Updates in ED Management of Trauma Patients
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Introduction

Early hospital management of trauma patients is a daily activity for most emergency physicians. The ability to quickly assess, stabilize and initiate treatment of these patients is critically important to optimize outcomes. This issue of “Resident Journal Review” focuses on selected updates in the trauma literature. We specifically review new developments in trauma pharmacology, biomarkers in trauma, modalities of trauma diagnostics, and management of head trauma in anticoagulated patients.

Trauma Pharmacology: Early Administration of Tranexamic Acid

Tranexamic acid is an amino-acid derivative which binds to plasminogen and inhibits conversion to its fibrinolytic form plasmin. Initially used to minimize bleeding during surgical cases, tranexamic acid is now becoming more widely used in management of trauma patients. The CRASH-2 trial[1] was a randomized controlled, multi-center trial examining the use of tranexamic acid in trauma patients with significant hemorrhage after trauma. The initial study, which examined use of tranexamic acid [loading dose of 1g over 10 minutes then 1g infusion for 8 hours] demonstrated reduced risk of death from bleeding if administered within 8 hours of injury. More recently this data has been examined to maximize the benefit of tranexamic acid use on trauma patients with traumatic bleeding as well as to quell apprehension about possible adverse events secondary to its use.


In this study, the CRASH-2 collaborators looked to optimize the use of tranexamic acid in trauma patients with hemorrhage, specifically to examine the effects of early administration on morbidity and mortality. Toward this end, the authors utilized the CRASH-2 data set of 20,211 adult trauma patients randomized to receive tranexamic acid or placebo at 274 hospitals internationally. The primary outcome examined was death, secondary to hemorrhage within four weeks of injury. Causes of death were categorized as bleeding, vascular occlusion (myocardial infarction, pulmonary embolism, and stroke), multi-organ failure, head injury, and other. Patients were broken into sub-groups determined by time of tranexamic acid administration (<1hr, 1-3hr or >3hr after injury), systolic blood pressure (<75, 75-89, or >89), GCS on hospital arrival (3-8, 9-12, or 13-15), and type of trauma (blunt, penetrating, or both). Patients receiving tranexamic acid within one hour showed a significant reduction in the risk of death secondary to bleeding relative to those in the placebo group, 5.3% [tranexamic group] versus 7.7% [placebo], RR 0.68, CI 0.57-0.82, p<0.0001. This trend continued between hours 1 and 3, 4.8% [tranexamic group] versus 6.1% [placebo], RR 0.79, CI 0.64-0.97, p=0.03. These benefits were found to not exist after 3 hours, and in fact, after 3 hours there was an increased risk of death due to bleeding 4.4% [tranexamic group] versus 3.1% [placebo], RR 1.44, CI 1.12-1.84, p=0.004. It was concluded that if tranexamic acid was given immediately after injury the estimated odds ratio (OR) for survival was 0.61 (95% CI 0.50-0.74). This OR is multiplied by 1.15 (95% CI 1.08- 1.23) for each hour after injury that passes. Stratification by blood pressure, GCS or type of injury did not reveal significant variances in the effect of tranexamic acid.

It is unclear as to why after 3 hours the benefit of tranexamic acid decreases and actually begins to cause harm. The authors provided some possible explanations for this phenomenon. They note that D-dimer concentrations are often found to be elevated at hospital admission in trauma patients, suggesting that the process of fibrinolysis begins quickly in this population. They postulate that only by early antifibrinolytic support can this be suppressed. On a similar note, patients presenting late after injury could have thrombotic disseminated intravascular coagulation which would be in...
fact a contraindication for the antifibrinolytic effects of tranexamic acid. It would also be important to consider that trauma patients with delayed presentation have an increased prevalence of acidosis and hypothermia that could also contribute to decreased efficacy of tranexamic acid after 3 hours.

