Emergency Medicine: Open Access
ISSN: 2165-7548

Chmayssani and Vespa, Emergency Med 2013, 4:1
DOI: 10.4172/2165-7548.1000172

Review Article Open Access

Prehospital Triage and Emergency Room Care in TBI

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Keywords: Brain trauma; Triage; Emergency department management

During the last 30 yrs, there has a been remarkable reduction in severe TBI mortality from 50% to 25% [1]. To ensure further improvement in TBI related mortality and to minimize related morbidity, formalization of further protocols to reduce delays in triage, transfer and treatment of patients should be implemented. Neurointensivists and Neurosurgeons have a long held belief that a decrease in the time between injury and definitive care improves the outcome. The Brain Trauma Foundation endorsed expeditious transfer for patients with a Glascow Coma Score (GCS) of less than 14 to a trauma service with neurosurgery on-site where possible [2]. However, the data supporting any particular time limit remains open to discussion.

Little can be done about the inherent logistical constraints imposed by geography, but systematic transfer delays are potentially remedied. Delay in transfers and triaging is often subject to regional policies and is dictated by local political, cultural, and economical factors. The impact of the delay in receiving definitive care has significant implications for patient outcomes. Overall, patients spend 2-4 hours at non-trauma hospital, 11-18% of those die awaiting transfer [3]. Surgery within 4 hours of injury has been shown to reduce mortality by as much as 60% among patients with acute subdural hematoma [4]. Another study was in favour of rapid surgical intervention showing poor outcomes for patients undergoing subdural or extradural hematoma evacuation only 2 hours following loss of consciousness [5].

It continues to be a challenge to convince pre hospital providers to bypass hospitals closest to injury scene. However, over the past few years, extensive body of evidence endorsing direct transport of injured patients to definitive care center has been studied, established, and well accepted. In a prospective study using compulsory protocol, Hart et al. [6] evaluated prospectively whether direct transport to Level I or Level II trauma center would be associated with decreased mortality at 2 weeks following injury when compared to indirect transfers. Their findings supported the hypothesis that time may indeed be of essence. They showed 50% increase in mortality associated with indirect transfer of TBI patients [6]. These findings were a replica of studies performed a decade earlier [7,8]. Along the same lines, patients that suffered Intracranial Hemorrhages (ICH) and were subject to direct admission from emergency department to neurocritical care unit were less likely to experience ICH expansion and more likely to have to better outcomes [9]. Authors attributed improvement in outcome due prompt implementation of standardized protocol when patients were admitted directly from their own emergency department [9].

Arrival to a definitive care center is paramount for better outcomes. Differences in patient survival between direct and indirect transfers cannot be explained solely on the basis of differences in transport times; in fact, the significance of being directly admitted to a tertiary center is believed to overshadow the importance of overall time to care for mortality [6]. The study conducted by Gerber et al. [10] lends further support for such a finding. They showed that transfer from an emergency department to a tertiary care ICU is associated with better outcomes when compared to transfer from an outside ICU.

To date, it is unclear what subtypes of patients benefit most from prompt initial transfer to trauma centers. Several investigators failed to distinguish subgroups of injured patients that would be best served by direct transport to a level one trauma center [7,11]. The current state of evidence supports the paradigm that, when feasible, major trauma patients should be directly sent to definitive care centers.

The use of civilian helicopters to expedite the transfer of critically TBI is a subject of heated debate. There is a concern in the medical and political community from over triage and financial burden [12]. Applying liberal policy for the use of civil helicopters to transport patients failed to demonstrate clear benefits [13,14]. On the other hand, a number of reports have provided evidence of positive impact in patients' outcomes [15-17]. Some investigators advocated that helicopter evacuations have a considerable influence on the survival of the more severely injured patients but does not demonstrate significant impact on the less injured [16]. The effectiveness for helicopter evacuations is also debatable for rural vs. urban trauma patients [18-20]. Current data raises questions about effective hospital utilization. Further studies with regard to helicopter transport on patient survival and cost-effective utilization is warranted.

