dying in severely head-injured patients was increased twofold if the mesencephalic cisterns were compressed or obliterated. The risk of elevated ICP for those patients with abnormal cisterns was increased threefold compared to patients with normal cisterns. The value of the status of the basal cisterns as an indicator for presence of increased ICP has been confirmed in many other studies. Cordobes, et al. (1986), in a small study of 78 patients with post-traumatic diffuse axonal injury, showed increased ICP to be present in 50% of the patients with CT scan evidence of ventriculocisternal collapse and this phenomenon was also associated with an unfavorable outcome.<sup>4</sup> Similar conclusions were drawn by Colquhoun, et al. (1989), and Teasdale, et al. (1984).<sup>3, 12</sup>

Yanaka, et al. (1993), in a retrospective study on 170 patients with acute subdural hematoma also show in these patients a positive predictive value of 77% to unfavorable outcome in the presence of compressed basal cisterns.<sup>16</sup>

#### Conclusions

- Compressed or absent basal cisterns indicate a threefold risk of raised ICP.
- Status of basal cisterns is related to outcome.
- Mortality is increased two- to threefold in the presence of compressed or absent basal cisterns.
- Strong association exists between the status of the basal cisterns and pupil reactivity.
- Some association of the status of the basal cisterns is reported with GCS score, presence of focal lesions, or early hypoxic and hypotensive insults.

#### Recommendation for Future Research

- Define and test better definition of open, partially compressed, or absent basal cisterns.
- Determine of observer reliability.
- Need to further investigate the independent value of the status of basal cisterns as predictive parameter.
- Need to further investigate the relative value of status of basal cisterns and compression of third ventricle as indicator of raised ICP and CT-predictor.

#### Evidentiary Table: Basal Cisterns and Outcome

Van Dongen,<sup>15</sup> 1983

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Years of Study: 1977-1979

Description: Prospective consecutive series examining prognostic value of CT in 121 patients with severe head injury.

Classification: Class I Study

Conclusions: Status of the basal cisterns was shown to be a powerful prognostic indicator, but is strongly related to pupil reactivity. Based on status of the basal cisterns and the presence or absence of lesions in the brain parenchyma, sharp predictions were possible in 30% of cases. Adding CT features to clinical features increased the rate of sharp predictions from 48% to 62%.

Outcome 12 Months:

	Unfavorable	Favorable
Open Cisterns	12	19
Compressed Cisterns	10	11
Absent Cisterns	57	2

PPV = 84% (67/80)

Teasdale,<sup>12</sup> 1984

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Description: Prospective analysis of 37 patients with severe diffuse injury.

Classification: Class II Study

Conclusions: Compression of third ventricle and basal cisterns closely correlated with increased ICP and worse prognosis. Association between pupil reactivity and status of the basal cisterns.

Status Basal Cisterns/Third Ventricle:

	Unfavorable Outcome	Favorable Outcome
Present	9	9
Absent	15	4

Toutant,<sup>14</sup>1984

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Years of Study: 1981-1982

Description: Prospective study of 218 patients with severe head injury (GCS < 8) from the pilot phase of the National Traumatic Coma Data Bank analyzing prognostic importance of basal cisterns.

Classification: Class III Study

Conclusions: Mortality was doubled when basal cisterns were compressed and increased threefold when absent. Prognostic value remained strong after adjusting for GCS score. Status of the cisterns was more important in patients with higher GCS scores.

	Unfavorable Outcome	Favorable Outcome
Open Cisterns (n = 82)	44	56
Compressed Cisterns (n = 70)	64	46
Absent Cisterns (n = 48)	85	15

Cordobes,<sup>4</sup> 1986

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Years of Study: 1977-1984

Description: Selected series of 78 patients with diffuse axonal injury.

Classification: Class II Study

Conclusions: Collapsed or absent basal cisterns present in 59 out of 78 (75%) patients.

Compression or absence of basal cisterns is correlated to unfavorable outcome

Outcome at 6 Months:

	Unfavorable	Favorable
Open Cisterns	12	7
Compressed Cisterns	20	7
Absent Cisterns	29	

PPV = 87%

Colquhoun,<sup>3</sup> 1989

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Years of Study: 1985-1986

Description: Retrospective study on prognostic significance of third ventricle and basal cisterns in 60 patients whose CT scan showed evidence of primary brain injury.

Classification: Class III Study

Conclusions: Compression and obliteration of the third ventricle and basal cisterns were shown to have a close correlation with raised ICP and poor prognosis.

Outcome at 6 Months:

	Unfavorable	Favorable
Normal Third Ventricle and Basal Cisterns		2 9
One or Both Compressed	10	8
One or Both Absent	26	5

Eisenberg,<sup>5</sup> 1990

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Years of Study: 1984-1987

Description: CT features studied in National Traumatic Coma Data Bank.

Classification: Class II Study

Conclusions: Compressed cisterns were noted in 58% of patients. Abnormal cisterns indicate a threefold risk of abnormal ICP and a threefold increase in mortality. An association exists between diffuse swelling as defined by abnormal cisterns and/or small ventricles and early hypoxia/hypotension.

Selladurai,<sup>11</sup> 1992

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Years of Study: 1989-1991

Description: Prospective consecutive series of 109 patients with severe head injury studied within 48 hours of injury.

Classification: Class II Study

Conclusions: Status of basal cisterns strongly correlated to outcome. Complete obliteration of basal cisterns doubles unfavorable outcome (34% to 81%)

Outcome at 6 Months:

	Unfavorable	Favorable
Patent Basal Cisterns	13	22
Partial Obliteration	16	10
Complete Obliteration	38	10

PPV = 73%

Athiappan,<sup>2</sup> 1993

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Years of Study: 1990-1992

Description: Study of 107 patients with moderate and severe head injury (GCS < 11). CT examination within 24 hours.

Classification: Class III Study

Conclusions: Obliteration of basal cisterns increases mortality threefold (27% to 76%).

Correlation between status of the basal cisterns and type of pathology and GCS score.

Outcome at 3 Months:

	Dead	Alive
Normal Cisterns	17	45
Obliterated Cisterns	35	10

Yanaka,<sup>16</sup> 1993

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Years of Study: 1985-1992

Description: Retrospective study of 170 patients with acute subdural hematoma, identifying clinical and radiologic prognostic variables.

Classification: Class III Study

Conclusions: Obliteration of cisterns indicates a poorer prognosis. Rating of prognostic effectiveness:

1. Pupils
2. Obliteration ambient cistern
3. Midline shift
4. Age
5. GCS score

Prognostic equations including the status of the ambient cisterns were formulated; association existed between the status of the basal cisterns and presence of contusions.

Status of Basal Cisterns:

	Poor Outcome	Functional Outcome (3 Month)
Basal Cisterns Open	12	63
Basal Cisterns Compressed	73	22

PPV = 77%

Liu,<sup>10</sup> 1995

Years of Study: 1985-1987

Description: Retrospective study on 334 consecutive cases of head injury evaluating grading system of status of basal cisterns and brainstem changes versus outcome.

Classification: Class III Study

Conclusions: Good correlation between proposed grading system and outcome.

Outcome 12 Months:

	Unfavorable	Favorable
Grade 0	9	25
Grade 1	6	7
Grade 2	6	8
Grade 3	17	8
Grade 4	4	1
Grade 5	48	4

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#### Traumatic Subarachnoid Hemorrhage

Definition of parameter: presence of blood in the subarachnoid space, either over the convexity or in the basal cisterns.

#### Reliability of Scoring

No formal investigation has been performed concerning the reliability of scoring this parameter. In the European Nimodipine trial a difference of opinion concerning the presence or absence of traumatic subarachnoid hemorrhage (tSAH) was reported between the review committee and investigators in “a number of cases.” In the paper by Harders, et al. (1996), on treatment of tSAH with Nimodipine, in patients of varying clinical severity the review committee could not confirm the presence of subarachnoid blood on the initial CT scan in 26 of the 123 patients (21%) included in the study.<sup>7</sup> Kakarieka (1997) in his monograph on tSAH concludes that the CT findings of tSAH do not have a high reliability.<sup>8</sup> This conclusion is supported by El Tabou, et al. (1995).<sup>16</sup> Greene, et al. (1995), however, although not directly reporting results, describe in the presence of tSAH a 94% interobserver reliability in grading the degree of tSAH.<sup>6</sup>

#### Incidence and Grading

An overview of the reported incidence of tSAH in patients with head injury of varying severity is shown in Table 1.

