

GUIDELINES

Guidelines for the management of severe head injury

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INTRODUCTION

Head injury, a clinical problem treated frequently by neurosurgeons, is a major cause of disability, death, and economic cost to our society. In the past two decades, we have increased remarkably our understanding of the pathophysiology of head injury. One of the central concepts that emerged from clinical and laboratory research is that all neurological damage does not occur at the moment of impact, but evolves over the ensuing hours and days. Furthermore, we now recognize the deleterious effects of these various delayed insults to the injured brain at the clinical and biochemical levels. This has led to an interest in developing better monitoring and treatment methods as well as the development of new pharmaceuticals, all of which show great promise in improving the outcome for patients who have suffered a head injury.

Past efforts to develop guidelines for the management of patients with severe head injury relied on authors' expert opinion and practice experience and, therefore, had an element of subjectivity. Recently, with the advent of a methodology to develop guideline documents based on scientific method, there has been a dramatic increase in clinical practice guidelines with subsequent

reports showing improvement in patient care and a reduction in medical time and cost (Woolf, 1993). The interest in developing guidelines for head injury intensified after a recent national study documented considerable variability in the management of patients with severe head injury (Ghajar *et al.*, 1995).

The task force developing these guidelines for the management of severe head injury used a meticulous process relying on scientific evidence rather than expert opinion. In addition, the task force actively involved representatives of national and international medical societies and individuals with demonstrated expertise and interest in the care of patients with severe head injury.

These guidelines address key issues relating to the management of severe head injury in adult patients with a Glasgow Coma Scale score of 3-8. They are by no means an exhaustive treatise on severe head injury. Due to the enormous effort required to develop evidence-based guidelines, the task force selected topics that were deemed to have an impact on outcomes in patients with severe head injury. Other important aspects of patient management which were not covered in the present effort will be considered for study in subsequent editions of this document. Examples of such topics include indications for neurosurgical intervention, special consideration in paediatric head injury, the management of penetrating head injury, and prognosis. We intend that these guidelines will be continually improved in response to new scientific evidence.

Our intent is that these guidelines will clearly state the current scientific basis for our clinical

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† These guidelines are supported by the Brain Trauma Foundation, and further information can be obtained from the Executive Director, 523 E 72nd Street, 7th Floor, New York, NY 10021, USA. Tel: (212) 772-0608; Fax: (212) 772-0357.

practice. For most clinical practice parameters, scientific evidence is insufficient for standards of care, as is generally the case in most of current medical practice. Upgrading clinical practice parameters from option to guidelines to standard will require focused, well-designed and carefully implemented clinical research trials.

The process used in the development of these guidelines

This guidelines document is comprised of 14 topics ranging from trauma systems and prehospital resuscitation to monitoring and treatment of intracranial hypertension and intensive care. In 1993, a head injury guidelines task force was formed and supported by the Brain Trauma Foundation. Members of the task force were selected based upon their academic expertise in head injury.

The Brain Trauma Foundation is a nonprofit foundation dedicated to improving the outcome of patients with severe head injury. The Foundation has supported select neurotrauma research in collaboration with the Joint Section on Neurotrauma and Critical Care of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) over the past 8 years. The Foundation provides generous financial and administrative support that enables this guidelines effort to proceed expeditiously and focus on the tasks necessary to accomplish our goals.

Initially, each person on the task force was assigned a topic and conducted a MEDLINE search, reviewed and graded clinical articles pertinent to the topic, then wrote a report. These reports were reviewed and critiqued by the entire task force in February 1994 and resulted in the draft Version I of the guidelines. Four subsequent meetings were held, resulting in Version VI. At each meeting, the entire document was reviewed by the task force with, at times, representatives of various medical societies, individuals with expertise in head injury care, and members of the AANS Guidelines and Outcomes Committee. Each new draft version was improved either in terms of scientific review, content, or layout — as in the inclusion of evidentiary tables in draft Version IV. Two topic sections from the document were presented to neurosurgeons in attendance at the Joint Section on Neurotrauma and Critical Care meeting at the October 1994 CNS meeting. In addition, Version III was critiqued in detail by a group of European neurosurgeons with expertise in neurotrauma.

In January 1995, Version V was reviewed and approved by the AANS Guidelines and Outcomes Committee and recommended for review to the AANS Board of Directors and CNS Executive Committee. Versions V and VI were also sent to the American Academy of Neurology, the American College of Surgeons, the American College of Emergency Physicians, the American Society of Neuroradiology, the Society for Critical Care Medicine, the American Association of Neuroscience Nurses, and the American Academy of Physical Medicine and Rehabilitation for their reviews and comments. This final version (VII) was improved editorially without a change in content.

Degrees of certainty

In assessing the degree of certainty associated with a particular recommendation, the following terminology is the most widely accepted and is used in this document.

- Standards: represent accepted principles of patient management that reflect a *high degree of clinical certainty*.
- Guidelines: represent a particular strategy or range of management strategies that reflect a *moderate clinical certainty*.
- Options: are the remaining strategies for patient management for which there is *unclear clinical certainty*.

Note that the term 'guidelines' is used both in a global sense, i.e. clinical practice guidelines, as well as in a more specific sense, as noted above.

Classification of evidence

When assessing the value of therapies or interventions, the available data is classified into one of three categories according to the following criteria:¹

- Class I evidence: prospective randomized controlled trials (PRCT) — the gold standard of clinical trials. However, some may be poorly designed, lack sufficient patient numbers, or suffer from other methodological inadequacies.
- Class II evidence: clinical studies in which the data were collected prospectively, and retrospective analyses which were based on clearly reliable data. Types of studies so classified include: observational studies, cohort studies, prevalence studies, and case-control studies.
- Class III evidence: most studies based on retrospectively collected data. Evidence used in

¹ A single study may be of a different class depending upon the parameter studied in each topic.

this class indicates clinical series, databases or registries, case reviews, case reports, and expert opinion.

- **Technology assessment:** the assessment of technology, such as intracranial pressure monitoring devices, does not lend itself to classification in the above-mentioned format. Thus, for technology assessment the devices were evaluated in terms of their accuracy, reliability, therapeutic potential, and cost effectiveness.

Correlation between evidence and recommendations

Standards are generally based on Class I evidence. However, strong Class II evidence may form the basis for a standard, especially if the issue does not lend itself to testing in a randomized format. Conversely, weak or contradictory Class I evidence may not be able to support a standard.

Guidelines are usually based on Class II evidence or a preponderance of Class III evidence.

Options are usually based on Class III evidence and are clearly much less useful except for educational purposes and in guiding future studies.

Attributes of clinical practice guidelines

To ensure the development of scientifically sound, clinically relevant guidelines that are applicable to the day-to-day practice of medicine, the American Medical Association (1990) developed a list of attributes which are listed here in an abbreviated form.

Attribute I. Practice guidelines should be developed by or in conjunction with physician organizations and should be characterized by the following:

- scientific and clinical expertise in the content areas of the parameters;
- broad-base representation of physicians likely to be affected by the parameters.