This paper demonstrated the importance of prompt (within 3 hours) administration of tranexamic acid to hemorrhaging trauma patients. There were several limitations to the study. Though the authors attempted to focus on actively hemorrhaging patients, this diagnosis was made based on clinical signs, and ability to identify these patients with total certainty was impossible. Furthermore, though every effort was made to accurately estimate time from injury to treatment, down times in the field were not always known, leading to uncertainties in this estimate.


Roberts, et al., examined not only the risk of death after receiving tranexamic acid but also the risk of thrombotic events. The authors stratified the CRASH-2 subjects into four groups according to risk of mortality as determined by the authors’ own risk model based on age, GCS, blood pressure, heart rate, respiratory rate, and type of injury; these were <6%, 6-20%, 21-50%, and >50%. Only patients who had treatment started within 3 hours after injury were included. End points were inhospital death within four weeks, death from bleeding, and occurrence of thrombotic events. Those treated demonstrated fewer overall deaths and deaths from bleeding than those not treated in all strata except the lowest strata (<6%). In patients treated with tranexamic acid there was a significant reduction in arterial thrombotic events (OR 0.58, CI 0.40-0.83, p=0.003) and in risk of all thrombotic events (OR 0.69, CI 0.53-0.89, p=0.005). A similar effect was seen in the initial CRASH-2 trial analysis[1] including all patients receiving tranexamic acid within 8 hours of injury. The relative risk of non-fatal and fatal myocardial infarction and other thrombotic events was 0.64 (95% CI 0.42-0.97, p=0.035). This phenomenon is possibly explained by the reduction in bleeding as well as a theorized anti-inflammatory effect of tranexamic acid.

In each of the risk strata, except those in the lowest strata, there was a 30% reduction in the odds of death from bleeding and thrombotic events. This, according to the authors, suggests that tranexamic acid can be administered safely to a wide variety of patients and not only to those with severe hemorrhage.

The authors’ analysis demonstrated reduction in overall thrombotic events, arterial thrombotic events, and death due to bleeding, providing reassurance that there is no increased risk in use of tranexamic acid in the bleeding trauma patient.

Limitations of this study include use of only a subset of the CRASH-2 data set (those receiving tranexamic acid within 3 hours), and the effective difficulty in identifying all thrombotic events occurring in the study population.

Trauma Biomarkers: Monitoring of End Tidal CO\textsubscript{2} and Lactate Clearance

Rapid and accurate triage is imperative to optimizing outcomes for trauma patients. Primary and secondary surveys as well as information about mechanism and circumstances of injury provide important prognostic information. Additionally, early lactic acid levels have been shown to predict outcomes for trauma patients, including risk of mortality.[2] Two recent studies now expand on this with further identification of prognostic factors in trauma patients.


Caputo, et al., explored the use of end tidal carbon dioxide (ETCO\textsubscript{2}) measurements as a surrogate for lactate levels and predictor of need for surgery in penetrating trauma patients. In a prospective cohort study, they enrolled 105 patients with penetrating trauma at a single urban Level-I trauma center. Subjects underwent measurement of ETCO\textsubscript{2}
by nasal cannula and arterial serum lactate on arrival to the hospital. Inclusion criteria were any penetrating trauma patient for whom the trauma team was activated (criteria include blood pressure in adults less than 90 mmHg at any time, gunshot wounds to the head, chest or abdomen, GCS less than 8, respiratory compromise, or emergency physician discretion). Exclusion criteria were loss of vital signs before reaching the trauma bay, intubation prior to arrival, or need for surgical airway support. The primary end point was determination of correlation between ETCO\(_2\) level and serum lactate level. The secondary end point was determination of correlation between ETCO\(_2\) level and need for surgical intervention.