Table 1  
Incidence of Subarachnoid Hemorrhage

First Author	Patient Population	Incidence tSAH		Remarks
Eisenberg, <sup>3</sup> 1990	GCS $\leq$ 8 (within 48 hours n = 753)	40 %		No absolute numbers reported
Selladurai, <sup>15</sup> 1992	GCS $\leq$ 8	32/109	29.4	
Vollmer, <sup>19</sup> 1991	GCS $\leq$ 8	237/588	40	TCDB
Kakarieka, <sup>10</sup> 1994	Severe head injury in adults (GCS $\leq$ 8)	268/819	33	Population European Nimodipine Trial
Lang, <sup>11</sup> 1994	Head injury with diffuse brain swelling (children and adults)	46/118	39	tSAH + intraventricular hemorrhage
Gaetani, <sup>6</sup> 1995	Head injury GCS 3-15	148/515	28.7	
Greene, <sup>7</sup> 1995	GCS 3-15 GCS 3-9	355/3157 178/704	11 26.6	Higher incidence of tSAH in more severe injuries
Taneda, <sup>18</sup> 1996	Head injury GCS 3-15	130/883	14.7	
Murray, <sup>13</sup> 1998	EBIC* survey GCS 3-12	385/953	40	EBIC Survey
Marshall, <sup>12</sup> 1998	GCS 4-12	568/1067	53	International Tirilazad Trial

\*EBIC = European Brain Injury Consortium

A few investigations have been performed concerning the degree and localization of blood in the subarachnoid space. Most investigators studying the influence of the extent of SAH use the grading system proposed by Fisher et al. for patients with spontaneous SAH. Greene, et al. propose a different grading system, specific for trauma patients (Table 2).

Table 2  
Grading Systems for Subarachnoid Hemorrhage

Fisher	Greene
Grading of SAH:	Proposed grading system for scoring tSAH:
Group 1: no blood	Grade 1: thin ( $\leq$ 5 mm)
Group 2: layer < 1 mm thick	Grade 2: thick (> 5 mm)
Group 3: layer > 1 mm thick	Grade 3: thin ( $\leq$ 5 mm) with mass lesion
Group 4: ventricular involvement	Grade 4: thick (> 5 mm) with mass lesion

There is no consistent reporting on the location of subarachnoid blood after trauma. Some authors describe the location in various basal cisterns, in the fissures, on the tentorium, or over the convexity,<sup>10</sup> others only differentiate between the presence of blood in basal cisterns, over the convexity, or a combination of the two.<sup>6</sup> The most frequent location is over the convexity, followed by the fissures and basal cisterns. Location of tSAH in the Sylvian fissure has been reported to be indicative of the development of local contusions.<sup>16</sup>

### Associations with Other Lesions and/or Prognostic Variables

Patients with tSAH have a higher incidence of contusions, acute subdural hematomas, intraventricular hemorrhage, and increased ICP signs. Kakarieka reports contusions as associated lesions in 77% of patients with tSAH and acute subdural hematoma in 44% of patients. Gaetani, et al. (1995), report an association of contusions or other intracranial lesions in 63% of patients.<sup>6</sup> Both Gaetani, et al. (1995), and Greene, et al. (1995), report an association between admission GCS score and CT grade of tSAH.<sup>6,7</sup>

### Traumatic SAH as Prognostic Variable

There is Class I evidence supporting a 72% PPV for unfavorable outcome in patients with CT scans showing tSAH in the suprasellar or ambient cisterns. A 78% PPV of an unfavorable outcome is associated with Fisher's Grade 4 tSAH.

Although attention was already called to the presence of SAH in severely head-injured patients as an important risk factor in the Japanese literature in 1983,<sup>14</sup> it is only recently that this aspect has gained attention in the international literature. Takaneka, et al. (1990), described the poor prognostic significance of the presence of tSAH, especially in the perimesencephalic region in a limited series of 30 patients with severe shearing injuries.<sup>17</sup> Among 17 patients with tSAH there were 11 cases with perimesencephalic hemorrhage of which 10 died. Selladurai, et al. (1992), in a consecutive series of 109 patients with severe head injury also report a significant correlation between the presence of CT visible subarachnoid blood and poor outcome ( $p = 0.002$ ).<sup>15</sup> The presence of tSAH is correlated to the occurrence of secondary deterioration<sup>11</sup>; degree and location of tSAH have been reported to be an indication of delayed ischemic symptoms, caused by vasospasm (Table 3).

Table 3

tSAH and Delayed Ischemia: Relation Between Degree of tSAH and Occurrence of Delayed Ischemia (Taneda,<sup>18</sup> 1996)

Degree of tSAH	Number	Delayed Ischemia	
		yes	no
small (< 1 mm)	101	3	98
extensive (> 1 mm)	29	7	22
Total	130	10	120

In the population of the U.S. Traumatic Coma Data Bank an incidence of tSAH of 40% was reported. A twofold increase in the risk of dying was noted in the group with subarachnoid blood. The presence of subarachnoid blood also appeared to predict an abnormal ICP and the predictive value of tSAH was shown to be additive to other CT scan parameters, such as the presence of abnormal cisterns, mass lesion, and midline shift. Eisenberg, et al., showed CT scan parameters to be of greater prognostic significance than clinical variables, such as age and post-resuscitation GCS score, when employing a predictive model including CT scan features and clinical variables.<sup>3</sup> Traumatic SAH rated second to effacement of the basal cisterns. The calculated odds ratios were 2.13 for tSAH, versus 1.03 for age and 0.71 for post-resuscitation GCS score. Upon analyzing the relative predictive value of CT parameters alone, tSAH also rated second to effacement of the basal cisterns. In the report on the European trial on Nimodipine in severe head injury, a trend toward a favorable effect in the Nimodipine-treated group was seen in patients exhibiting tSAH (1994). The clinical significance of the finding of subarachnoid blood on the CT scan in this series has been

further analyzed and reported by Kakarieka, et al. (1994).<sup>9</sup> The outcome of patients with traumatic SAH was significantly worse than that of patients whose first CT scan did not show subarachnoid blood. The outcome was unfavorable in 60% of tSAH patients compared to 30% in patients without SAH ( $p < 0.01$ ). Logistic regression analysis showed the presence of subarachnoid blood to be one of the most important factors of independent prognostic significance (odds ratio 0.29). The presence of tSAH was shown to have a PPV of 60% for an unfavorable outcome. When differentiated to the location of tSAH, the presence of blood in the various basal cisterns demonstrated a PPV of 69% to 72% and blood over the convexity had a PPV of 61% (Table 4). Gaetani, et al. (1995) also show the presence of tSAH in the basal cisterns to be more indicative of unfavorable outcome than tSAH over the convexity.<sup>6</sup>

A larger extent of SAH is related to poorer outcome.<sup>8,9,18</sup> Kakarieka shows in Fisher's Grade 3 a PPV of 62% and in Fisher's Grade 4 a PPV of 79% toward unfavorable outcome (Table 5); Harder's study (1996) shows a PPV of 78% to unfavorable outcome in Fisher's Grades 3 and 4. The independent predictive value of tSAH has also been found by Greene, et al. (1995), with a 78% PPV for the presence of tSAH and poor outcome in patients with severe head injury.<sup>7</sup> However, in patients with mild and moderate head injury the adverse influence of tSAH on outcome was much less pronounced. In patients with acute subdural hematomas, Domenicucci, et al. (1998), report a PPV of 86% to mortality in the presence of tSAH.<sup>2</sup>

Table 4  
Distribution of tSAH and Outcome (Kakarieka,<sup>9</sup> 1997)

Distribution of tSAH	Unfavorable	Favorable	PPV
No tSAH	87	193	31%
Convexity	56	38	60
Interhemispheric Fissure	38	17	69
Lateral Sylvian Fissure	46	22	68
Suprasellar Cisterns	21	8	72
Ambient Cisterns	26	10	72
Quadrigeminal Cisterns	9	4	69

(n= 409)

Table 5  
Relation Between Degree of tSAH and Outcome (Kakarieka,<sup>9</sup> 1997)

Fisher Grade	Unfavorable	Favorable
1	87	193
2	23	26
3	29	18
4	26	7

(n= 409)

## Conclusions

- tSAH is a frequent occurrence in severe head injury (26%-53%).
- Most frequent location is over the convexity.
- Mortality is increased twofold in the presence of tSAH.
- Presence of blood in the basal cisterns carries a PPV to unfavorable outcome of approximately 70%.
- Extent of tSAH is related to outcome.
- tSAH is a significant independent prognostic indicator.