Attribute II. Relevant scientific literature and expert clinical opinion should be reviewed as evidenced by:

- a description of the process of the review;
- a description of the evidence reviewed;
- the speciality affiliations and other credentials of the physician organizations, groups, and individuals conducting the review;
- a description of the methods used to evaluate the scientific literature and other appropriate research findings;
- the rationale for including or excluding studies is noted;

- the process for selection of clinical experts/reviewers is noted or available upon request;
- at least two-thirds of clinical experts/reviewers were actively involved in clinical practice in relevant clinical areas;
- the clinical experts/reviewers thoroughly reviewed and assessed the scientific literature.

Attribute III. Practice parameters should be as comprehensive and specific as possible.

Attribute IV. Practice parameters should be based on current information. There should be provisions for periodic reviews and revisions, when appropriate.

Attribute V. The guidelines should be widely disseminated.

Every effort has been made in the formulation of these guidelines to achieve these ideals.

DISCLAIMER OF LIABILITY

The information contained in these guidelines reflects the current state of knowledge at the time of completion, July 1995. The information is designed to provide accurate and authoritative information in regard to the subject matter covered. In view of the fact that there will be future developments in scientific information and technology, it is anticipated that there will be periodic review and updating of these guidelines. These guidelines are distributed with the understanding that the Brain Trauma Foundation, the American Association of Neurological Surgeons, and the other organizations that have collaborated in the development of these guidelines are not engaged in rendering professional medical services. If medical advice or assistance is required, the services of a competent physician should be sought. The recommendations contained in these guidelines may not be appropriate for use in all circumstances. The decision to adopt any particular recommendation contained in these guidelines must be made by a treating physician in the light of all the facts and circumstances in each particular case and on the basis of the available resources.

TRAUMA SYSTEMS AND THE NEUROSURGEON

I. Recommendations

(A) Standards

There are insufficient data to support a treatment Standard for this topic.

(B) Guidelines

All regions in the United States should have an organized trauma care system.

(C) Options

As delineated in the American College of Surgeons Committee on Trauma *Resources for Optimal Care of the Injured Patient: 1993*, neurosurgeons should have an organized and responsive system of care for patients with neurotrauma. They should initiate neurotrauma care planning including prehospital management and triage, maintain appropriate call schedules, review trauma care records for quality improvement, and participate in trauma education programmes.

Trauma facilities treating patients with severe or moderate head injury must have a neurosurgery service, an in-house trauma surgeon, a neurosurgeon promptly available, and a continuously staffed and available operating room, intensive care unit and laboratory with proper equipment for treating neurotrauma patients. A computed tomography (CT) scanner must be immediately available at all times.

In rural or occasionally weather-bound communities without a neurosurgeon, a surgeon should be trained to perform accurate neurological assessment and to initiate immediate neurotrauma care. Such a surgeon also should be trained to perform life-saving surgical treatment of an extracerebral haematoma in a deteriorating patient.

II. Overview

Trauma causes about 150 000 deaths in the United States each year, about half due to fatal head injuries. Every year another 10 000 persons sustain spinal cord injuries: some 200 000 people in the US live with the disabilities caused by these injuries. Thus, trauma, including neurotrauma, is a serious public health problem requiring continuing improvement in the care of injured patients. Trauma system development and organization and better injury prevention appear to be lowering the incidence of death and disability due to intentional and unintentional injury, and should be available to all people in the United States and other countries.

III. Process

A MEDLINE search from 1966 to the present identified 102 articles with the key words 'trauma systems' and 'outcome' and that literature was used as a basis to assess the value of trauma systems. The guidelines and options listed are derived from studies and the opinions of many 'experts' in neurotrauma care from a variety of

peer-reviewed and other articles. *Resources for Optimal Care of the Injured Patient: 1993*, published by the American College of Surgeons Committee on Trauma, provides the basis for most recommendations regarding trauma hospital organization. This document, originally published in 1976, is written, reviewed, and revised regularly by highly recognized North American trauma surgeons. Revision of the next document begins as soon as the latest version is completed; the 1993 version is the sixth edition.

IV. Scientific foundation

Since the late 1970s, various investigators have tried to demonstrate the efficacy of trauma systems. Early studies generally attempted to show that excessive, 'preventable' trauma deaths occurred in regions without organized trauma care (West *et al.*, 1979; Kreis *et al.*, 1986; Campbell *et al.*, 1989) but this methodology was criticized as being too subjective (Wilson *et al.*, 1992). Additional studies relied on series of patients treated at one or more trauma centers and compared them with those treated within a region (J. Smith *et al.*, 1990) or across the United States (Shackford *et al.*, 1987) using prospectively collected standardized data for severity and outcome. In all comparisons between organized and non-organized trauma systems, patient outcome was worse without organization. A number of studies and their methodologies have been summarized (Roy, 1987; Mendeloff and Cayten, 1991). There are no published data suggesting that unorganized trauma care is superior to organized systems.

Published reports indicate that centres treating larger volumes of trauma patients have better patient outcomes than centres with fewer admissions (R. Smith *et al.*, 1990). One report states that organized Level II trauma centers with attending trauma surgeons who are available but not 'in-house' have outcomes as good as those with surgeons present in the hospital at all times (Thompson *et al.*, 1992). However, at another centre, in-house attending surgeons achieved better than expected survival rates in patients who had blunt or penetrating trauma treated within 20 min of hospital arrival (Hoyt *et al.*, 1989) (both of these studies examined data prospectively collected at their centre against data collected prospectively at many trauma centres across the United States).

Organization of neurotrauma care

Several kinds of arrangements can provide optimal management of trauma, including neurotrauma, and depend on the presence and interest of the local neurosurgeon, trauma surgeon, emergency physician, and critical care specialist. The injured patient, particularly the patient with

injury to several body regions, must have a surgeon available for overall management. A trauma surgeon or an appropriately qualified neurosurgeon may fill this role in collaboration with the trauma service. He or she most often assumes overall responsibility in patients with isolated head or spinal cord injuries, and in multitrauma patients after their other injuries have stabilized and when management of neurotrauma is the most pressing problem. When multiple organ injuries require active treatment, appropriate consultants may be called upon to deliver care for respiratory, nutritional, infectious, and haematological needs (Pitts *et al.*, 1987; ACS-COT, 1993).

The surgeon qualified for the care of trauma patients is defined as a board-certified, Advanced Trauma Life Support certified surgeon with active trauma clinical involvement, continuing medical education, and participation in national or regional trauma organizations (ACS-COT, 1993). The *Resources for Optimal Care* further directs the surgeon's practice in the following areas: emergency intervention, critical care, acute care, and discharge planning.

That same document (ACS-COT, 1993) also directs neurosurgical involvement in the care of the injured patient. Neurosurgeons should participate in defining prehospital care in their region including on-site resuscitation and trauma centre referral criteria, and in training emergency medical providers in the early management of neurotrauma. It is imperative that neurosurgeons define and maintain on-call schedules and formulate trauma centre bypass procedures when a neurosurgeon is unavailable to treat injured patients, and be available when called to provide trauma care. They must assure that the trauma facility has adequate computed tomography scanning capabilities, operating room, and intensive care resources for patients to be treated optimally. Neurosurgeons also should participate in the trauma system's review, quality improvement, and teaching efforts within their hospital and trauma system.