As triage and resuscitation protocols evolve, it is essential to expand focus to preventing secondary injury. Following the initial insult, a cascade of pathological events compounds the initial damage in the ensuing hours and days. Unlike various risk factors that are predictors of poor outcome and are fixed at the time of injury such as GCS [21] and mechanism of injury [22], secondary injury is amenable to medical intervention. Elevated ICP, cerebral ischemia and seizures, in addition to other extracranial variables such as hypotension, hypoxemia, and hyperglycemia, are implicated in secondary injury and influence outcomes. The following section will shed light on early resuscitation of TBI patients highlighting the essential physiological endpoints and systemic complications that are frequently encountered (Figure 1).

Hypotension

It is not ethically feasible to subject a patient to experimental hypotension. Current evidence of hypotension and outcome stems from prospective cohorts. Hypotension is a commonly encountered complication in TBI patients [23]. Both pre-hospital and in-hospital hypotensive episodes impact adverse outcomes. A single episode of hypotension was associated with an approximate doubling of mortality and a comparable increase in morbidity [24]. Furthermore, the duration and number of episodes correlated with mortality [25]. Careful attention should be paid to trauma patients that undergo emergent

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Received June 10, 2013; **Accepted** December 29, 2013; **Published** December 31, 2013

Citation: Chmayssani M, Vespa PM (2013) Prehospital Triage and Emergency Room Care in TBI. Emergency Med 4: 172. doi:10.4172/2165-7548.1000172

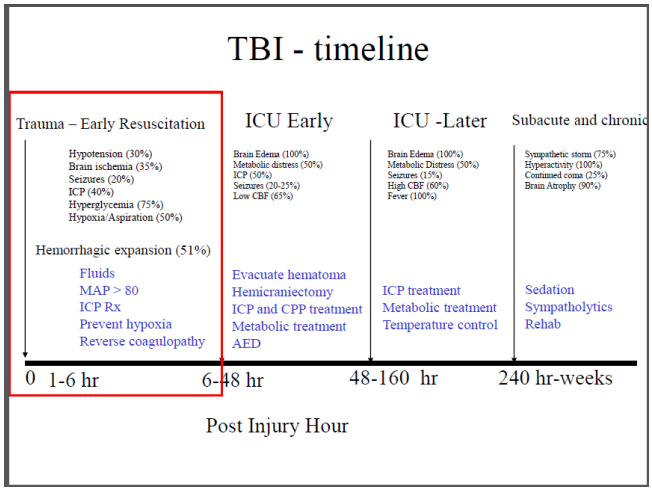

Figure 1: TBI management and complications evolve over time.

surgical intervention, as intra operative hypotension is associated with three-fold increase in mortality [26].

It is not clear what threshold of SBP should be defined as resuscitation end point. The value of 90 mm Hg has been defined by blood pressure distribution for normal adults, thus, 90 mg Hg is more a statistical threshold than a physiologic reference. This traditional definition has come into question in a recent report examining patients with isolated moderate to severe TBI suggesting to raise threshold to 110 mm Hg [27].

Fluid resuscitation represents a cornerstone in the treatment of hemodynamically unstable patients; however, the data for the optimal fluid of choice has evolved influencing the practices over time. Albumin was the mainstream of resuscitation among TBI patients until SAFE study was conducted [28]. The Saline versus Albumin Fluid Evaluation (SAFE) study was an international trial that randomized critically ill patients to either 4% albumin or normal saline fluid resuscitation for 28 days [28]. There was no overall difference in 28-day mortality between the two groups. However, there was a trend toward increased mortality in patients with trauma randomized to albumin resuscitation that was prominent among trauma patients with TBI. A post hoc analysis confirmed that usage of albumin for patients with severe TBI, GCS ≤ 8, was associated with increased mortality at 24 months [29]. It is proposed that following TBI there is increased propensity for extravasation of albumin across the capillary that could lead to increased interstitial oncotic pressure and exacerbate cerebral edema [30,31].