## Recommendations for Future Research

- There should be further development of a grading system for tSAH, specific to head injury
- There should be observer reliability studies using grading systems
- There should be identification of the relative prognostic value of grading and location of tSAH

## Evidentiary Table: Traumatic Subarachnoid Hemorrhage and Outcome Shigemori,<sup>16</sup> 1990

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Year of Study: Unknown

Description: Study of 20 patients with tSAH; GCS scores 3-15.

Classification: Class III Study

Conclusions: Most frequent location is the Sylvian fissure; this location may be indicative of development of local contusions. Extensive hemorrhage in basal cisterns indicates a poorer outcome.

## Takaneka,<sup>17</sup> 1990

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Year of Study: Unknown

Description: Retrospective study on 30 patients with shearing injury.

Classification: Class III Study

Conclusions: Presence of tSAH indicates a poor prognosis.

	Outcome	Unfavorable	Favorable
tSAH+		16	1
tSAH-		4	9

## Eisenberg,<sup>3</sup> 1990

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Years of Study: 1984-1987

Description: Prospective consecutive series of 753 patients with non-penetrating severe head injury from the NIH Traumatic Coma Data Bank in whom admission CT examination was performed.

Classification: Class II Study

Conclusions: tSAH occurs in 29 of 753 (39%). Mortality increases by twofold in presence of tSAH (26% to 55%). Presence of tSAH is predictive of raised ICP. The presence of tSAH has independent predictive value.

Selladurai,<sup>15</sup> 1992

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Years of Study: 1989-1991

Description: Prospective consecutive series of 109 patients with severe head injury studied within 48 hours of injury.

Classification: Class III Study

Conclusions: Presence of CT visible subarachnoid blood correlates with a poor outcome ( $p \leq 0.0002$ ). Mortality increased twofold in the presence of tSAH.

Outcome 6 Months	Unfavorable	Favorable
tSAH +	29	3
tSAH -	38	39

Lang,<sup>11</sup> 1994

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Years of Study: 1978-1982

Description: Selected, prospective series of 118 patients (59 adults and 59 children), secondarily referred with diffuse brain swelling as defined by absent basal cisterns or absent third ventricle without a shift of more than 6 mm.

Classification: Class III Study

Conclusions: tSAH or intraventricular hemorrhage occurred in 46 of the 118 cases and is significantly correlated to the occurrence of secondary deterioration.

Kakarieka,<sup>10</sup> 1994

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Years of Study: 1989-1991

Description: Population consisted of patients with severe, non-penetrating head injury enrolled in the randomized, prospective, double-blind study on the effect of Nimodipine in severe head injury. Prognostic evaluation on basis of 414 placebo-treated patients.

Classification: Class I Study

Conclusions: Incidence of tSAH was 33% and adversely influenced outcome. Unfavorable outcome in the presence of tSAH was doubled (30% to 60%). Logistic regression analysis showed tSAH to be one of the most important prognostic factors. The number of hypotensive episodes was higher in patients with tSAH.

Outcome at 6 Months	Unfavorable	Favorable
tSAH+	87	58
tSAH-	81	188

Gaetani,<sup>6</sup> 1995

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Years of Study: 1992-1994

Description: Retrospective series of 148 patients with head injury of varying degrees (mild, moderate, and severe) with demonstrated presence of subarachnoid blood on CT examination. Evaluation of clinical significance of degree and extent of SAH was according to Fisher's grade.

Classification: Class III Study

Conclusions: Degree of tSAH is significantly related to GCS score on admission and to outcome. Distribution of tSAH is also of prognostic significance. Patients with blood both over the convexity and in the basal cisterns have worse outcomes.

Outcome at 6 Months		
Distribution of tSAH	Unfavorable	Favorable
Spaces Over Convexity	37	54
Basal Cisterns	17	19
Mixed	17	4

Greene,<sup>7</sup> 1995

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Years of Study: 1988-1991

Description: Retrospective cohort study of 252 patients with head injury of variable degrees showing CT evidence of tSAH.

Classification: Class III Study

Conclusions: Degree of SAH as defined by proposed grading system is related to admission GCS score and outcome at discharge. Stepwise regression analysis confirmed the independent predictive value of the presence of tSAH.

CT Grade of tSAH	Outcome at Discharge		Outcome at Discharge	
	Severe Head Injury GCS 3-9		Mild and Moderate GCS 10-12	
	Unfavorable	Favorable	Unfavorable	Favorable
Grade 1	11	7	1	34
Grade 2	8	3	0	6
Grade 3	45	16	7	35
Grade 4	48	6	4	21

PPV = 78% (112/144)

Harders,<sup>8</sup> 1996

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Year of Study: 1994

Description: Prospective, randomized trial on the effect of Nimodipine in 61 patients with tSAH of varying severity (n = 61).

Classification: Class II Study

Conclusions: Most frequent location of blood in the subarachnoid space is over the convexity (67%); less frequently in the basal cisterns (40%). Some relationship between the presence of subarachnoid blood and contusions or acute subdural hematoma. The amount of blood as graded by the Fisher system was related to poorer outcome.

Relation Between Degree of tSAH and Outcome:

Outcome at 6 Months:

Fisher Grade	Unfavorable	Favorable
1	0	14
2	6	13
3	15	6
4	7	0

Taneda,<sup>18</sup> 1996

Years of Study: 10-year period

Description: Prospective study of 130 patients with head injury of varying severity (mild, moderate, severe) with CT evidence of subarachnoid blood on admission.

Classification: Class III Study

Conclusions: Ten patients in this series developed delayed ischemic symptoms. The degree and location of tSAH was a predictive indicator of delayed ischemic symptoms. In the patients with symptoms of delayed ischemia, vasospasm was angiographically proven. Mortality was significantly higher in the presence of more subarachnoid blood.

tSAH	Number	Outcome at 3 Months	
		Dead	Alive
Small (< 1 mm)	101	27	74
Extensive (> 1 mm)	29	17	12

Domenicucci,<sup>2</sup> 1998

Years of Study: 1993 and 1994

Description: Retrospective study of 31 patients with severe head injury and ASDH. Analysis of subarachnoid spaces and shift.

Classification: Class III Study

Conclusions: Overall mortality was 68%; in the presence of tSAH; 86%.

Outcome at 6 Months

	Dead	Alive
Absence of tSAH or undetectable subarachnoid space	9	8
tSAH+	12	2

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Table 2  
Description of Studies

First Author	> 25 patients	GOS/ Mortality 6 Months	Prospective	Indicator Measured within 24 Hours	Statistics	Class
Lang, <sup>11</sup> 1994	+	-	+	?	-	III
Eisenberg, <sup>3</sup> 1990	+	-	+	+	+	II
Selladurai, <sup>15</sup> 1992	+	+	+	-	-	III
Gaetani, <sup>6</sup> 1995	+	+	-	+?	-	III
Taneda, <sup>18</sup> 1996	+	-	+	+	-	III
Shigemori, <sup>15</sup> 1990	-	-	-	+	-	III
Greene, <sup>7</sup> 1995	+	-	-	+	+	III
Harders, <sup>8</sup> 1996	+	+	+	+	-	II
Kakarieka, <sup>10</sup> 1994	+	+	+	+	+	I
Takaneka, <sup>17</sup> 1990	+	-	-	+	-	III
Domenicucci, <sup>2</sup> 1998	+	-	-	+	-	III

#### Midline shift

Definition of Parameter: The presence of midline shift is defined as the absolute distance (in mm) that midline structures of the brain are displaced in respect to the midline determined by averaging the distance between the inner tables of the skull. Most authors describe the degree of displacement of the septum pellucidum relative to the midline. Ross, et al. (1989) further examined shift of the pineal gland and of the aqueduct.<sup>10</sup>

#### Reliability of Scoring Midline Shift

No formal observer reliability studies concerning the scoring of midline shift were found. It is remarkable that in three manuscripts authors quantify the degree of midline shift down to 1.1 mm.<sup>5,6</sup> <sup>16</sup> At the same time, Young states that two observers would agree down to the limit of 1 mm.<sup>5</sup> The degree of midline shift and quantification of this is highly variable in the various reports. An overview of the various classifications, as mentioned by the different authors, is given in Table 1.