Prehospital care and emergency department treatment of patients with neurotrauma may have profound importance in their ultimate morbidity and mortality. Many key individuals provide critically important patient care in the early minutes and hours after trauma, including appropriately credentialed emergency physicians, anaesthesiologists, emergency medical technicians and paramedics, and emergency department and operating room nurses, among others, whose skills and training are essential in the management of these critically injured patients. Because

treatment of nervous system injury must be done correctly, involvement by neurosurgeons in the planning and implementation of treatment protocols is extremely important, along with input from other trauma specialists. Reviews of specific treatments are given in the following sections in these neurotrauma guidelines.

V. Summary

Published case series and cohort comparison studies of patients treated in regions where planned trauma systems are in place compared with regions without trauma systems, or before and after instituting a trauma system, conclude that mortality is reduced after major trauma in patients treated in a trauma system. For optimal care of neurotrauma, neurosurgeons should be involved in the planning and implementation of trauma systems, and in support of a system once it is in place.

VI. Key issues for future investigation

In order to establish trauma system development as a standard for treatment, a prospective study would have to compare the outcome of treatment of patients randomly taken to hospitals within and without a planned trauma system. This would be required both for trauma patients in general, and for neurotrauma patients in particular. Given the preponderance of data supporting trauma systems, such studies are unlikely to be undertaken.

THE INTEGRATION OF BRAIN-SPECIFIC TREATMENTS INTO THE INITIAL RESUSCITATION OF THE SEVERE HEAD INJURY PATIENT

I. Recommendations

(A) Standards

There are insufficient data to support a treatment standard for this topic.

(B) Guidelines

There are insufficient data to support a treatment guideline for this topic.

(C) Options

The first priority for the head-injured patient is complete and rapid physiologic resuscitation. No specific treatment should be directed at intracranial hypertension in the absence of signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial explanations. When either signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial explanations are present, however, the physician should assume that intracranial hypertension is present and treat it aggressively. Hyperventilation should be

Table 1.

Reference	Description of study	Data class	Conclusions
ACS-COT (1993)	Sixth revision of these guidelines for organization of trauma centres and trauma personnel. Defined by expert opinion and supported by published data where possible	III	Trauma is a surgical disease, and neurotrauma care should be planned and managed by neurosurgeons in concert with other trauma surgeons. Trauma systems and hospitals should be defined and maintained according to these guidelines
Campbell <i>et al.</i> (1989)	Retrospective case series in an undesignated trauma system showing 23% 'preventable' deaths other than head injury judged by group review ($n = 452$)	III	Study demonstrates that a self-designation system without regulatory control results in a high percentage of preventable trauma deaths
Hoyt <i>et al.</i> (1989)	Retrospective analysis of indications for OR resuscitation of trauma patients with cardiac arrest, persistent hypotension despite resuscitation, or uncontrolled external haemorrhage ($n = 323$)	III	No patients survived after blunt trauma and cardiopulmonary arrest. Patients with blunt trauma who have persistent hypotension rarely have surgery started within 20 min of injury. They can be resuscitated in the emergency department. Only patients with penetrating chest and abdominal injuries who have persistent hypotension after resuscitation may benefit from OR resuscitation
Kreis <i>et al.</i> (1986)	Retrospective case series in an undesignated trauma system showing 21% 'preventable' non-CNS deaths judged by group review. A Level I trauma centre had a 12% preventable mortality compared with 21% in planned Level II centres and 30% at 16 other hospitals ($n = 1201$)	III	The authors concluded that severely injured patients should be triaged and taken to trauma centres and that there is a need for an organized trauma system
Mendeloff and Cayten (1991)	Review of trauma system studies and implications for public policy	Review	Evidence suggests that the introduction of trauma systems in urban areas can prevent deaths at a relatively low cost. The federal government should require states or regional organizations to designate appropriate hospitals as trauma centres and to mandate the development of transfer agreements among hospitals
Pitts <i>et al.</i> (1987)	Editorial comment on the need for neurosurgeon involvement in neurotrauma care and planning	III	It is essential for neurosurgeons to take an active role in defining triage schemes for neurotrauma, in helping establish the needed hospital organization for neurotrauma care, in maintaining appropriate call schedules, and in helping in trauma education and quality assurance
Roy (1987)	Review of published literature on the value of local and regional trauma care systems, emphasizing study methodology. Evidence in the reports includes case series reports, before and after studies, and intersystem comparisons	Review	The literature overwhelmingly suggests that the main determinants of survival are the adequacy of resuscitation and the early recognition of serious injuries

Table 1. continued

Reference	Description of study	Data class	Conclusions
Shackford <i>et al.</i> (1987)	Analysis of patients admitted after traumatic injury, of whom 283 were severely injured (trauma score < 8). Of those who had sufficient data ($n = 189$) to compare with a national cohort study that provided a model for predicting survival in patients, actual survival was 29% whereas Ps was 18%. In patients with penetrating injury, Ps was 8% and actual survival was 20% ($n = 3393$)	II	The improved survival was attributed to the integration of prehospital and hospital care and expeditious surgery
J. Smith <i>et al.</i> (1990)	Analysis of data abstracted from computerized discharge information about patients with femoral shaft fractures requiring operation over a one-year period in two states ($n = 1332$)	II	Patients treated in trauma care centres had significantly fewer deaths and complications than in non-trauma centres
R. Smith <i>et al.</i> (1990)	A cohort analysis was performed on data from severely injured patients using three statistical methods to determine the relationship between trauma centre volume and mortality ($n = 1643$)	II	Low-volume trauma centres (fewer than 140 patients annually) had significantly higher mortality when adjusted for head injury, than did high-volume trauma centres (more than 200 patients annually) ($p < 0.04$)
Thompson <i>et al.</i> (1992)	Cohort analysis of trauma admissions at a level II trauma centre showed no difference between survival in that centre and survival among patients in the Major Trauma Outcome Study ($n > 15\ 000$). Whether the trauma surgeon was on call out of the hospital did not adversely affect survival in patients with severe thoracoabdominal injury, compared with the trauma surgeon available in house ($n = 3689$)	II	Level II trauma centres can achieve mortality rates equal to that shown in a large multicentre trauma study, and trauma surgeons promptly available from outside a hospital can produce mortality rates equal to in-house trauma surgeons
West <i>et al.</i> (1979)	Retrospective case series of motor vehicle trauma victims in two California counties, one with a trauma system ($n = 92$) and another without ($n = 90$). About 2/3 of the non-CNS deaths and 1/3 of the CNS deaths in the county with no trauma system were judged by the authors to be potentially preventable. Only one death in the county with a trauma system was judged to be potentially preventable	III	The authors suggested that survival rates for major trauma can be improved by an organized system of trauma care
Wilson <i>et al.</i> (1992)	Compared three methods by which a panel identified preventable trauma deaths other than from head injury, showing different rates of preventable deaths among the three methods	II	Precise determination of preventable deaths is difficult and should not be used to measure institutional quality of care. The authors recommended that assessment of performance should be based on the study of patient population outcomes, rather than on subjective methods in which individual cases are reviewed

CNS, central nervous system; OR, operating room; Ps, predicted survival

rapidly established. The administration of mannitol is desirable, but only under conditions of adequate volume resuscitation.