Physiologically, the metabolic acidosis caused by elevated lactate levels should cause an accompanying decrease in blood and ETCO\(_2\) levels. For this study, an elevated serum lactate level was considered to be greater than 4.0, and a depressed ETCO\(_2\) was considered to be less than 35 mmHg. Of the 105 subjects, 58 had a depressed ETCO\(_2\) and 43 had an elevated serum lactate. The authors found a strong inverse correlation between measured ETCO\(_2\) and serum lactate (R=-0.86, p=0.74; 0.63-0.81 for 95% CI, p=0.0001). Interestingly, they found no correlation between either serum lactate or ETCO\(_2\) with systolic blood pressure on hospital arrival. Of the 105 subjects, 61 required operative intervention, and of those 54% had elevated serum lactate and 82% had depressed ETCO\(_2\). The odds ratio of requiring surgical intervention for those having depressed ETCO\(_2\) was 20.4 (7.47-55.96 for 95% CI). For those with elevated serum lactate or systolic hypotension they were 4 (1.68-9.53 for 95% CI) and 3.01 (0.32-27 for 95% CI) respectively. The sensitivity and specificity of depressed ETCO\(_2\) for predicting need for surgery were 0.82 (0.69-0.9 for 95% CI) and 0.82 (0.66-0.91 for 95% CI) respectively.

This study suggests a role for end tidal CO\(_2\) measurement by nasal cannula as a fast and easily-obtainable surrogate for serum lactate level in penetrating trauma patients. Additionally, the ETCO\(_2\) measurement has a strong predictive value for patients requiring surgical intervention. Limitations of this study include exclusion of blunt trauma patients, restriction to a single center, and the possibility of breath-to-breath measurement error intrinsic to nasal cannula capnography.


Régnier, et al., expand on the use of serum lactate as a marker of outcome in trauma patients by exploring trends in lactate clearance. In an observational study, they measured serum lactate on hospital arrival, and again at 2 and 4 hour time intervals for 586 patients of blunt and penetrating trauma at a single level I trauma center. Specific inclusion and exclusion criteria were not laid out, but of the 730 patients in the trauma center during the study dates, 586 had lactic acid levels drawn and were included in the study. The primary end point was 30-day survival. Secondary end points included death within 48 hours, ICU stay longer than two days, massive hemorrhage (requiring six or more units of packed red blood cells within 24 hours or causing death), and the need for emergent procedures (surgery, embolization, transfusion, or thoracic drainage). For each endpoint, the authors generated receiveroperating characteristic (ROC) curves to determine the predictive value of lactate clearance. End points were examined both for the study population as a whole, and for the following two subgroups: patients with high (>5mM/L) initial lactate, and normotensive (SBP>90) patients.

The strongest conclusions of this study were made in the subgroup of patients with initially elevated serum lactate. In this group, initial blood lactate, lactate clearance, and Trauma Related Injury Severity Score (TRISS) were each independent predictors of mortality (area under ROC curve 0.77, 0.60-0.87 for 95% CI; 0.67, 0.51-0.78 for 95% CI; and 0.90, 0.79-0.95 for 95% CI, respectively). The authors note, though, that a predictive model incorporating lactate clearance with TRISS did not provide additional information when compared with using TRISS alone (area under ROC curve 0.92 in both cases).

This study demonstrates that lactic acid clearance over 4 hours can add prognostic information in the evaluation of trauma patients. Limitations of this study include restriction to a single center, and inclusion of only adult patients.
Additionally, lactate clearance may be impaired by serious liver injuries. While the authors acknowledge this and note that 68 patients (12%) in their population had severe hepatic contusion, these patients were not excluded from the study or analyzed separately.

Trauma Diagnostics: Streamlining Use of Computed Tomography (CT) Scans and Surgery

Balancing the risk of a missed injury with efforts to reduce unnecessary radiation exposure and exploratory surgery remains a challenge to emergency providers. While high-resolution CT scanners have improved ease and accuracy of diagnosis, their wide spread use has an associated cost from both a financial and public health perspective. Similarly, for patients with penetrating zone 2 neck injuries an exploratory dissection of the area to rule out injury has traditionally been mandatory. Though this has proved effective in ruling out injury, in many cases it represents an unnecessary surgery. Two recent studies suggest a more conservative approach to CT use in trauma patients and mandatory exploration of neck injuries.


