Neurotrauma: 50th Anniversary Year Review Article of the *Journal of Trauma*

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The *Journal of Trauma* over its 50 years in publication has grown from being a minor source of information on neurotrauma and neurocritical care to now the third largest US resource outside the major neurosurgical journals—*Journal of Neurosurgery and Neurosurgery*. Publications have run the basic science gamut from cellular mechanisms of central nervous system injury to biomechanics and the clinical spectrum from brachial plexus injuries to traumatic intracranial aneurysms.

For traumatic brain injury (TBI), spine/spinal cord injury (SCI) and peripheral nerve injury topics of investigation have included prehospital care, basic science, epidemiology, direct and secondary injury, surgical and critical care management, outcome, and prevention.

In the early years, there were few publications on neurotrauma in the journal. Indeed, the first two articles published in 1961 were related to lumbar disc disease. Nevertheless, there was a progressive and exponential rise in important neurotrauma contributions in subsequent decades (Fig. 1).

For this "landmark" neurotrauma article review, we have chosen to focus on topics that are arguably responsible for some of the most significant advancements in care over the past several decades—prehospital care; a topic of ongoing debate in intracranial pressure management—hypertonic saline; and two vexing clinical issues—cervical spine clearance and mild/minor TBI.

PREHOSPITAL CARE

The importance of early, definitive airway management in the care of severe TBI was extended from the Emergency Department to the field in the late 1970s and early 1980s. Hypoxia has clearly been associated with an increase in mortality. With a scene or transport $Paco_2$ of <60 mm Hg, more than one-third of severe TBI patients will die and 25% will have a poor outcome. Thus, invasive airway management with rapid intubation of the comatose patient became the de facto prehopsital "standard," even though there was little evidence to support that there was an associated improvement in outcome, so long as hypoxia was prevented/treated.

In an important study in 2003, the Maryland Shock Trauma group, focusing on 191 patients with a Glasgow Coma Score (GCS) <8 and a head Abbreviated Injury Score >3, found prehospital intubation to be associated with a significant increase in morbidity and mortality.

Of the 191 patients, 78 (41%) were intubated in the field and 113 (59%) immediately on hospital arrival. There was no significant difference in any of the factors that have been shown to affect outcome—age, Injury Severity Score, GCS, systolic blood pressure (SBP). There was, however, significantly increased mortality in the field intubation group—23% versus 12.4% ($p = 0.05$; odds ratio [OR] 1.85).[1]

In 2005, a much larger study of more than 13,000 patients from the San Diego Trauma System found similar results. Of the 18.1% of TBI patients undergoing prehospital intubation, mortality was 55% compared with 15% without invasive airway management ($p = <0.001$; OR 0.14). Even when adjusting for confounding factors such as GCS, Injury Severity Score, Abbreviated Injury Score, and prehospital hypotension, there was still a significant increase in mortality ($p < 0.01$; OR 0.36).[2]

Although it remains undisputed that appropriate prehospital airway management and effective ventilation are central tenets of TBI management, *Journal of Trauma* articles have shown that this need not necessarily require an invasive airway. It has been speculated that with an invasive airway, hyperventilation is more common; aspiration is more likely; positive pressure ventilation may exacerbate hypotension; and transport to definitive care is delayed—each individually or collectively potentially having an adverse effect on outcome.

When an invasive airway is used, another issue of importance is the prehospital use of rapid sequence intubation (RSI). The first prospective study of prehospital RSI appeared in the *Journal of Trauma* in 2003.

In a study of 209 prospectively enrolled TBI patients, matched to 627 historical controls, Davis et al. demonstrated increased mortality and worsened outcomes with RSI.

Paramedics were rigorously trained through a special course in RSI, GCS, and ventilation protocols before being allowed to participate. Rigid inclusion criteria were established.

Study findings included longer scene times for RSI patients ($p < 0.0001$), higher Emergency Department arrival Po_2 ($p < 0001$), and lower arrival Pco_2 ($p < 0.0001$).

Submitted for publication July 14, 2010.
Accepted for publication July 19, 2010.

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DOI: 10.1097/TA.0b013e3181f2b713

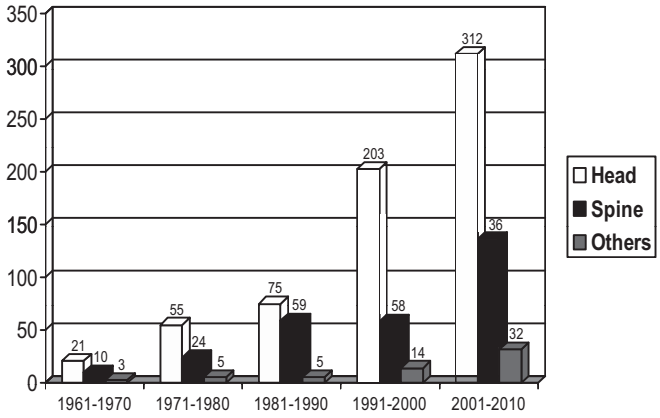

Figure 1. Distribution of neurotrauma articles published in the *Journal of Trauma* over the last 50 years.