Sedation and neuromuscular blockade can be useful in optimizing transport of the head injury patient. However, both treatments interfere with the neurological examination. In the absence of outcome-based studies, the choice of sedative is left to the physician. Neuromuscular blockade should be employed when sedation alone proves inadequate and short-acting agents should be used when possible.

II. Overview

Although there is no present technology for its quantification, intracranial hypertension has the potential to exert a detrimental influence on outcome during the period between injury and insertion of an intracranial pressure (ICP) monitoring device. Unfortunately, not only do all treatment modalities for intracranial hypertension have serious potential complications, but many of them can directly interfere with resuscitation procedures (e.g. use of diuretics). The efficacy of cardiopulmonary resuscitation in improving survival from trauma in general is well accepted. In addition, the acknowledged negative influence of secondary insults such as hypertension and hypoxia on outcome from severe head injury establishes systemic resuscitation as the critical foundation upon which treatment of intracranial hypertension must be based. Therefore, in the absence of obvious evidence of elevated ICP, any presumptive or prophylactic treatment must be consistent with optimal systemic resuscitation.

Alternatively, signs of transtentorial herniation are strong evidence of intracranial hypertension and should initiate rapid treatment to lower ICP. Under such circumstances, it is necessary to reassess the balance of cerebral and systemic priorities for the individual situation.

III. Process

The process leading to this section differs from that of the other chapters in this document in that many of the conclusions have been derived from analyses outlined in those other sections. In particular, material from the sections on hyperventilation, mannitol, and management of blood pressure and oxygenation were incorporated. The summary sections from these chapters are reproduced here and the relevant articles included in Table 2.

For the subject of sedation, a MEDLINE search back to 1966 was undertaken using the following key words: 'head injury', 'sedation', and 'human

subjects'. This produced 35 references which were reviewed for clinical relevance and outcome orientation. No articles met these criteria.

For the subject of neuromuscular blockade, a MEDLINE search back to 1966 was undertaken using the following key words: (1) 'head injury' and 'neuromuscular blockage' or 'pharmacologic paralysis' or 'relaxation' and (2) 'human subjects'. This produced 11 references which were reviewed for clinical relevance and outcome orientation. One article met these criteria.

IV. Scientific foundation

There is a dearth of data focused on the efficacy of head-injury specific resuscitation therapy with respect to either the subsequent in-hospital neurologic course or outcome. Therefore, all therapeutic conclusions regarding protocols must remain at the level of treatment options.

- *Sedation.* Approaches to sedation and neuromuscular blockade in the severely head-injured patient vary widely and there is evidence that both sedation and pharmacologic relaxation influence the initial evaluation and treatment of the neurotrauma patient (Marion and Carrier, 1994). Unfortunately, there have been no studies on the influence of sedation on outcome from severe head injury (Chiolero, 1992). Therefore, decisions about the use of sedation and the choice of agents are left to the practitioner to make based on individual circumstances.
- *Neuromuscular blockade.* There has been only one study (Class II) of the influence of neuromuscular blockade on outcome from severe head injury. Hsiang *et al.* (1994) studied the effect on outcome in 514 severe head injuries entered into the Traumatic Coma Data Bank of prophylactic neuromuscular blockade (i.e. pharmacologic paralysis beginning early in the patient's course and lasting at least 12 hours not administered for control of intracranial hypertension). They reported that such use of neuromuscular blockade was associated with a longer intensive care unit course, a higher incidence of pneumonia, and a trend towards more frequent sepsis without providing an improvement in outcome. They suggested that neuromuscular blockade should be reserved for specific indications (e.g. intracranial hypertension and transport) rather than be routinely administered to severe head injury patients.
- *Blood pressure and oxygenation.* Early post-injury episodes of hypertension or hypoxia greatly increase the morbidity and mortality from severe head injury. The literature contains no adequate definition of their actual

physiologic values. However, there is abundant Class II evidence suggesting that early hypotension, defined as a single observation of a systolic blood pressure of less than 90 mmHg, or hypoxia, defined as apnoea or cyanosis in the field, or a $\text{PaO}_2 < 60$ mmHg by arterial blood gas analysis, are associated with increased mortality and morbidity (Chesnut *et al.*, 1993; Fearnside *et al.*, 1993; Pigula *et al.*, 1993). With respect to the efficacy of early treatment, there is now evidence from *post hoc* (Class II) analysis of data from a prospective, randomized, controlled trial that enhanced blood pressure resuscitation improves outcome from severe head injury (Vassar *et al.*, 1993).

A recent single-centre, prospective, randomized, controlled trial suggested that delayed resuscitation was more beneficial than immediate resuscitation in improving outcome from penetrating torso injuries (Bickell *et al.*, 1994). Notably, head injury patients were specifically excluded from this trial. Therefore the concept of delayed resuscitation cannot be considered applicable in head injury.

- **Mannitol.** There are two Class I studies (Schwartz *et al.*, 1984; Smith *et al.*, 1986) and one Class II study (Gaab *et al.*, 1990) that can be used to support mannitol in ICP control (see Mannitol section).
- **Hyperventilation.** Hyperventilation provides a reduction in ICP by causing cerebral vasoconstriction and a subsequent reduction in cerebral blood flow (CBF). Research conducted over the past 20 years clearly demonstrates that CBF during the first day after injury is less than half that of normal individuals (Boama *et al.*, 1991, 1992; Marion *et al.*, 1991) and that there is a risk of causing cerebral ischaemia when aggressive hyperventilation is employed (Obrist *et al.*, 1984). These findings are corroborated by arteriovenous oxygen content different and jugular venous saturation measurements (Robertson and Ryan, 1992; Sheinberg *et al.*, 1992). Aggressive hyperventilation ($\text{PaCO}_2 < 30$ mmHg) will reduce CBF values even further but will not consistently cause a reduction of ICP and may cause loss of autoregulation (Obrist *et al.*, 1984). While the CBF level at which irreversible ischaemia occurs has not been clearly established, ischaemic cell changes are seen in 90% of those who die following severe head injury (Graham *et al.*, 1988). A recent prospective, randomized study found improved outcome at 3 and 6 months when prophylactic hyperventilation was not used compared with when it was (Muizelaar *et al.*, 1991). Thus, limiting the use of hyperventilation following

severe head injury may help improve neurologic recovery following injury or, at least, avoid iatrogenic cerebral ischaemia.

Committee consensus

Consistent with the analyses outlined above and discussed elsewhere in this document, the recommended management approach (Class III-treatment option) is that the management of the severe head injury patient prior to ICP monitoring be predicated on clinical evidence of intracranial hypertension as manifest by signs of herniation. These signs include unilateral or bilateral pupillary dilatation, asymmetric pupillary reactivity, motor posturing, or other evidence of deterioration of the neurologic examination. The most convincing evidence of the development of intracranial hypertension is the witnessed evolution of one or more of these signs.