Further evidence exists showing the futility of using colloids in resuscitation of TBI patients. Among patients with severe TBI not in hypovolemic shock, initial resuscitation with either hypertonic saline or hypertonic saline/dextran, compared with normal saline, did not result in superior 6-month neurologic outcome or survival [32] Presently, Crystalloids are safe as first line fluids. Costly Colloids offer no advantage over crystalloids and may be detrimental in patients with traumatic brain injury. Data is lacking as to what specific crystalloid is safest and most efficacious for TBI patients.

Hypoxemia

Hypoxemia is a serious and known complication among patients with TBI. The influence of hypoxemia on outcome has not been subject to manipulative investigation, as it is not experimentally feasible to subject patients to hypoxemia, but the evidence suggesting an adverse affect of hypoxemia on outcome is compelling in both transport and in hospital studies [23]. In one study, on route, patients who suffered hypoxemia independent of hypotension had mortality rate as high as 50% vs. 14.3% in hypoxemic patients [33]. In a hospital-based study, the duration of hypoxemia was found to be an independent predictor of mortality [34].

Although the evidence linking hypoxemia to poor outcome is very well established, the timing as to when to institute mechanical ventilation is controversial. In an Australian based randomized trial, pre hospital rapid sequence intubation was associated with improved outcome at 6 months [35]. On the contrary, another randomized trial pre hospital intubation was associated with adverse outcome compared with intubation in hospital [36]. Lack of adequate experience of paramedics was attributed to an adverse outcome for pre hospital intubations [37]. The current guidelines recommend aggressive airway management in hypo ventilated or hypoxemia TBI patients, either by endotracheal intubation or by mask ventilation [38]. However, rapid sequence intubation does not appear to be beneficial to patients with SaO_2>90% [38].

Seizures

Post traumatic seizures are classified as early, occurring within 7 days of injury, or late, occurring beyond one week from the initial insult. The incidence of seizures among patients with severe TBI is 30% [39,40]. Studies utilizing continuous monitoring with electroencephalography (cEEG) showed nonconvulsive status in 15-25% of patients with coma and severe head injury [41,42].

Seizures have detrimental effect and could precipitate secondary injury. Seizures results in increased blood flow resulting in elevation in ICP, and poses metabolic demand on an already injury brain tissues further aggravating neuronal demise. A randomized, double-blinded, placebo-controlled trial showed that early post traumatic seizures can be effectively reduced by administering phenytoin for 1 to 2 weeks without significant increase in serious drug related side effects or in mortality [43]. Another study showed that administration of Valproic acid may also have a comparable effect to phenytoin on reducing early post-traumatic seizures but may, however, be associated with higher mortality [44]. To date, current evidence does not support the use of prophylactic anticonvulstant to prevent late posttraumatic seizure [43,45]. However, it is proposed that preventing early seizures could decrease the incidence of chronic epilepsy by preventing kindling which would be a nidus for permanent seizures [46].

Hyperglycemia

Hyperglycemia has been repeatedly found to correspond with worsened clinical outcome after traumatic brain injury [47,48] and the extent of hyperglycemia has been correlated with the severity of brain injury [47]. Surprisingly, none of the major guidelines suggest what, if any, treatment should be instituted [2]. By means of microdialysis, Vespa et al. [49] showed that intensive insulin therapy (90-120) vs. loose control (120-150) was associated with increases in micordialysis markers of cellular distress. However, microdialysis is not available in acute stage of TBI management. Presently in the ER, a safe approach is to avoid both extreme hypo- and hyperglycemia until further studies are available to confirm the optimal serum glucose during the acute stage of TBI management when ancillary tools of cerebral monitoring are not available.

ICP

Elevation in intracranial pressure is a frequently encountered complication in TBI patients, and is a robust predictor of poor mortality and worsened outcome [50,51] Indications for ICP monitoring in TBI are a GCS score ≤ 8 and an abnormal CT scan showing evidence of mass effect from lesions such as hematomas, contusions, or swelling [52]. ICP monitoring in severe TBI patients with a normal CT scan may be indicated if two of the following features are present: age >40 years; motor posturing; systolic BP <90 mmHg.