The risk/benefit profile of the whole-body or “liberal” CT in trauma patients has long been contested. Some physicians argue that a more conservative approach, with targeted scans and serial examinations, lessens the radiation exposure to patients without sacrificing diagnostic accuracy or delaying time to intervention. A study out of the University of California, Los Angeles, by Gupta, et al., demonstrated that although trauma surgeons and emergency physicians (EPs) do not necessarily agree on the clinical significance of missed diagnoses, EP decision to not perform a specific CT in all-comer trauma patients had a negative likelihood ratio of 0.05 for a missed abnormal result that would require a critical action. The authors commented that this value, as an indicator of test performance, is comparable to or better than that of most laboratory tests used in clinical medicine. On the other hand, the FIRST (French Intensive care Recorded in Severe Trauma) group found a 30% mortality reduction in the whole-body CT cohort as compared to a selective CT group.

In the midst of this debate, Mahoney, et al., attempted to determine whether or not institution of limited-CT protocol practice guidelines would affect patient outcomes.

This pseudoprospective case-control study compared 612 patients liberally scanned according to the conventional treatment (CONV) in place in 2008 to 611 patients treated according to “evidence-based treatment guidelines” (EBG) — algorithms involving selective CTs with serial examinations — instituted in 2010. At baseline, patients in the EBG group had a higher Injury Severity Score (ISS) (11.93 v. 8.77, p<0.001) but the groups were otherwise similar. There were reportedly no missed injuries in either group, although it should be noted that as long as a diagnosis was eventually made in the EBG group, it was not considered to be delayed or missed, as it occurred according to the serial examinations guideline. As would be expected, there were fewer CTs and a reduction in estimated radiation exposure per patient in the EBG group. There was no difference in average mortality or length of stay in ICU or hospital, but there were significantly more complications and 30-day readmissions in the EBG group. The authors comment that this may be due to the EBG group’s higher ISS, and an expansion in the categorization and documentation of complications in their institution’s trauma registry in 2009 (after data collection for the CONV group, but just prior to that for the EBG group). Although the authors minimize the importance of these complications and readmissions, the additional morbidity and cost associated with them is not clear. The investigators also attempt to analyze cost savings in the EBG group and present a decrease in charges for CT in this group. However, they do not compare total hospital costs between the groups citing difficulty in obtaining these records. The accuracy of CT costs only as a surrogate for total cost of care for each group is not self-evident.

The article would have been strengthened by discussion of the EBG algorithms themselves, how well the serial exam protocols (which are time-intensive and subjective to the examiners performing them) were followed, and how complications occurred and were diagnosed, whether by serial exam or CT. It would also be interesting to know
whether or not the additional days of readmission observed in the EBG group would result in an increased length of stay as compared to the CONV group. Lastly, this study is unfortunately limited somewhat by its generalizability only to admitted patients, so does not help guide management of patients who might be appropriate for discharge, nor can the results be extrapolated to patients with severe trauma as defined by ISS (score>15).


Although representing less than 2% of all penetrating trauma, evaluation and treatment of patients who sustain penetrating neck injuries is particularly challenging for the emergency physician and trauma surgeon.[5] Numerous vital structures, in close proximity, make reliance on any external wound location as a means of determining underlying structural injury impossible. Furthermore, these injuries can be distracting, both for the patient and physician, delaying identification of potentially more serious injuries. Finally, the benefit of mandatory surgical exploration of these injuries has been called into question due to a large number of negative explorations.[6] In this recent article in the *Journal of Trauma* by Inaba and colleagues a clinical protocol for the evaluation of patients with these injuries is reviewed.