Successful systemic resuscitation is fundamental to maintaining the possibility of satisfactory neurologic recovery. Therefore, the Advanced Trauma Life Support (ATLS) evaluation remains the first priority. The considerations contained in this chapter are to be applied within the framework of the ATLS approach. An algorithm describing an approach to the resuscitation of the severe head injury patient is presented in Fig. 1.

Management in the absence of clinical signs of herniation

In the absence of clinical evidence of transtentorial herniation, sedation and pharmacologic relaxation should be used when indicated for safe and efficient patient transport. The confusion and agitation frequently attendant to head injury often makes sedation desirable. Pharmacologic relaxation, however, has the undesirable effect of limiting the neurologic examination to the pupils and, upon arrival at the hospital, the CT scan. Therefore, its use in the absence of evidence of herniation should be limited to situations where sedation alone is not sufficient to optimize safe and efficient patient transport and resuscitation. When used, short-acting agents are strongly preferred.

This protocol opinion does not support the 'prophylactic' administration of mannitol due to its volume-depleting diuretic effect. In addition, although it might be desirable to approximate the lower end of the normal range of PaCO_2 during transport of a suspected brain injury, the risk of exacerbating early ischaemia (see Hyperventilation section) outweighs the questionable benefit in the patient without evidence of herniation. Therefore, the protocol option derived here recommends ventilatory parameters consistent with optimal oxygenation and 'normal' ventilation.

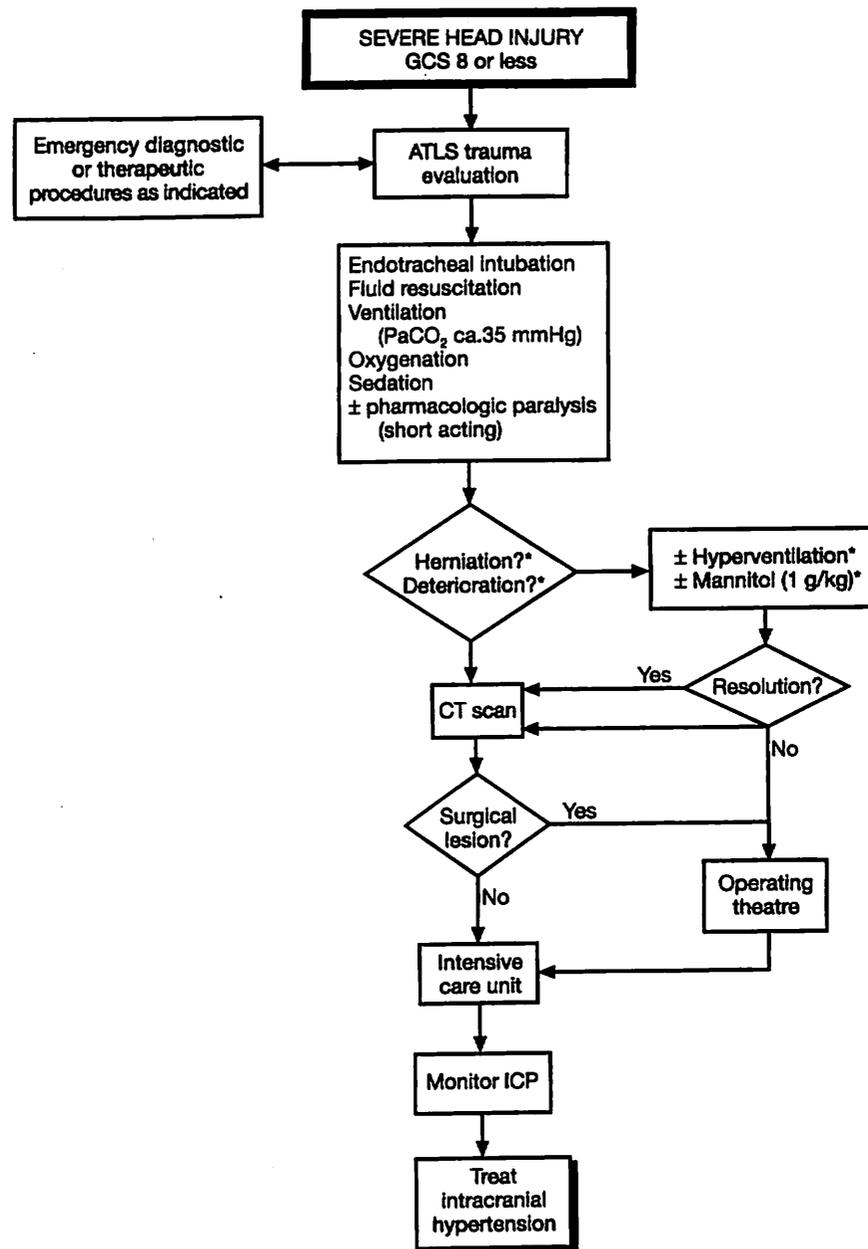


Fig. 1. Initial resuscitation of the severe head injury patient (treatment option). *Only in the presence of signs of herniation or progressive neurologic deterioration not attributable to extracranial factors.

Management in the presence of clinical signs of herniation

When there is evidence of transtentorial herniation (or progressive neurologic deterioration not attributable to extracranial explanations), aggressive treatment of suspected intracranial hypertension is indicated. Hyperventilation is easily accomplished by increasing the ventilatory rate and does not depend on or interfere with successful volume resuscitation. Since hypotension can produce both neurologic deterioration and intracranial hypertension, the use of mannitol is less desirable unless adequate volume resuscitation has been accomplished (see Mannitol section). If

complete volume resuscitation has been attained, however, mannitol should be administered by bolus infusion. Under these circumstances, it is critical that the patient be transported to the hospital with utmost haste.

V. Summary

The fundamental goals of resuscitation of the head-injured patient are the restoration of circulating volume, blood pressure, oxygenation, and ventilation. The physicians should initiate manoeuvres that serve to lower ICP and do not interfere with these aims as early as possible during

resuscitation of any patient with a head injury. Treatment modalities such as hyperventilation and mannitol administration that have the potential of exacerbating intracranial ischaemia or interfering with resuscitation should be reserved for patients who show signs of intracranial hyper-

tension, such as evidence of herniation or neurologic deterioration.

VI. Key issues for future investigation

The key issues discussed in all the chapters relevant to this section are germane to this discussion.

Table 2.