Table 1  
Variable Classification of Shift Between Authors

First Author	Classification of shift
Kotwica and Brzezinski, <sup>5</sup> 1993	< 1.5 mm, 1.5-3 mm, ≥ 3 mm
Young, <sup>16</sup> 1981	< 4.1 mm, ≥ 4.1 mm
Lobato, <sup>8</sup> 1991	≤ 5 mm, 6-15 mm, ≥ 15 mm
Quattrochi, <sup>9</sup> 1991	Absent / Present
Lipper, <sup>6</sup> 1985	< 3.8 mm, ≥ 3.8 mm
Fearnside, <sup>4</sup> 1993	< 5 mm, 5-10 mm, > 10 mm
Selladurai, <sup>12</sup> 1992	< 5 mm, 5-10 mm, > 10 mm
Eisenberg, <sup>3</sup> 1990	≤ 3 mm, > 3 mm
Vollmer, <sup>19</sup> 1991	≤ 5 mm, > 5 mm

## Incidence

Midline shift is a relatively frequent occurrence in series of patients with severe head injury. An overview of the reported incidence is shown in Table 2.

Table 2  
Incidence of Midline Shift

First Author	Patient Population	Incidence	Remarks
Young, <sup>16</sup> 1981	170 head-injured patients with focal neurological deficit or unconsciousness for 6 hours	69/170 40.6% 25/170 14.7	All shift Shift $\geq$ 4.1 mm
Lipper, <sup>6</sup> 1985	128 patients with severe head injury	46/128 36	Shift $\geq$ 3.8 mm
Eisenberg, <sup>3</sup> 1990	GCS $\leq$ 8 within 48 hours	255/753 34	Shift $\geq$ 3 mm
Lobato, <sup>8</sup> 1991	211 patients who talk and deteriorate	89/211 42.2 46/211 21.8	Shift 6-15 mm Shift > 15 mm
Quattrocchi, <sup>9</sup> 1991	56 patients with intracranial hematoma and 19 patients with normal CT	28/75 37.3	
Selladurai, <sup>12</sup> 1992	109 patients with severe head injury	27/109 24.7 17/109 15.6	Shift 5-10 Shift > 10 mm
Athiappan, <sup>1</sup> 1993	107 patients with moderate and severe head injury	35/107 32.7	
Kotwica, <sup>5</sup> 1993	200 adult patients with acute subdural hematoma	96/200 48 63/200 31.5	Shift 1.5-3 mm Shift $\geq$ 3 mm
Vollmer, <sup>14</sup> 1991	661 patients with severe head injury (GCS $\leq$ 8) in whom CT was available	176/597 29	Shift > 5 mm

## Association with Other Prognostic Variables

A few studies describe the relative importance of the degree of midline shift in respect to other prognostic CT variables. A relation to the presence or absence of focal lesions<sup>5</sup> and the GCS score<sup>16</sup> is described. Athiappan, et al. (1993), found the prognostic value of midline shift more important in patients with single contusions or intracerebral hematoma than for those with multiple lesions and extraaxial or subdural hematoma.<sup>1</sup> They conclude that the presence of midline shift is better correlated with the type of pathology and GCS score, rather than that the degree of midline shift can be taken alone.

## Prognostic Value of Midline Shift

Class I and Class II evidence demonstrate the prognostic significance of both presence or absence as well as degree of midline shift in patients with severe head injury<sup>3, 4, 6, 14</sup>; Class II evidence supports the greatest prognostic value of brain shift in patients with GCS scores 5-7.<sup>16</sup> In the study by Fearnside, et al. (1993), midline shift and other CT parameters were third in strength (after age and motor score) in a logistic regression analysis of the relative importance of prognostic variables.<sup>4</sup> Lobato, et al. (1991), showed in patients with secondary deterioration to coma that the degree of midline shift rates third after GCS score and highest mean ICP.<sup>8</sup> Other authors, however, have not

been able to show such prognostic significance; Selladurai, et al. (1992), describing a poor outcome in the majority of patients with a midline shift greater than 10 mm, could not show overall statistical significance in the total population of 109 patients with severe head injury.<sup>12</sup> The limited prognostic value of midline shift in this study could in part be explained by the presence of diffuse axonal injury and bilateral hemorrhagic lesions in the significant proportion of patients with midline shift less than 10 mm. In patients comatose due to acute epidural hematoma, Seelig, et al. (1984), found no correlation between the degree of midline shift and outcome.<sup>11</sup>

In patients with subdural hematoma some authors report a good correlation between midline shift and outcome, others a less evident relation: Kotwica and Brzezinski showed 42% favorable outcomes and a mortality of 39% when the shift was below 1.5 cm, and a 76% mortality when shift exceeded 3 cm.<sup>5</sup> Yanaka reports a mean midline shift of 2.9 mm in those patients with a functional recovery and 12.8 mm in those with a poor outcome.<sup>15</sup> Lobato, et al. (1991), only found a relation at extreme values of shift comparing a midline shift less than 4 mm versus a shift of more than 12 mm.<sup>8</sup> The outcome in the intermediate values did not differ. Domenicucci, et al. (1998), describe slightly larger average shift in patients dying with acute subdural hematoma than in survivors, but these results are not statistically significant.<sup>2</sup> Zumkeller, et al. (1996), also reporting on acute subdural hematomata, describe a decrease in survival density curves at shifts greater than 12 mm, but 50% survival occurs at a shift of 20 mm. A PPV of 70% to mortality can be calculated at a shift of approximately 23-24 mm.<sup>17</sup>

In the initial report on the Traumatic Coma Data Bank (TCDB),<sup>3</sup> a midline shift of 3 mm or more was noted in 34% of patients. In contrast to other studies they find a midline shift, regardless of the underlying pathology, a very strong predictor of abnormal ICP. The risk of dying was proportional to the degree of midline shift. From the published best fit curve between degree of midline shift and outcome, it can be inferred that a PPV of 70% for mortality can be calculated at a midline shift of 1.5 cm or more. This is in agreement with the PPV of 68% to fatal outcome reported by Lobato, et al. (1991), when the shift exceeds 1.5 cm.<sup>8</sup> From the data presented by Vollmer, et al. (1991), on a more definitive analysis of the TCDB, including six-month outcome, a PPV of 78% for poor outcome, as defined by the Glasgow Outcome Scale (GOS) categories dead and vegetative, can be calculated in the presence of a shift of 5 mm or greater in patients over 45 years of age. The relation between shift and poor outcome is, however, more evident in younger patients, in whom poor outcome is doubled. Because of the better, age-dependent prognosis in these patients, the PPV of this parameter at ages below 45 is only 53%.<sup>14</sup> Young, et al. (1981), however, report a PPV of 68% versus unfavorable outcome already at shifts of more than 4.1 mm.<sup>16</sup>

Quattrocchi, et al. (1991), in a retrospective study of 75 consecutive patients with head injury, also found a prognostic significance of the presence or absence of midline shift on the admission CT. The presence of midline shift was associated with a poor outcome in 50% of cases, whereas the absence of midline shift was associated with a poor outcome in only 14% of cases ( $p < 0.05$ ). Significant predictive factors for poor outcome in this study were the presence of intracranial hemorrhage (34%), intracranial hemorrhage with midline shift (61%), and midline shift out of proportion to the extent of intracranial hemorrhage (88%).<sup>9</sup>

## Conclusions

- Presence of midline shift is inversely related to prognosis; however, interaction with the presence of intracranial lesions and other CT parameters exists.
- Class I evidence shows a PPV of 78% to poor outcome in the presence of shift greater than 5 mm in patients over 45 years of age.
- Class II evidence shows a PPV of 70% to unfavorable outcome at midline shift greater than 1.5 cm.
- Presence of midline shift is indicative of increased intracranial pressure. The degree of midline shift has not been well studied and authors report widely differing values.
- The value of shift seems less important than other CT parameters, because the degree of shift is also influenced by the location of intracerebral lesions and the presence of bilateral abnormalities. Moreover, the presence and degree of midline shift as seen on the admission CT scan can be significantly altered on subsequent investigations, following the evacuation of mass lesions.

## Recommendations for Future Research

- Further observer reliability studies.
- Further uniform classification of degree of shift.
- Further investigations concerning association with other prognostic variables.
- Further investigation of independent predictive value of midline shift as CT predictor.

## Evidentiary Table: Midline Shift and Outcome Domenicucci,<sup>2</sup> 1998

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Years of Study: 1993-1994

Description: Retrospective study of 31 patients with severe head injury and acute subdural hematoma; analysis of subarachnoid spaces and shift.