Mortality in RSI patients was significantly higher (OR 1.6) and outcomes significantly worse (OR 1.6).[3]

In a follow-up article in 2004, the same authors studied the incidence of hypoxia and hypocapnia in a larger group of RSI patients. Mortality in RSI patients was 40.7% versus 21.5% in matched controls ($p < 0.01$; OR 2.51) Prolonged O_2 desaturations during RSI were associated with higher mortality (OR 1.52); however, the highest mortality occurred in those who were inadvertently significantly hyperventilated ($p < 0.05$; OR 9.94) based on end-tidal CO_2 ($ETco_2$) measurements.[4]

The *Journal of Trauma*, through these studies, has led us to the conclusion that the routine use of O_2 saturation and $ETco_2$ monitors in the prehospital phase may be of significant clinical benefit to TBI patients and that adequate ventilation can be achieved in many circumstances without resorting to an invasive airway.

HYPERTONIC SALINE

The use of hypertonic saline (HS) as a resuscitative fluid and as a treatment for elevated intracranial pressure (ICP) became of clinical interest in the 1990s based in large part on a number of basic science studies published in the *Journal of Trauma*.

An excellent review article by Doyle et al. in 2001 outlines the pertinent hemodynamic effects and mechanisms of action of HS in TBI patients. Aside from its low-volume (1 mL/kg) resuscitative capabilities, HS seems to attenuate cerebral edema by osmotic/bulk flow dynamics and secondary injury through various vascular and cellular mechanisms such as minimizing endothelial cell edema responsible for vasospasm and decreased cerebral blood flow, modulating the inflammatory immune response, and inhibiting excitotoxicity.[5]

In 1989, Zomow et al. published their observations on the use of HS on ICP and cerebral water content in a rabbit model of cryogenic brain injury using lactated Ringer's solution as a control. HS was superior in reducing ICP ($p = 0.0015$) and brain water content in noninjured tissue ($p < 0.01$). The latter finding is of significance because with disruption of the blood-brain barrier, it is not possible to establish an effective osmotic gradient with any agent and a reverse gradient may develop.[6]

In a sheep model combining hemorrhagic shock with cryogenic TBI, Battistella et al.,[7] comparing HS to isotonic fluid resuscitation, found no cardiovascular advantage to HS, but a similar ICP lowering effect ($p < 0.05$) was found, and brain water content decreased in the uninjured brain ($p < 0.05$).

Studies such as these led to the concept that HS may be useful in TBI patients. Such concept has subsequently borne out in a number of nonprospective, nonrandomized trials. Currently, there is an ongoing large, multicenter, prospective, randomized prehospital trial of HS in TBI by the Resuscitation Outcomes Consortium.

MINOR TBI

While the majority of TBI literature focuses on severe TBI, minor TBI occurs at a rate of 130/100,000 and is responsible for >50% of trauma hospital admissions and is a part of the overall injury complex in >60% of multitraumatized patients.

Early, pre-computed tomography (CT) scan era, articles in the *Journal of Trauma* attempted to determine the risk of significant underlying brain injury in the face of clinically minor TBI.

In 1981, Fischer studied their policy of admitting all minor TBI patients for "precautionary" observation for 24 hours. Irrespective of their specific presentation, 99% of the 333 consecutively admitted patients underwent skull X-rays.

Skull fractures were found in 43 patients (13%) and were of "grave prognostic significance." All neurologic morbidity and the single death occurred in those patients with skull fractures of which eight required neurosurgical intervention.[8]

These findings were somewhat contradictory to the prevailing literature and raised some presaging issues on the cost-effective, guidelines-driven practice of medicine.

A similar CT-era study was published in the *Journal of Trauma* in 1992. By this time, CT had become standard in the evaluation of TBI; however, there was ongoing debate over its routine use to guide selective admission of patients with no other reason for admission.

A prospective study was undertaken by seven trauma centers in the Western Trauma Associations Multicenter Trial Group. During the study period, 9,626 patients with head injuries were evaluated and treated. Of this group, 2,826 (29%) had an isolated minor TBI—GCS score 13 to 15.

It was hypothesized that minor TBI patients with a normal neurologic examination and a normal CT should have a vanishing risk of neurologic deterioration or require surgical intervention.

Indeed, it was found that one in 50 such patients have a very small risk of requiring treatment and no risk of requiring craniotomy.

It was thus concluded that "reliable" patients with minor TBI and normal neurologic and CT exams can be safely discharged from the emergency room "provided there is a mechanism for follow-up."[9]

This study thus confirmed the importance of routine CT in patients presenting with minor TBI.