In this prospective study, patients with penetrating neck trauma who presented to one of two Level-I trauma centers were reviewed between 2009 and 2011. These patients were classified, by an attending trauma surgeon after clinical examination, into one of three groups with respect to possible vascular or aerodigestive injury. Patients with “hard signs” were those who demonstrated active hemorrhage, pulsatile hematoma, bruit or thrill adjacent to injury, shock unresponsive to fluid resuscitation, massive hemoptysis, hematemesis, or air bubbling at the injury site. This group was taken to the operating room for immediate surgical exploration. Patients with “no signs” were those who were completely asymptomatic and were observed for a minimum of 24 hours. All other patients were considered to have “soft signs” such as minor venous bleeding, nonexpanding hematomas, or subcutaneous emphysema. Soft sign patients were evaluated with multidetector computed tomographic angiography (MDCTA) for further injury.

Of the 453 patients evaluated in this study, 8.6% had hard signs with nearly 90% of these patients having at least one significant vascular or aerodigestive injury identified intraoperatively. A total of 189 patients or 41.7% had no signs of injury and were observed for 24 hours prior to discharge. Of this group, no injuries were missed after 24 hours and no injuries had a delayed presentation identified at a subsequent follow up visit. The 49.7% of patients who were identified as having soft signs underwent MDCTA. The sensitivity and specificity of this technique in identifying significant vascular or aerodigestive injury was 100% and 97.5% respectively. The authors concluded that an initial physical exam of a patient sustaining penetrating neck trauma is a safe and effective way of determining which patients may benefit from immediate surgery, noninvasive imaging or, observation. Overall, this approach can reduce total imaging and unnecessary surgical exploration.

Limitations to this study include the possibility that some patients, whose initial injury was missed, followed up with a clinically significant injury at another facility. Additionally, the initial physical examination, which determined group assignment, was completed by highly experienced surgeons at large volume trauma centers perhaps not reproducible at smaller centers. Finally, the CT scanners utilized in this study were 40 and 64 slice scanners; in contrast many emergency departments have older 16 slice scanners. Again, this potentially makes these findings less generalizable.

Despite limitations, it should be noted these conclusions are not isolated to this one article. In fact, a recent article by Shiroff, et al., reviewed a number of additional studies comparing more traditional algorithms in evaluating penetrating neck trauma against contemporary approaches that employ reliance on physical exam as a means of determining what, if any, further workup may be necessary.[5] Like Inaba, et al., this review found that physical exam findings could be used to direct whether patients should go immediately to the operating room, undergo noninvasive imaging such as MDCTA, or only need a period of observation. Together, these studies suggest a new paradigm for management of penetrating neck injuries, suggesting that management decisions be made based on physical exam findings of aerodigestive injury, rather than simply identification of the zone injured.
Trauma Management: Minor Head Injury in Anticoagulated Patients

Anticoagulation by inhibition of platelets or coagulation cascades improves outcomes in patients at risk for acute coronary syndromes, cerebrovascular accidents, or embolic events. These benefits come at a price, though, of increased tendency toward bleeding, and impaired ability to mount a coagulation response at sites of hemorrhage. This is particularly dangerous for victims of head trauma, who may harbor small but steadily growing intracranial hematomas in the absence of outward signs. Two recent articles address this problem, and propose a protocol for managing minor head trauma in anticoagulated patients while minimizing risk of missed intracranial injury.


This is an observational cohort study done over a two-year period in six centers (two trauma centers and four community hospitals), that evaluated patients suffering a head injury while taking either clopidogrel or warfarin. The study’s aim was to identify the prevalence of immediate intracranial hemorrhage from each of these groups and evaluate the incidence of delayed intracranial hemorrhage up to two weeks after the original injury.

Included patients were greater than 18 years of age, used warfarin or clopidogrel within seven days preceding the injury, and suffered any blunt head trauma. Patients were excluded if they had concomitant use of both warfarin and clopidogrel.

A total of 1,064 patients were included in the cohort analysis. Seven hundred sixty-eight patients were warfarin users and 296 patients were clopidogrel users. The mechanism of injury was a ground level fall in 83%, a direct blow to the head in 6%, and a motor vehicle crash in 5%. Eighty-eight percent of patients had an initial GCS of 15 and 70% of patients displayed evidence of trauma above the clavicles.