Classification: Class III Study

Conclusions: Average shift higher in patients dying (10.7 mm) than in survivors (8.9 mm), but no significant difference.

## Eisenberg,<sup>3</sup> 1990

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Years of Study: 1984-1987

Description: Prospective study of early head CT in 753 patients with severe head injury. Analysis of shift at the level of the septum pellucidum and mortality examined as one subset.

Classification: Class II Study

Conclusions: At 1.5 cm shift or greater there was a 70% or higher percent of patients dying. Other parameters such as basal cisterns, mass lesions, tSAH, and ICP were examined.

Fearnside,<sup>4</sup> 1993

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Years of Study: Study duration 2-year period

Description: Prospective series of 315 consecutive patients with a GCS score less than 8 or deterioration to this level within 48 hours of injury. Analysis of prognostic significance of clinical and CT variables; outcome 6 months after injury.

Classification: Class II Study

Conclusions: CT parameters with predictive value concerning mortality were: cerebral edema, compressed/absent basal cisterns, shift, and presence of intraventricular hemorrhage. Cerebral edema was considered present in three of the following four variables:

1. Loss of grey/white matter differentiation
2. Compressed ventricles
3. Effaced sulci
4. Effaced or compressed perimesencephalic cisterns.

Degrees of shift defined were as follows: none, less than 5 mm, 5-10 mm, and greater than 15 mm. Logistic regression analysis concerning clinical and CT variables showed predictors of mortality to be: 1) age, 2) motor score, and 3) any of the 3 CT parameters. Predictors of disability in survivors were different: 1) hypotension, 2) abnormal motor response, 3) tSAH, and 4) intracerebral contusion or hemorrhage.

Kotwica and Brzezinski,<sup>5</sup> 1993

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Years of Study: 1982-1990

Description: Consecutive series of 200 adult patients operated on for acute subdural hematoma with a GCS score less than 10 prior to operation. Analysis of relationship between age, GCS score, operative timing, concomitant presence of focal lesions, shift, and outcome at 3 months.

Classification: Class III Study

Conclusions: Significant correlation between midline shift, presence of contusions, and outcome.

Shift	Outcome at 3 Months	
	Unfavorable	Favorable
< 1.5	24	17
1.5-3	72	24
> 3	58	5

Lipper,<sup>6</sup> 1985

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Year of Study: Unknown

Description: Retrospective analysis of CT findings in 128 patients with head injury as defined by not obeying commands and unable to formulate formal words.

Classification: Class II Study

Conclusions: Number of slices on which a lesion was seen under presence of shift were related to outcome. Favorable outcome was seen in 80% of patients with a normal CT scan.

Relation Between Shift and Outcome (3 Months or 1 Year)

Shift	Unfavorable	Favorable
shift < 3.8 mm	25	57
shift ≥ 3.8 mm	29	17

Lobato,<sup>7</sup> 1988

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Years of Study: 1977-1986

Description: Retrospective analysis of 64 consecutive cases of patients in comas with epidural hematoma.

Classification: Class III Study

Conclusions: Significant correlation between outcome and mechanism of injury, interval between trauma and surgery, motor score before operation, hematoma CT density and hematoma volume. 57% of patients had one or more associated intracranial lesions.

Lobato,<sup>8</sup> 1991

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Years of Study: 1977-1989

Description: 211 patients with secondary deterioration to coma out of a series of 838 head-injured patients. Analysis of cause of deterioration and prognostic indicators. Time of outcome determination not reported.

Classification: Class III Study

Conclusions: 80.5% of the 211 patients showing secondary deterioration were shown to have a focal mass lesion. In 52.3% of these patients it was an intracerebral mass lesion. Multivariate regression analysis showed prognostic values of the following parameters: 1) GCS, 2) highest mean ICP, 3) degree of midline shift, 4) type of lesion, and 5) age.

Relation between Midline Shift and Outcome:

Midline Shift	Fatal	Functional
≤ 5 mm	14	62
6-15 mm	23	66
> 15 mm	31	15

Quattrocchi,<sup>9</sup> 1991

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Year of Study: 1987

Description: Retrospective study of 56 patients with head injury (GCS 3-12) with intracranial

hematoma. Data were compared to a randomly selected series of 19 patients with normal CT scans. Purpose of the study was to determine specific CT criteria for predicting outcome. GOS score determined at 6 months and 1 year.

Classification: Class III Study

Conclusions: Significant factors for poor outcome were intracranial hemorrhage, intracranial hemorrhage plus shift, and shift out of proportion to intracranial hemorrhage.

Relationship Between Presence and Absence of Shift and Outcome:

Shift	Unfavorable	Favorable
shift -	4	24
shift +	14	14

Relationship Between Degree of Shift and Outcome:

Shift	Unfavorable	Favorable
shift = mass	8	12
shift > mass	7	1
PPV $\geq$ 70% for mortality		

Ross,<sup>10</sup> 1989

Year of Study: No year of study reported.

Description: Prospective blinded trial on 46 patients with acute post-traumatic intracerebral hematoma; the relation between the degree of midline shift, GCS score and outcome at 3 months was investigated. The study included 19 patients with acute subdural hematoma, 14 with intracerebral hematoma, and 13 with epidural hematoma.

Classification: Class III Study

Conclusions: Significant relation between level of consciousness and lateral pineal or septal shift. Significant correlation between outcome (3 months) and septal shift, but not between outcome and pineal or aquaductal shift. No difference in shift between patients with acute subdural hematoma, epidural hematoma, or intracerebral hematoma.

Relation Between GCS, Shift, and Outcome:

	Outcome at 3 Months	Lateral Pineal Shift	Lateral Septal Shift
GCS 3-5	Poor	6.8 mm	12.6 mm
	Alert	6.0	10.5
GCS 6-8	Poor	8.2	13.4
	Alert	5.2	9.4

Seelig,<sup>11</sup> 1984

Years of Study: 1980-1982

Description: Prospective series of 51 patients, comatose with epidural hematoma. Study population formed part of the pilot National Traumatic Coma Data Bank (581 patients). Analysis of clinical and CT variables.

Classification: Class III Study

Conclusions: Motor score before operation was most powerful predictor. No relationship between presence or absence of contusions, location of contusion, and midline shift to outcome. Time of outcome determination and tables not given in manuscript.

Servadei,<sup>13</sup> 1988

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Years of Study: 1980-1986

Description: Out of 158 patients examined in CT era with epidural hematoma, 87 were comatose. Separate analysis of these patients. Study of changing characteristics in connection with increased availability of CT scanners.

Classification: Class III Study

Vollmer,<sup>14</sup> 1991

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Year of Study: 1984-1987

Description: Prospective study on 661 patients from the Traumatic Coma Data Bank in whom CT examination was performed.

Classification: Class I Study

Conclusions: Primary focus of this report is on the relationship between age and outcome. Older patients had a greater frequency of shift greater than 5 mm than younger patient groups. Shift of midline, ventricular asymmetry, and effacement of the mesencephalic cisterns was closely correlated with higher rates of poor outcome (vegetative or dead).

	Age ≤ 45		Age > 45	
	Dead/Veg	SD/M/GR	Dead/Veg	SD/M/GR
Shift > 5 mm	67	59	39	11
Shift ≤ 5 mm	97	275	32	17
	PPV: 53%		PPV: 78%	

Year of Study: Unknown

Description: Prospective series of 170 patients with head injury; severity defined as major neurological deficits and/or unconsciousness at 6 hours after injury. Study population includes patients with missile wounds. Analysis of predictive value of GCS score, age, and shift. Data are related to 1-year outcome. The value of shift as measured on CT scan was separately studied in 69 patients with GCS scores 5-7.

Classification: Class II Study

Conclusions: In patients with a GCS score less than 5 or greater than 7, there was a high predictive value of GCS score. Strong relationship between presence or absence of shift more than 4.1 mm and outcome. However, outcome prediction was not significantly improved when adding data concerning shift to the GCS score. Adding shift to GCS score later than 24 hours after admission, however, did improve predictive value.

Relation Between Midline Shift and Outcome at 1 Year:

Midline shift	Unfavorable	Favorable
< 4.1 mm	17	27
≥ 4.1 mm	17	8

Years of Study: 10-year period

Description: Retrospective study of 174 patients with isolated severe head injury and unilateral acute subdural hematoma; analysis of shift and hematoma thickness.

Classification: Class III Study

Conclusions: Survival density decreases markedly at shift greater than 12 mm. Survival rate of 50% at shift is 20 mm. Shift exceeding hematoma thickness is unfavorable sign.