In 2001, the *Journal of Trauma* published the first practice management guidelines to "facilitate a safe, more uniform and cost-effective approach to the understanding and management of minor TBI," which remain in wide use today.[10]

CERVICAL SPINE CLEARANCE

One of the more controversial issues in trauma care is the means, mechanisms, and safety of clearance of the cervical spine in patients with an altered mental status. In such patients, the incidence of C-spine injury has been reported as high as 20%.

While some advocate continued immobilization until such a time as a reliable clinical examination can be established, such examination is oftentimes impossible or very prolonged. It has been shown that maintenance of hard cervical collars for as few as 5 days can result in occipital decubiti and compromise airway management.

In 1998, the *Journal of Trauma* published the EAST practice guidelines on determination of cervical spine instability, which have subsequently gone through several iterations.[11]

Currently, the recommended primary screening modality is axial CT with sagittal and coronal reconstruction. According to the guidelines, "plain radiographs contribute no additional information" and the role of magnetic resonance imaging (MRI) "remains to be determined."

Schenarts et al. prospectively evaluated the EAST guidelines in a consecutive series of 1,356 multitrauma patients.

All eligible patients (n = 136) underwent upper cervical spine (occiput to C3) CT (2-mm cuts) with subsequent reconstruction with saggital and coronal reformatting as well as a five-view plain C-spine X-ray series—lateral, anteroposterior, odontoid, and oblique views.

C-spine injury was found in 20 patients (5.2%) with identification of 95 bony injuries.

CT alone missed three injuries—atlanto-occipital subluxation, C2-C3 subluxation, C3-C4 subluxation—all of which were identified on plain films. Plain films alone missed 46% of the injuries.[12]

Thus, although CT was clearly superior to plain films in identifying potentially clinically significant upper C-spine injury, this study did not provide justification for the complete elimination of plain spine films in the evaluation of trauma patients such as these.

In addition, it is well known that significant ligamentous injury cannot be directly evaluated by CT or plain films alone or in combination.

The role of MRI for assessing ligamentous injury was studied by Stassen et al. Of 52 patients in the study population, 13 (25%) had a negative CT and a positive MRI ($p = 0.01$), 31 had both negative CT and MRI, and 8 had both positive CT and MRI for spine/ligamentous injury.

While in 25% of patients an injury was only diagnosed with MRI, all these patients were simply maintained in a hard cervical collar for 6 weeks and none ultimately required surgery.[13]

Thus, although it could be argued that MRI is "oversensitive," it needs to also be borne in mind that if the MRI is negative, it seems very safe to discontinue spine immobilization.

SPECIAL CONTRIBUTIONS TO NEUROTRAUMA CARE

Cerebral perfusion pressure (CPP) management became a hallmark of TBI treatment based on a seminal article published in *Journal of Trauma* in 1990. The research, undertaken by Rosner et al., advanced targeted CPP treatment over ICP treatment as a "safe, rational and enhanced" therapeutic option. The theory was based on the principal that if control of ICP could not be established/maintained by traditional means, elevation of systolic blood pressure through hypervolemia and pressors would "overcome" the ICP elevations and maintain adequate cerebral blood flow to prevent ischemia.

In 34 patients, increase in CPP to as high as 107 mm Hg despite the consistent ICP of >20 mm Hg resulted in an overall mortality of 21%—but more importantly a mortality of only 8% from uncontrollable ICP. Prior studies had shown a mortality approaching 100% in this patient population.

The physiologic rationale for the effectiveness of this treatment was based on cerebral autoregulation. Rosner and Daughton[14] argued that in "most" TBI patients, autoregulation was intact, thus an increase in CPP would result in a decrease in cerebral vasodilatation and an associated decrease in cerebral blood flow and ICP.

Thus, CPP management was widely adopted in clinical practice until a randomized trial in 1998 demonstrated no significant difference in clinical outcome in CPP- versus ICP-managed patients primarily based on pulmonary complications due to fluid overload.

While CCP remains an important component of TBI management, it is currently recommended that CPP be optimally kept in the 60 to 70 mm Hg range.

The *Journal of Trauma* has published two landmark supplements in neurotrauma: Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children and Adolescents (2003) and Management and Prognosis of Penetrating Brain Injury (2001).

These evidence-based guidelines codified best practices in managing the unfortunately common problem of severe TBI and the relatively uncommon but devastating effects of penetrating injuries.[15,16]

Both sets of guidelines were equally important in providing recommendations for clinical care and identifying gaps in knowledge to spur further research.

CONCLUSION

The *Journal of Trauma*, although not a mainstream neurosurgical journal, has contributed significantly to the advancement of knowledge in the fields of neurotrauma and neurocritical care. It is important to point out that the work of

trauma surgeons has been as prominent in this advancement as the work of neurosurgeons. This emphasizes the importance of a multidisciplinary team approach to both basic science and translational research in continually improving quality clinical care for neurotrauma patients.

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