ICP measurements are useful for prognosis and in guiding therapy. ICP lowering therapies is coupled to improvement in outcomes [53]. Often times, ICP elevation is the first sign of worsening of intracranial pathology and surgical mass lesion [54]. Current data supports 20-25 mm Hg as an upper threshold above which treatment to lower ICP should be implemented [55-58]. Any chosen threshold should be carefully interpreted in context of a clinical setting since herniation depends on location of intracranial mass lesion and can occur when ICP measures <20 [59,60]. ICP cannot be reliably predicted solely on CT scan alone [61]. More importantly, ICP is essential in guiding therapy to optimize CPP [62]. CPP is defined as the MAP minus ICP. CPP is utilized as a index of perfusion and a marker for brain ischemia. It appears that the critical threshold for ischemia appears for CPP values <60 mm Hg. Elevated CPP targeted therapy >70 mm Hg offered no clinical benefit and was associated with detrimental systemic complications [63]. Therefore, in the acute stage of TBI management, a CPP >60 and MAP >80 is the recommended goals of therapy. Past the acute stage of TBI management, the critical threshold for CPP indicating ischemia can be further delineated on individual basis by ancillary monitoring such as brain tissue oxygen probe, jugular venous oximetry and cerebral micordialysis. Recent study further supported the utility of microdialysis to optimize management of TBI, but the use of such monitoring is applicable for second stage of TBI care when patient is transferred to the Neurological ICU [64].

Hemorrhagic Expansion

Acutely following moderate to severe TBI, the initial CT scan captures the full extension of hemorrhagic injury in nearly 50% of patients [65,66]. Coagulopathy among TBI patients is either iatrogenic from existing medication or is induced secondary to a systemic release of tissue factor and brain phospholipids leading to a cascade of coagulation dysfunction predisposing patients to microvascular thromobosis and bleeding diasthesis [67].

Hemorrhagic expansion has been shown to be associated with elevated ICP [66] and worse clinical outcomes [68]. A phase II dose-escalation clinical trial of recombinant factor VIIa in TBI patients demonstrated a non-significant trend towards limiting hematoma expansion but no mortality benefit, although this was not directed exclusively at patients with TBI-related INR elevation [65]. Another medication, Tranxeamic acid, that is commonly administered to surgical patients to reduce bleeding and the need for blood transfusion, was studied in patients with TBI and extracranial injuries [69]. Investigators showed that with the use of Tranexamic acid there is a trend towards lower risk of hemorrhagic conversion and formation of new ischemic strokes [69]. This data sets the basis for an ongoing large clinical trial to confirm the beneficiary impact of Tranexamic acid on hemorrhagic conversion in patients suffering solely of intracranial injuries [70].

Presently there are no set guidelines for the evaluation and reversal of coagulopathy. When coagulopathy is identified in the setting of warfarin consumption, it is advised to use Prothrombin Complex Concentrate (PCC), Fresh Frozen Plasma (FFP), and vitamin K. A realistic, somewhat arbitrary target for INR is <1.4. [65] In our institution, in the setting of thrombocytopenia we aim for Platelet count >100 K for TBI associated ICH.

A recent study showed that in spite optimal resuscitation and adherence to guidelines, cerebral metabolic crisis, a marker of ongoing neuronal injury, occurred in the first 72 hours post injury in nearly three quarters of patients. The duration of metabolic crisis was substantially longer for patients with unfavorable outcomes [64]. Hence, we should focus on expediting triage to a tertiary center and accelerating the ER phase of treatment. The goal is to transition to ICU care, to deploy ancillary neuromonitoring modalities and further optimize management.

Triage of the Future

Alternative means of improving care for neurotrauma patients is to: (i) provide early diagnosis and point of care tests (ii) implement Mobile ICU (iii) start resuscitation and specific treatment before hospital arrival.