Reference	Description of study	Data class	Conclusions
Bickell <i>et al.</i> (1994)	Single-centre, prospective, randomized, controlled trial to determine the effects of delaying fluid resuscitation until the time of operative intervention in 598 adult hypotensive patients with penetrating injuries to the torso. This study excluded patients with head injuries. Survival to discharge was improved in the delayed resuscitation group	I	Delaying resuscitation in patients with penetrating torso wounds but without severe head injuries may improve outcome
Bouma <i>et al.</i> (1991)	Cohort studies of 186 patients with severe TBI designed to measure early CBF after injury and correlate it with outcome	II	The mean CBF during the first 6 h after injury was 22.5 ± 5.2 ml/100 g/min and CBF was highest at 36–42 h after injury
Bouma <i>et al.</i> (1992)	Cohort studies of very early CBF in 35 patients with severe TBI studied a mean of 3.1 ± 2.1 h after injury	II	Global or regional CBF < 18 ml/100 g/min, defined as ischaemic threshold, was found in 31.4% of the patients
Chesnut <i>et al.</i> (1993)	A prospective study of 717 severe head injury patients admitted consecutively to four centres investigated the effect on outcome of hypotension (systolic blood pressure [SBP] < 90 mmHg) occurring from the time of injury through resuscitation. Hypotension was a statistically independent predictor of outcome. A single episode of hypotension during this period increased mortality 150% and also increased morbidity. Patients in whom hypotension was not corrected in the field had a worse outcome than those who were corrected by time of arrival	II	Early hypotension (SBP < 90 mmHg) significantly increases mortality in a statistically independent manner
Fearnside <i>et al.</i> (1993)	A prospective study of 315 severe head injury patients admitted consecutively to a single centre with respect to pre-hospital and in-hospital predictors of outcome. Hypotension (SBP < 90 mmHg) was an independent predictor of increased mortality and morbidity	II	Hypotension (SBP < 90 mmHg) occurring at any time during a patient's course independently predicts worse outcome
Gaab <i>et al.</i> (1990)	A comparative analysis of THAM in traumatic brain oedema ($n = 21$ patients, not randomized)	II	Mannitol boluses produced a 32% reduction in ICP and the effect was seen for 60 min. THAM was 'at least as effective as mannitol'
Graham <i>et al.</i> (1988)	Histologic study of 71 victims of fatal severe TBI who had no premortem evidence (clinical, radiologic, or pathologic) of elevated ICP	II	Ischaemic cell changes were found in 70% of the brains

Table 2. continued

Reference	Description of study	Data class	Conclusions
Hsiang <i>et al.</i> (1994)	A prospective study of 514 severe head injury patients admitted consecutively to four centres investigated the effect on outcome of prophylactic neuromuscular blockade (i.e. pharmacologic paralysis beginning early in the patient's course and lasting at least 12 h not administered for control of intracranial hypertension). Such use of neuromuscular blockade was associated with a longer intensive care unit course, a higher incidence of pneumonia, and a trend towards more frequent sepsis without providing an improvement in outcome	I	Neuromuscular blockade should be reserved for specific indications (e.g. intracranial hypertension and transport) rather than be routinely administered to severe head injury patients
Marion and Carlier (1991)	Cohort study of 32 patients with severe TBI aimed at defining temporal changes in CBF that occur during the first 5 days after injury	II	Mean CBF was in the first 1–4 h after injury was 27 ml/100 g/min, and CBF was always lowest during the first 12–24 hours after injury. Regional CBF was substantially heterogeneous
Muizelaar <i>et al.</i> (1991)	Prospective, randomized clinical trial of 77 patients with severe TBI comparing clinical outcome for a group hyperventilated to a PaCO ₂ of 25 ± 2 mmHg for 5 days after injury and a group with a PaCO ₂ kept at 35 ± 2 mmHg during that period	I	At 3 and 6 months after injury, the patient with an initial GCS motor score of 4–5 had a significantly better outcome if not hyperventilated
Obrist <i>et al.</i> (1984)	Cohort study of 31 patients with severe TBI in whom the effect of aggressive hyperventilation on ICP, CBF, and arteriovenous difference in oxygen content (AVdO ₂) was examined	II	Hyperventilation had a much more direct effect on CBF reduction (29/31 patients) than it did on ICP reduction (15/31 patients). Aggressive hyperventilation in 10 patients (PaCO ₂ 23.2 ± 2.8 mmHg) led to AVdO ₂ values of 10.5 ± 0.7 vol% and CBF values of 18.6 ± 4.4 ml/100 g/min
Pigula <i>et al.</i> (1993)	58 children (< 17 years old) with severe head injuries were prospectively studied for the effect of hypotension (SBP < 90 mmHg) on outcome. An episode of hypotension decreased survival fourfold. This finding was confirmed in a concomitant analysis of the effect of hypotension on outcome in 509 patients in the National Pediatric Trauma Registry. Hypotension appeared to eliminate any neuroprotective mechanisms normally afforded by age	II	The detrimental effects of hypotension (SBP < 90 mmHg) on outcome appear to extend to children
Robertson and Ryan (1992)	Cohort study of 102 patients with severe head injury examining the time course and relationship of AVdO ₂ , CBF, and ICP	II	AVdO ₂ values were always widest during the first 24 h after injury

Table 2. continued

Reference	Description of study	Data class	Conclusions
Schwartz <i>et al.</i> (1984)	The University of Toronto Head Injury Treatment Study: a prospective, randomized comparison on pentobarbital and mannitol	I	Prospective, randomized comparison of mannitol vs. barbiturates for ICP control. Crossover permitted. Sequential analysis $n = 59$. 'Pentobarbital was not significantly better than mannitol.' Mannitol group had better outcome mortality 41% vs. 77%. Cerebral perfusion pressure much better with mannitol than barbiturates (75 mmHg vs. 45 mmHg)
Sheinberg <i>et al.</i> (1992)	Cohort study of jugular venous O ₂ saturation in 45 patients with severe head injury monitored for 1-8 days	II	Hyperventilation was the second most common identifiable cause of jugular venous desaturations (O ₂ saturation < 50%), and was the cause for desaturation in 10/33 cases
Smith <i>et al.</i> (1986)	Comparison of two mannitol regimens in patients with severe head injury, undergoing intracranial pressure monitoring: effect of bolus mannitol given only when ICP > 25 mmHg, v.s. 'empirical mannitol' (every 2 h until serum osmolarity > 310 mOsm/l, or neurodeterioration)	I	No difference between ICP-directed, and empiric mannitol use. ICP smoother and lower in empiric group. (Power too low to detect an effect, $n = 8$, randomized)
Vassar <i>et al.</i> (1993)	Prospective, randomized, controlled, multicentre trial comparing the efficacy of administering 250 ml of hypertonic saline 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. <i>Post hoc</i> analysis of the severe head injury group (Class II analysis), however, revealed that the hypertonic saline group had a statistically significant improvement in survival-to-discharge	II	Raising the blood pressure in hypotensive, severe head injury patients improves outcome in proportion to the efficacy of the resuscitation

GCS, Glasgow Coma Scale; THAM, tromethamine

Specific to this section is the question of combining these modalities into a protocol and testing the efficacy of that protocol in optimizing resuscitation and improving outcome from severe head injury. The 'prophylactic' treatment of intracranial hypertension in patients suspected of severe head injury is of particular interest and would lend itself to a prospective, randomized trial.

RESUSCITATION OF BLOOD PRESSURE AND OXYGENATION

I. Recommendations

(A) Standards

There are insufficient data to support a treatment standard for this topic.