## Description of Studies

First Author	> 25	GOS 6 Month	Prospective	Indicator < 24 Hours	Statistics	Class
Ross <sup>10</sup>	+	-	+	+	-	III
Seelig <sup>11</sup>	+	-	+	+	-	III
Kotwica <sup>5</sup>	+	-	+	+	-	III
Young <sup>16</sup>	+	+	+	+	+/-	II
Lobato, <sup>8</sup> 1991	+	?	+	-	+	III
Lobato, <sup>7</sup> 1988	+	+	-	+	-	III
Fearnside <sup>4</sup>	+	+	+	-	+	II
Quattrocchi <sup>9</sup>	+	+	-	-	-	III
Lipper <sup>6</sup>	+	+	-	?	+	II
Servadei <sup>13</sup>	+	+	-	+	-	III
Eisenberg <sup>3</sup>	+	-	+	+	+	II
Domenicucci <sup>2</sup>	+	-	-	+	-	III
Zumkeller <sup>17</sup>	+	-	-	+	-	III
Vollmer <sup>14</sup>	+	+	+	+	+	I

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### Intracranial Lesions

Intracranial lesions are differentiated into extracerebral and intracerebral lesions; extracerebral lesions in the acute phase after head injury consist of epidural and acute subdural hematomas. Identifying such lesions is important for purposes of management, but at the same time allows quantifying severity of primary damage by determining number of lesions, type of lesions, their sizes, location, and mass effect.

Definitions: Epidural hematoma: high/or mixed density blood collection, between dura and skull. Acute subdural hematoma: high/or mixed density blood collection in the subdural or "intradural" space. Parenchymal lesions: Intraparenchymal lesions are ill defined in the literature and definitions inconsistently applied. Intraparenchymal lesions may be differentiated in low-density, mixed-density, and high-density lesions. High-density lesions may be small, located in the subcortical white matter, basal ganglia or brain stem and then form part of so-called "diffuse axonal injury."<sup>49</sup> Other lesions, of variable density, may be larger and cause mass effect. There is no sharp demarcation between contusions of a hemorrhagic nature and intracerebral hematoma.

### Reliability of Scoring

No observer reliability studies concerning the scoring of intracranial lesions were found.

## Incidence of Intercranial Lesions

First Author	Sweet, <sup>43</sup> 1978; n = 140	Kobayashi, <sup>17</sup> 1983; n = 138	Gennarelli, <sup>10</sup> 1982; n = 107	Marshall, <sup>22</sup> 1991; n = 746 evacuated lesions	European Nimodipine Trial, <sup>1</sup> 1994; n = 819
Epidural					
Hematoma	5 (25%)	23 (16%)	96 (9%)	45 (6%)	134 (16%)
Acute Subdural					
Hematoma	32 (23%)	45 (33%)	319 (29%)	159 (21%)	248 (30%)
Contusions	32 (23%)	33 (38%)	134 (12%)		501 (61%)
Contusions (mass lesion)			71 (6%)		96 (12%)
Intracerebral Hemorrhage		32 (23%)	71 (9.5%)		70 (8.5%)

### Association with Other Lesions and/or Prognostic Variables

Intracerebral lesions occur frequently in patients with epidural hematoma.<sup>11, 14, 15, 19, 21, 29, 36</sup> In patients with acute subdural hematoma, intracerebral lesions are common.<sup>8, 18, 46, 48</sup> Haselsberger, et al. (1988), demonstrated that patients with “pure” epidural hematomas had a good outcome in 70% of cases as compared to 44% of those with associated intracerebral lesions.<sup>11</sup>

Jamjoom, et al. (1992), compared two series of patients with epidural hematoma with and without intracerebral lesions and showed with statistical significance that patients with intracerebral lesions were older, had more falls as mechanism of injury, had a lower GCS score at the time of treatment, and presented with more extracranial injuries.<sup>14</sup> The correlation between age and outcome in patients with epidural hematoma can be explained in part by the incidence of associated intracerebral lesions. Only 20% of patients aged 20 or younger had associated intracerebral lesions, whereas such lesions were present in 80% of patients over the age of 60. In patients with acute subdural hematomas, the presence of associated intracerebral lesions is negatively related to outcome. Kotwica and Brzezinski (1993) describe a mortality of 85% for an acute subdural hematoma with an associated unilateral contusion, and 17% when no such lesion exists.<sup>18</sup> In the study by Wilberger, et al. (1991), patients with acute subdural hematomas had a mortality rate of 72% when associated with contusions versus 52% of those without contusions.<sup>46</sup>

This difference was related to the highest postoperative increased ICP. Seelig, et al. (1981), as well as Domenicucci, et al. (1998), however, showed no significant difference in outcome for patients with acute subdural hematoma with and without associated contusions.<sup>8, 32</sup> Similarly, Seelig, et al. (1984), and Servadei, et al. (1988), could not confirm the relationship between intracerebral associated lesions and outcome in patients with epidural hematoma.<sup>33, 35</sup> Hemorrhagic contusions occur more frequently in the elderly, where falls are the common most cause of head injury. Intraparenchymal hemorrhage is more frequent in patients with alcohol use.<sup>7, 31</sup>

### Predictive Value

The analysis of the predictive value of the presence or absence of intracranial lesions in patients with severe head injury is complicated by the fact that many studies reporting on such lesions include patients with injuries of less severity (i.e., GCS > 8). Time to operation and widely varying

indications for operation, particularly concerning intracranial lesions, are factors possibly influencing treatment results and prognosis. The mortality of comatose patients with epidural hematoma is lower than in patients with acute subdural hematoma (Table 1). A higher percentage of favorable outcome is described in patients with severe head injury and an epidural hematoma, and a lower percentage of favorable outcome in patients with acute subdural hematoma is described in comparison to patients with diffuse lesions.<sup>10</sup> Class II evidence shows a PPV of 77% for unfavorable outcome in severely head-injured patients in whom mass lesions were present and evacuated, and a PPV of 89% when mass lesions were not evacuated.<sup>22</sup> Class I evidence shows a PPV of 67% to unfavorable outcome in the presence of a combination of high-density intracerebral and extracerebral lesions.<sup>24</sup> Other Class I evidence shows a PPV of 79% to poor outcome (dead/vegetative) in the presence of lesions greater than 15 ml in patients over 45 years of age.<sup>45</sup>

Table 1  
Mortality Reported in Series of Patients with Epidural or Acute Subdural Hematoma

Epidural Hematoma		Acute Subdural Hematoma	
First Author	% Mortality	First Author	% Mortality
Phonprasert, <sup>25</sup> 1980	24%	Seelig, <sup>32</sup> 1981	57%
Cordobes, <sup>4</sup> 1981	26	Gennarelli, <sup>10</sup> 1982 (GCS 3-5)	74
Gennarelli, <sup>10</sup> 1982 (GCS 3-5)	36	Gennarelli, <sup>10</sup> 1982 (GCS 6-8)	36
Gennarelli, <sup>10</sup> 1982 (GCS 6-8)	9	Klun, <sup>16</sup> 1984	79
Bricolo, <sup>2</sup> 1984	14	Stone, <sup>42</sup> 1986	59
Seelig, <sup>33</sup> 1984	41	Stening, <sup>40</sup> 1986	76
Reale, <sup>28</sup> 1984	27	Haselsberger, <sup>11</sup> 1988	57
Dan, <sup>6</sup> 1986	59	Marshall, <sup>22</sup> 1991	50
Haselsberger, <sup>11</sup> 1988	38	Wilberger, <sup>46</sup> 1991	66
Lobato, <sup>21</sup> 1988	28	Phuenpathom, <sup>26</sup> 1993	74
Servadei, <sup>34</sup> 1988	27	Hatashita, <sup>12</sup> 1993	55
Marshall, <sup>22</sup> 1991	18	Kotwica, <sup>18</sup> 1993	55

No correlation is found between hematoma localization and outcome in patients with epidural hematoma.<sup>19, 21, 29, 35</sup> Hematoma volume in epidural hematoma,<sup>21, 29, 35</sup> subdural hematoma,<sup>13, 42, 48, 50</sup> as well as in intraparenchymal lesions correlates well with outcome.<sup>20</sup>

Lobato, et al. (1988), show poor outcomes in only 20% of patients with epidural clots less than 150 cc versus 58% when the clot volume is greater than 150 cc.<sup>21</sup> Yanaka, et al. (1993), shows in patients with acute subdural hematoma that the mean hematoma volume was 31 cc for patients with functional recovery and 104 cc for those patients with an unfavorable outcome.<sup>48</sup> Stone, et al. (1983), demonstrates that patients with an acute subdural hematoma volume of less than 100 cc had a mortality rate of 51% and those with hematoma over 100 cc had a 79% mortality. Zumkeller, et al. (1996), on analysis of patients comatose with an acute subdural hematoma, found a 50% survival rate at a hematoma thickness of 18 mm or less. A PPV toward mortality of 70% can be inferred to occur at a hematoma thicknesses of approximately 23 mm. A PPV of 75% for mortality was demonstrated when midline shift exceeded hematoma thickness by more than 5 mm.<sup>50</sup> Lipper, et al. (1985), in a retrospective analysis of 128 patients with severe head injury, developed a prognostic

equation based on the number of slices of the CT scan on which hemorrhagic lesions were visible. The equation allowed accurate prediction in 69% of cases. The model was less accurate in extra-axial lesions.<sup>20</sup> The presence of visible subarachnoid spaces without signs of tSAH has been shown to be indicative of favorable outcome in patients with acute subdural hematoma.