Early identification of intracranial hematoma in TBI patients allows faster triage and earlier surgical evacuation which is a robust determinant of outcome. Robertson and associates [71-73] evaluated the performance of a near-infrared (NIR)-based, non-invasive, portable device to screen for traumatic intracranial hematomas. The NIR device demonstrated sensitivity of 88% and specificity of 90.7% in detecting intracranial hematomas larger than 3.5 ml in volume and less than 2.5 cm from the surface [73]. Previous studies reported higher sensitivities [74,75]. The device can be used to supplement clinical information, but it is prudent to be aware that the NIR device is limited to detecting other traumatic processes such as diffuse axonal injury or cerebral edema. Hence, severe TBI could exist in the presence of a normal NIR exam. NIR technology should not replace structural imaging when it is readily available.

Frequently, the details of the incident are unclear as a result patients are erroneously triaged as TBI when they actually suffered a primary intracerebral hemorrhage or stroke. The existence of serum biomarker testing and their availability as point of care tests in the scene or on route serves as a valuable adjunct to routine clinical examination and will aid in the most apt triage and cause-specific management decision making. Unfortunately, we are still lagging behind; current serum biomarkers lack reliable sensitivity and specificity precluding their use in diagnostic algorithms [71]. Presently, current evidence supports their use solely for prognostication [72].

The future of triage systems lies in the implementation of mobile intensive-care units. Mobile intensive care units enable patients to withstand the rigors of long distance travels. More importantly, it shortens the distance between the emergency department and patient allowing earlier delivery of cause-specific management. For instance, in Australia, neurosurgeons and neurointensivists are faced with the great challenge of managing head injuries over great distance. For this reason, a mobile neurosurgical service was recommended more than 2 decades ago for patients whose transport times are likely to be greater than 2 hours from a trauma center [76]. Subsequently, this system has been adopted in the official Neurosurgical Society of Australasia (NSA) and Royal Australasian College of Surgeons (RACS) neurotrauma guidelines [77]. This system has proved its validity in stroke patients [78,79] and in treating myocardial infarctions [80].

Time to definitive care is a sum of many time intervals: pre-hospital time, referring hospital time, and transit time. In addition to expediting

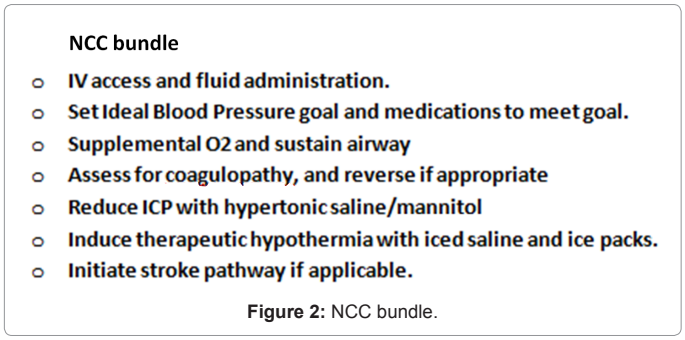

Figure 2: NCC bundle.

transfers, one effective way to overcome the challenge of delays in transfer is to allow different phases to coexist simultaneously; i.e. initiate a basic treatment bundle on triage. A similar system of trauma transfer check has proven validity and was implemented successfully in UK and Australia, resulting in both the reduction of the time required to transfer patients as well as improvement of management [81].

In our institution, we have established an enhanced triage system that is based on the foundation that delayed assessment and treatment can result in lost opportunities to improve outcomes. Telemedicine is a vital part of triage. We are using a telemedicine approach with various hospitals and emergency departments. The sequences of events of this paradigm starts with either pre hospital or emergency room notification of neurocritical care followed by face-to-face contact with patient via Robotic Telepresence (RTP), [82] instead of the traditional telephonic paradigm. The types of information shared would be routine laboratory data, trends of point-of-care testing, radiologic imaging, and electronic reports. This brief encounter is followed by initiation of neurocritical care bundle which highlights the key management goals that could be detrimental to patients care. Nevertheless, the bundle is simple and applicable in a generalized and efficient manner (Figure 2). This enhanced triage protocol remains yet to be tested and is the next wave of progress in the field of triage.

Funding Acknowledgement

UCLA Brain Injury Research Center, supported by NS-058489.

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