Table 3. Outcome by secondary insult at time of arrival at traumatic coma data bank hospital for mutually exclusive insults

Secondary insults	Number of patients	% total patients	Outcome (%)		
			Good or moderately disabled	Severely disabled or vegetative	Dead
Total cases	699	100	43	20	37
Hypoxia	78	11	45	22	33
Hypotension	113	16	26	14	60
Neither	456	65	51	22	27
Both	52	8	6	19	75

Hypoxia = PaO₂ < 60 mmHg; hypotension = SBP < 90 mmHg
Adapted from Chesnut *et al.* (1993), with permission

(B) Guidelines

Hypotension (systolic blood pressure < 90 mmHg) or hypoxia (apnoea or cyanosis in the field or a PaO₂ < 60 mmHg) must be scrupulously avoided, if possible, or corrected immediately.

(C) Options

The mean arterial pressures should be maintained above 90 mmHg throughout the patient's course to attempt to maintain cerebral perfusion pressure (CPP) > 70 mmHg.

II. Overview

For ethical reasons, a prospectively controlled study of the effects of hypotension or hypoxia on outcome from severe head injury has never been done. Nevertheless, there is a growing body of evidence that secondary insults occur frequently and exert a profound influence on outcome from severe head injury. This influence appears to differ markedly from that resulting when hypoxic or hypotensive episodes of similar magnitude occur in trauma patients without neurologic involvement. Therefore, we do need to determine if there is any strong evidence that suggests threshold value for oxygenation and blood pressure support.

III. Process

A MEDLINE search back to 1996 was undertaken using the following queries: (1) 'head injury' and 'hypoxia or hypotension' and 'human subjects'; (2) 'head injury' and 'field or pre-hospital or in-hospital' and 'treatment or management or resuscitation'. These produced 188 references. Of these, 79 references were found to be directly relevant with respect to outcome analysis and clinical orientation and were individually reviewed for design, content, and relevance. The results of this review were then incorporated into analysis presented here.

IV. Scientific foundation

The deleterious influence of hypotension and hypoxia on outcome from severe head injury was recently demonstrated by the analysis of a large, prospectively collected data set (717 patients) from the Traumatic Coma Data Bank (TCDB; Class II studies) (Marmarou *et al.*, 1991; Chesnut *et al.*, 1993). The TCDB study demonstrated that pre-hospital hypotension (a single observation of a systolic blood pressure of less than 90 mmHg) or hypoxia (apnoea/cyanosis in the field or a PaO₂ < 60 mmHg by arterial blood gas analysis) were among the five most powerful predictors of outcome and were statistically independent of the other major predictors such as age, admission Glasgow Coma Scale (GCS) score, admission GCS motor score, intracranial diagnosis, and pupillary status. A single episode of hypotension was associated with a doubling of mortality and increased morbidity compared with a matched group of patients without hypotension (Table 3). Hypoxia and hypotension occurred frequently, each occurring in over 1/3 of severe head injury patients. Notably, this study defined hypotension as a single reported incidence meeting the definition of hypotension or hypoxia without requiring either secondary insult to be protracted.²

² The question of the influence of hypoxia and hypotension on outcome is not subjectable to manipulative investigation. In addition, no prospective studies with concomitant cohort controls have been performed or are likely to be undertaken due to ethical considerations. Therefore, the large, prospectively collected, observational data set from the TCDB is the best information on the subject that can be expected to be available. Given the size and nature of this study and the unequivocal nature of the results, the avoidance of hypotension (systolic blood pressure ≤ 90 mmHg) and hypoxia (PaO₂ ≤ 60 mmHg) during the early post-injury period can be supported at the level of a guideline, if not a treatment standard.

A smaller Class II study from Australia supported the above findings, particularly with respect to the effects of hypotension on outcome (Fearnside *et al.*, 1993). The clinical predictors of mortality derived in this study were identical. Notably, in both studies, the only predictor with the potential of being altered through clinical manipulations is hypotension.

A recent retrospective review of prospectively collected data in children less than 17 years of age corroborated these results (Pigula *et al.*, 1993). In this study, hypotension markedly increased morbidity and mortality independently of other predictors of outcome, eliminating the improvement in survival generally afforded by youth.

These data validate similar retrospectively analysed Class II and III reports published previously (Rose *et al.*, 1977; Miller *et al.*, 1978; Jeffreys and Jones, 1981; Miller and Becker, 1982; Narayan *et al.*, 1982; Kohi *et al.*, 1984; Seelig *et al.*, 1986; Gentleman, 1992; Pietropaoli *et al.*, 1992; Hill *et al.*, 1993).

A Class I study has never directly addressed the efficacy of preventing or correcting early hypotension to improve outcome. However, a subgroup of severe head injury patients was subjected to *post hoc* analysis in a recent prospective, randomized, placebo-controlled, multicentre trial comparing the efficacy of administering 250 ml of hypertonic saline vs. normal saline as the initial resuscitation fluid in hypotensive trauma patients. In this trial, the hypertonic saline group had improved blood pressure responses, decreased overall fluid requirements, and associated improvements in survival. When they retrospectively examined the subgroup of patients with severe head injuries, this group had statistically significant improvement in survival-to-discharge (Vassar *et al.*, 1993). Although this was a *post hoc* analysis of Class I data, it strongly suggests that elevating the blood pressure in hypotensive, severe head injury patients improves outcome.

The value of 90 mmHg as a systolic pressure threshold for hypotension has arisen in a rather arbitrary fashion and is more of a statistical than a physiologic parameter. Given the evidence on the influence of CPP on outcome, it is possible that systolic pressures significantly higher than 90 mmHg would be desirable during the pre-hospital and resuscitation phase but no studies have been performed to corroborate this. The importance of mean arterial pressure, as opposed to systolic pressure, should also be stressed, not only because of its role in calculating CPP but because

the lack of a consistent relationship between systolic and mean pressures makes calculations based on systolic values unreliable. It may be valuable to maintain mean arterial pressures considerably above those represented by systolic pressures of 90 mmHg throughout the patient's course.

Once ICP monitoring has been established, manipulation of blood pressure should be guided by CPP management.

V. Summary

Early post-injury episodes of hypotension or hypoxia greatly increase morbidity and mortality from severe head injury. At present, the proper definition of hypotension and hypoxia is unclear in these patients. However, ample Class II evidence exists regarding hypotension, defined as a single observation of a systolic blood pressure of less than 90 mmHg, or hypoxia, defined as apnoea/cyanosis in the field or a PaO₂ < 60 mmHg by arterial blood gas analysis, to warrant the formation of guidelines stating that these values must be avoided, if possible, or rapidly corrected in severe head injury patients (Chesnut *et al.*, 1993; Fearnside *et al.*, 1993; Pigula *et al.*, 1993). Strong Class II evidence suggests that raising the blood pressure in hypotensive, severe head injury patients improves outcome in proportion to the efficacy of the resuscitation (Vassar *et al.*, 1993).