In patients with intraparenchymal lesions, the presence of multiple lesions is associated with a poorer outcome. Sweet, et al. (1978), describe in 52 patients with bilateral lesions an association between high-density lesions, higher ICP, and worse prognosis.<sup>43</sup> Patients with low-density lesions and small ventricles, however, generally show lower ICPs and a better prognosis. Chocksey, et al. (1993), in a retrospective study of 202 patients, describe a direct relationship between the number of intracerebral lesions and outcome. In patients with a single hematoma, 58% have a favorable outcome, in patients with two clots, 20%, while no patients with three or more hematomas have a favorable outcome.<sup>3</sup> Quattrocchi, et al. (1991), describe worse outcome when intracranial hemorrhage is associated with midline shift and especially when the midline shift is out of proportion to the extent of intracranial hemorrhage, 88% of the patients in this group showing a poor outcome.<sup>27</sup> Cordobes, et al. (1986), presenting results on 78 patients with diffuse axonal injury show a poorer outcome when intraparenchymal hemorrhage is associated with intraventricular hemorrhage or global brain swelling.<sup>5</sup> In the series reported from the Traumatic Coma Data Bank, 71 patients were operated on for an intracerebral hematoma. Nineteen (26.8%) died, while unfavorable outcome on discharge came to a total of 52 (74%).<sup>22</sup> Eide and Tysnes (1992), describe a poorer outcome at three months in patients with multifocal contusions when compared to those with focal contusions.<sup>9</sup>

CT examination yields by definition momentary information. When determining prognostic significance of lesions on the CT scan, the time elapsed between injury and CT examination must be taken into account. Various authors have addressed the issue of changes on CT appearance over time. Kobayashi, et al. (1983), describing a series of 138 patients, noted new lesions developing in 60 patients. In these patients outcome was favorable in only 12, while a favorable outcome was seen in 60 of the 78 patients not developing a new lesion.<sup>17</sup> Sweet, et al. (1978), in a series of 143 patients, show that 13 of the initial 75 patients with unilateral lesions on admission develop contralateral lesions during the first week.<sup>43</sup> Tseng (1992) describes 32 patients with delayed traumatic intracerebral hematoma. This delayed hemorrhage was found after a time interval varying from 7 hours to 10 days. Seventy-five percent of these patients had a favorable outcome; poor prognosis was associated with an earlier occurrence, larger hematoma, low GCS score, clinical deterioration, and obliteration of the supra chiasmatic cistern. In the majority of these patients, contusions were present on the initial CT scan. The delayed lesion was diagnosed between 12 hours and 6 days after trauma.<sup>44</sup> Soloniuk, et al. (1986), describe 35 patients with delayed traumatic intracerebral hematoma. In 20% of these patients, the diagnosis was made within 3 hours, in 6% between 3 and 6 hours, in 29% between 6 and 24 hours, and in 46% more than 24 hours after injury. Half of these patients were not comatose at the time of admission.<sup>37</sup> Yamaki, et al. (1990), shows the development of traumatic intracranial hematoma from brain contusions in 48 patients. In 56% of these patients, the lesion developed within 6 hours, in 81% within 12 hours, and in all patients within 24 hours after injury. Stein, et al. (1992), describe new lesions developing on the CT scan in 123 patients out of a series of 253 patients with head injury. Coagulation disturbances were present in the majority (55%) of these patients.<sup>39</sup> In a recent study by Servadei, et al. (1995), 37 patients are described, from a series of 412, developing new lesions within a 12-hour period from time of admission. In 22 patients, these hematomas evolved toward surgical removal. Lesions most prone to enlarge were epidural hematomas and intracerebral hemorrhages.<sup>35</sup>

When describing outcome results and prognosis in patients with demonstrable lesions on the CT

scan, it may be worthwhile to include results of subsequent CT examinations and to report the “full extent” of such lesions, i.e., the “worst CT” in addition to the initial CT scan results.

### Conclusions

- Extracerebral and intracerebral lesions occur frequently in comatose patients with head injury.
- Presence of mass lesions has a PPV of 78% to unfavorable outcome (Class II).
- Presence of mass lesions in patients over 45 years of age carries a PPV of 79% to poor outcome as defined by the categories dead and vegetative.
- Mortality is higher in acute subdural hematoma than in extradural hematoma.
- Outcome is more favorable in patients with severe head injury and an epidural hematoma and less favorable in acute subdural hematoma in comparison to patients with diffuse injuries.
- Hematoma volume is correlated to outcome.
- Intraparenchymal lesions are ill defined.

### Recommendations for Future Research

- There is a need for improved definition for intraparenchymal lesions.
- A more detailed recording of surgical indications is required in future studies. Standardized reporting of indications for surgery (clinical, such as occurrence of deterioration, CT, results of ICP monitoring), time to operation, and involving lesions are a prerequisite for comparison of different series and determination of prognostic value. Also reasons for not operating, i.e., poor prognosis or local “conservative” policy, should be explicitly stated.

### Evidentiary Table: Intracranial Lesions and Outcome Eide and Tysnes,<sup>9</sup> 1992

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Years of Study: 1984-1989

Description: Evaluation of outcome in 143 patients admitted with cerebral contusions, defined as non-homogeneous area of low- and high-attenuation values.

Classification: Class III Study

Conclusions: Outcome at 3 months was poorer in patients with multifocal contusions than in focal contusions. Longer-term evaluation did show increased occurrence of post-traumatic mental disturbances, also in patients with focal contusions.

#### Outcome in Patients with Brain Contusion

	Unfavorable	Favorable
Focal Contusion	0	57
Multifocal Unilateral	17	19
Multifocal Bilateral	31	19

### Gennarelli,<sup>10</sup> 1982

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Description: Retrospective analysis of 1,107 patients with severe head injury from seven centers analyzing outcome and type of CT lesion.

Classification: Class III Study

Conclusions: Differentiation of focal versus diffuse injuries being split into two categories of

severity: market heterogeneity of outcome; type of lesion as important on outcome as GCS score. Rank order of prognosis: subdural hematoma < diffuse injuries < extradural hematoma.

	Number of patients	Unfavorable	Favorable
Diffuse Injury	487	48%	52%
Focal Injury	620	67	33
Epidural Hematoma	96	37	63
Acute Subdural Hematoma	319	77	22
Other Focal Lesions		61	39

Kobayashi,<sup>17</sup> 1983

Years of Study: 1977-1981

Description: Analysis of serial CT scans performed in 138 patients with severe head injury.

Classification: Class III Study

Conclusions: New findings were visible on follow-up CTs in 91 of the 138 patients. Significant correlation was demonstrated between favorable outcome and absence of new lesions, and between poor outcome and development of new lesions.

Relationship Between Progression of Lesions and Outcome

	Unfavorable	Favorable
No New Lesion	18	60
New Lesions	48	12

Lipper,<sup>20</sup> 1985

Year of Study: Not Reported

Description: Retrospective analysis on 128 randomly selected patients with severe head injury. Evaluation of predictive significance of extent of hemorrhagic lesions. Outcome determinations at 3 months and 1 year.

Classification: Class II Study

Conclusions: Based on the number of slices (each 1 cm thick) of the CT scan on which hemorrhagic lesions were visible. A prognostic equation was developed, providing accurate prediction in 69.7% of cases. Model is less accurate in extra-axonal lesions.

Relationship Between Extent of Lesion and Outcome

Number of Slices with

Hemorrhagic Lesions	Unfavorable	Favorable
None	14	55
1 or 2	3	5
3 or 4	12	12
5 or 6	15	9
7 or 8	2	1

Lobato,<sup>21</sup> 1988

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Year of Study: Not Reported

Description: Analysis of 55 patients out of a series of 520 patients with severe head injury, showing post-traumatic hemispheric swelling.

Classification: Class III Study

Conclusions: Highest mortality (87%) in this category of patients with severe head injury. Strong association with the presence of acute subdural hematoma (85%) or epidural hematoma (9%). Also relation to arterial hypotension and/or hypoxia on admission.

Marshall,<sup>22</sup> 1991

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Description: Prospective study of a consecutive series of 746 severely head injured patients in four centers Traumatic Coma Data Bank (TCDB).

Classification: Class II Study

Conclusions: Outcome more unfavorable in patients with evacuated or non-evacuated mass lesions. Presence of mass lesions carries a PPV of 78% to unfavorable outcome.

	Outcome at Discharge	
	Unfavorable	Favorable
Diffuse Injury	294	120
Evacuated Mass Lesion	213	63
Non-Evacuated Mass Lesion	32	4

Miller,<sup>23</sup> 1979

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Year of Study: Not Reported

Description: Study of 74 patients with severe head injury ( $GCS \leq 9$ ) investigating relationship between CT scan, GCS score, and ICP versus outcome. Patients with epidural hematoma or subdural hematoma were excluded.

Classification: Class III Study

Conclusions: In the presence of high-density intraparenchymal lesions there was a 50% change of raised ICP and a strong correlation with poor outcome. In patients with cerebral contusion, admission GCS score was unrelated to outcome.

	Focal Lesions and Increased ICP	
	ICP Normal	ICP Raised
CT Normal/Diffuse Swelling	34	7
CT Contusion or Mixed Lesions	14	19

(n = 74)

GCS score on Admission	Relationship Between CT Scan, Coma Scale, and Outcome			
	CT Normal/ Diffuse Swelling		CT Contusion or Mixed Lesion	
	Unfavorable	Favorable	Unfavorable	Favorable
3-4	3	0	8	1
5-7	3	18	8	8
8-10	9	15	3	4
11	9	2	1	0

Narayan,<sup>24</sup> 1981

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Years of Study: 1976-1979

Description: Evaluation of prognostic parameters including CT scan in a consecutive series of 133 patients with severe head injury.

Classification: Class I/II Study

Conclusions: Concerning CT data, the presence of high-density lesions was the best, but not a very good prognostic indicator allowing 64% correct predictions. CT was less accurate than clinical predictors. In combination with clinical parameters, adding the CT scan improved confidence of prediction. CT was not selected on regression analysis for best prognosticators.

Intracerebral Lesion	Relationship Between Presence of Intracerebral Lesions and Outcome		
	None	Unfavorable	Favorable
Normal/Low Density	59	22%	78%
High Density Lesions	74	54	46

Quattrocchi,<sup>27</sup> 1991

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Year of Study: 1987

Description: Retrospective study on 75 patients (data fully available in 56) with intracranial hemorrhage of varying severity.

Classification: Class III Study

Conclusions: Predictive features for poor outcome with a presence of intracranial hemorrhage (34%), combination of intracranial hemorrhage and shift and shift out of proportion to intracranial hemorrhage (88% mortality).

	Relationship Between Intracranial Hemorrhage, Shift, and Outcome	
	Dead	Alive
No ICH	1	18
ICH	14	42
ICH Plus Shift	11	17
Shift Out of Proportion to Intracranial Hemorrhage	6	2

Rudnik,<sup>30</sup> 1992

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Years of Study: 1980-1986

Description: Evaluation of prognostic value of clinical and CT parameters in 146 patients with severe head injury (GCS  $\leq$  8).

Classification: Class III Study

Conclusions: GCS had the greatest prognostic significance, followed by degree of intracranial mass lesions. Isolated subdural hematoma or epidural hematoma were indicative of a good prognosis; the combination with multiple contusions or intracerebral hemorrhage indicated a poor prognosis.

Seelig,<sup>33</sup> 1984

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Years of Study: 1980-1982

Description: Description of treatment results in 51% operated on for epidural hematoma in comatose condition; part of 581 patients in a national pilot Traumatic Coma Data Bank.

Classification: Class III Study

Conclusions: Overall mortality 41%, in 50% of the cases association with intracerebral contusions. Motor score before operation was the most powerful prognostic indicator.

Servadei,<sup>35</sup> 1995

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Years of Study: 1990-1994

Description: Retrospective review of 37 patients out of a series of 412 showing changing lesions within 12 hours of admission.

Classification: Class III Study

Conclusions: Of the 37 patients showing changes, 15 cases evolved toward reabsorption and in 22 cases lesion size increased. Indications for control CT detecting these lesions were a raising ICP in 5 patients, clinical deterioration in 10, and scheduled controlled CT in 13 patients.

Stein,<sup>38</sup> 1993

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Years of Study: 1986-1989

Description: Retrospective review of 337 patients with moderate and severe head injury, who had follow-up CT within 72 hours.

Classification: Class III Study

Conclusions: 149 patients (44.5%) showed new lesions. Highly significant association between appearance of delayed insults and severity of initial injury, hypotension, pulmonary injury, coagulopathy or subdural hematoma on initial CT. Appearance of new lesions was strongly related to outcome and was shown to be of independent predictive value.

Sweet,<sup>43</sup> 1978

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Years of Study: 1976-1977

Description: Analysis of serial CT in 140 head-injured patients evaluating progression of lesion and relationship between intraparenchymal abnormalities and outcome.

Classification: Class III Study

Conclusions: Admission CT showed unilateral lesions in 75 patients and 39 bilateral lesions. Subsequent CT during the first week showed progression in 13 of the unilateral lesions, totaling 52 bilateral lesions. Bilateral increased density lesions were associated with a poorer motor score, a higher ICP, and worse outcome.

Type of Lesion versus Outcome		
CT lesion	Unfavorable	Favorable
Normal	5	21
Unilateral	21	41
Bilateral Swelling	8	21
Bilateral Hypodense	17	6

Tseng,<sup>44</sup> 1992

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Years of Study: 1987-1989

Description: Report on 32 patients with delayed traumatic intracranial hematoma (DTICH).

Classification: Class III Study

Conclusions: Incidence of DTICH was 5.9% of patients admitted with neurological signs or abnormal CT scan. Reason for control CT scan was clinical deterioration in 10 patients and failure to recover in 22 patients.

Vollmer,<sup>45</sup> 1991

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Description: Prospective analysis of 661 patients aged 15 years and older in relation to clinical outcome.

Classification: Class II Study

Conclusions: The proportion of patients with intracranial hematomas increases with age. Analysis based on the presence and evacuation of a large lesion showed that the increasing age was associated with poorer outcome in each subgroup.

	Age < 45		Age > 45	
	Dead/Veg	SD/M/GR	Dead/Veg	SD/M/GR
Lesion $\geq$ 15 ml	55	65	57	15
No lesion or lesion < 15	122	292	31	16
	PPV: 46%		PPV: -79%	

SD= severe disability; M=moderate disability; GR=good recovery

## Description of Studies

First Author	>25	GOS 6 Month	Prospective	Indicator within 24 Hours	Statistics	Class
Lobato <sup>21</sup>	+	?	-	+	-	III
Lipper <sup>20</sup>	+	+	-	+	+	II
Eide <sup>9</sup>	+	-	-	+	-	III
Kobayashi <sup>17</sup>	+	-	-	-	-	III
Seelig <sup>33</sup>	+	-	+	+	-	III
Tseng <sup>44</sup>	+	-	-	-	-	III
Sweet <sup>43</sup>	+	+	+	-	-	III
Stein <sup>38</sup>	+	?	-	-	-	III
Servadei <sup>35</sup>	+	?	-	+	-	III
Quattrocchi <sup>27</sup>	+	+	-	+	-	III
Miller <sup>23</sup>	+	+	-	+	-	III
Narayan <sup>24</sup>	+	+	+	+?	+	I/II
Rudnik <sup>30</sup>	+	?	?	?	+	III
Gennarelli <sup>10</sup>	+	-	-		-	III
Marshall <sup>22</sup>	+	-	+	+	-	II

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