VI. Key issues for future investigation

The major questions are the critical values for duration and magnitude of hypotensive episodes affecting neurological outcome and the optimal resuscitation protocol (fluid type, route of administration, etc.) for resuscitating the severe head injury patient. The former question is not a subject for a controlled trial for ethical reasons and, therefore, would be best addressed using a prospective data collection study with high-resolution collection of pre-hospital blood pressure data, correlating this with outcome. The latter question can be studied in prospective, randomized investigations, several of which are presently underway. Finally, since the actual parameter of interest is CPP, a simple, non-invasive method of determining ICP in the field warrants development.

APPENDIX

Participants: Robert Florin, MD, Chairman, AANS Guidelines & Outcomes Committee; Andrew Jagoda, MD, Representative, American College of Emergency Physicians; James P. Kelly, MD, Representative, American Academy of Neurology;

Table 4.

Reference	Description of study	Data class	Conclusions
Chesnut <i>et al.</i> (1993)	A prospective study of 717 severe head injury patients admitted consecutively to four centres investigated the effect on outcome of hypotension (systolic blood pressure [SBP] < 90 mmHg) occurring from injury through resuscitation. Hypotension was a statistically independent predictor of outcome. A single episode of hypotension during this period increased mortality 150% and also increased morbidity. Patients who hypotension was not corrected in the field had a worse outcome than those whose hypotension was corrected by time of arrival	III	Early hypotension (SBP < 90 mmHg) significantly increases mortality in an independent fashion
Fearnside <i>et al.</i> (1993)	A prospective study of 315 severe head injury patients admitted consecutively to a single-centre investigated pre-hospital and in-hospital predictors of outcome. Hypotension (SBP < 90 mmHg) was an independent predictor of increased mortality and morbidity	II	Hypotension (SBP < 90 mmHg) occurring at any time during a patient's course independently predicts worse outcome
Gentleman (1992)	A retrospective study of 600 severe head injury patients in three cohorts evaluated the influence of hypotension on outcome and the efficacy of improved pre-hospital care in decreasing its incidence and negative impact. Improving pre-hospital management decreased the incidence of hypotension but hypotensive insults remained a statistically significant, independent predictor of poor outcome	III	Management strategies that prevent or minimize hypotension in the pre-hospital phase improve outcome from severe head injury
Hill <i>et al.</i> (1993)	Retrospective study of the pre-hospital and emergency department resuscitative management of 40 consecutive, multitrauma patients. Hypotension (SBP ≤ 80 mmHg) correlated strongly with fatal outcomes. Haemorrhagic hypovolaemia was the major aetiology of hypotension	III	Improving the management of hypovolaemic hypotension is a major potential mechanism for improving the outcome from severe head injury
Jeffreys and Jones (1981)	Retrospective review of hospital records of 190 head injury patients who died after admission. Hypotension was one of the four most common avoidable factors correlated with death	III	Early hypotension appears to be a common and avoidable cause of death in severe head injury patients
Kohi <i>et al.</i> (1984)	Retrospective evaluation of 67 severe head injury patients seen over a 6-month period was correlated with 6-month outcome. For a given level of consciousness the presence of hypotension resulted in a worse outcome than would have been predicted	III	Early hypotension increases the mortality and worsens the prognosis of survivors in severe head injury
Marmarou <i>et al.</i> (1991)	From a prospectively collected database of 1030 severe head injury patients, all 428 patients who met intensive care unit monitoring criteria were analysed for monitoring parameters that determined outcome and their threshold values. The two most critical values were the proportion of hourly intracranial pressure (ICP) readings greater than 20 mmHg and the proportion of hourly SBP readings less than 80 mmHg	II	The incidence of morbidity and mortality resulting from severe head injury is strongly related to ICP and hypotension measured during the course of ICP management

Table 4. continued

Reference	Description of study	Data class	Conclusions
Miller and Becker (1982)	225 severe head injury patients were prospectively studied with respect to the influence of secondary insults on outcome. Hypotension (SBP < 95 mmHg) was significantly associated with increased morbidity and mortality. The predictive independence of hypotension in comparison to other associated factors, however, was not investigated	II	Strong statistical relationship between early hypotension and increased morbidity and mortality from severe head injury
Miller <i>et al.</i> (1978)	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 [see Miller and Becker, 1982]). Hypotension (SBP < 95 mmHg) associated with a trend (not statistically significant) toward worse outcome in entire cohort; trend met statistical significance for patients without mass lesions. Seminal report relating early hypotension to increased morbidity and mortality. Influence of hypotension on outcome not analysed independently from other associated factors	II	First prospective report implicating early hypotension as a major predictor of increased morbidity and mortality from severe head injury
Narayan <i>et al.</i> (1982)	Retrospective analysis of the courses of 207 consecutively admitted severe head injury patients. Management included aggressive attempts to control ICP using a threshold of 20 mmHg. Outcome was significantly correlated with the ability to control ICP	III	ICP control using a threshold of 20 mmHg as a part of an overall aggressive treatment approach to severe head injury may be associated with improved outcome
Pietropaoli <i>et al.</i> (1992)	Retrospective review of the impact of intraoperative hypotension (SBP < 90 mmHg) on 53 otherwise normotensive severe head injury patients who required early surgery (within 72 h of injury). The mortality rate was 82% in the hypotensive group and 25% in the normotensive group ($p < 0.001$). The duration of intraoperative hypotension was inversely correlated with Glasgow Outcome Scale using linear regression ($R = -0.30$; $p = 0.02$)	III	Early hypotension is correlated with significantly increased mortality from severe head injury in a duration-dependent fashion
Pigula <i>et al.</i> (1993)	58 children (< 17 years old) with severe head injuries were prospectively studied for the effect of hypotension (SBP < 90 mmHg) on outcome. An episode of hypotension decreased survival fourfold. This finding was confirmed in a concomitant analysis of the effect of hypotension on outcome in 509 patients in the National Pediatric Trauma Registry. Hypotension appeared to eliminate any neuroprotective mechanisms normally afforded by age	II	The detrimental effects of hypotension (SBP < 90 mmHg) on outcome appear to extend to children

Table 4. continued

Reference	Description of study	Data class	Conclusions
Rose et al. (1977)	Retrospective review of hospital records and necropsy material of 116 head injury patients who talked before dying. Hypotension was a major avoidable factor related to the increased mortality in this group	III	Hypotension is a major avoidable cause of increased mortality in patients with moderate head injury
Seelig et al. (1986)	Studied all patients ($n = 60$) with ICP ≥ 30 mmHg during the first 72 h after injury from a prospectively collected database of severe head injury patients ($n = 348$). Incidence and severity of intracranial hypertension as well as overall mortality were significantly correlated with systemic hypotension. The statistical independence of hypotension as a predictor was not evaluated	II	Early hypotension is significantly correlated with increased incidence and severity of intracranial hypertension and mortality
Vassar et al. (1993)	Prospective, randomized, controlled, multicentre trial comparing the efficacy of administering 250 ml of hypertonic saline 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. <i>Post hoc</i> analysis of the severe head injury group (Class II analysis), however, revealed that the hypertonic saline group had a statistically significant improvement in survival-to-discharge	II	Raising the blood pressure in hypotensive severe head injury patients improves outcome in proportion to the efficacy of the resuscitation

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