The prevalence of immediate traumatic intracranial hemorrhage was higher in patients receiving clopidogrel (33/276; 12.0%; 95% CI 8.4% to 16.4%) than warfarin (37/724, 5.1%, 95% CI 3.6% to 7.0%; relative risk 2.31, 95% CI 1.48 to 3.63; p<0.001). Delayed traumatic intracranial hemorrhage was identified in 4 of 687 patients receiving warfarin (0.6%; 95% CI 0.2% to 1.5%), and 0 of 243 patients receiving clopidogrel (0%; 95% CI 0% to 1.5%).

This is an observational study and not all patients presenting with head trauma received a CT on initial evaluation. Differences between groups existed in that more patients on clopidogrel were taking aspirin, which may confound the higher rate of intracranial bleeding. No difference in the prevalence of initial intracranial hemorrhage was noted when the subgroup of clopidogrel patients not taking aspirin underwent subgroup analysis. Given the observational nature of the study, other unmeasurable differences may explain the difference in bleeding between the two groups. Also, inclusion in the study was based on recent warfarin use, rather than measured INR. Those patients taking warfarin but with nearly normal INRs were treated equally in this study to those with therapeutic warfarin levels, which may skew results toward lower incidence and prevalence of bleed.

The study is helpful in estimating the prevalence and incidence of immediate and delayed intracranial hemorrhage. There is a high rate of hemorrhage among users of both groups, suggesting that a noncontrasted head CT should be strongly considered in all such patients.


Patients suffering mild head injury while taking an oral anticoagulant medication pose a disposition dilemma to the emergency clinician. The authors of this study looked at whether a 24 hour observation protocol with repeat head CT improved the recognition of delayed intracranial bleeding.

The study was set up as a prospective observational cohort study at a Level-II trauma center in Italy. Patients were
Included if they were >14 years of age, were taking warfarin for therapeutic anticoagulation, had an injury severity score <15, had any head injury with a GCS of 14-15, and presented to the ED within 48 hours of injury. Patients were excluded if the first CT showed any evidence of intracranial bleeding or a depressed skull fracture.

Ninety-seven consecutive patients were enrolled after initial negative head CT. Ten patients abstained from the repeat head CT leaving 87 patients with repeat imaging. Five patients developed a delayed intracranial hemorrhage on the second CT; three required hospitalization and one required surgery. Two additional patients presented 2 and 8 days after finishing the observation protocol with symptomatic intracranial hemorrhage. Analysis of patient variables collected on a structured data form at the time of enrollment indicates that an INR greater than 3.0 confers a relative risk of 14 (95% CI: 4 to 49) for delayed intracranial hemorrhage.

This study sets the stage for establishing ED-based observation protocols for minor head trauma in patients on anticoagulation. Of note, none of the patients enrolled had a GCS of 14 or had used any other anticoagulant or antiplatelet agent. The limitations of the study are that this is a single site and the numbers of patients with delayed intracranial hemorrhage was not high and limited the ability to determine predictors of intracranial hemorrhage. Further studies need to evaluate the reproducibility of these results in a multicenter population and also investigate the optimal timing for repeat imaging.

Conclusions

1. Tranexamic acid is most effective in reducing risk of death due to hemorrhage in trauma patients if used within 3 hours of the injury, after this time period it may cause harm. The benefits of tranexamic acid were noted in trauma patients of all injury severities except the most benign, and its use was not associated with increased risk of thrombotic event.

2. ETCO₂ monitoring is inversely correlated with serum lactate level, and is an accurate predictor of need for surgical intervention in penetrating trauma patients.

3. Though the merits of injury detection by serial examination versus whole-body CT scan continue to be debated, protocolled use of serial exams can lead to decreased radiation-exposure without sacrificing diagnostic sensitivity.

4. Penetrating neck injury patients with hard signs of aerodigestive or vascular injury should continue to receive immediate surgical intervention. Those with soft signs can be evaluated by MDCTA, and those without symptoms can safely be observed for 24 hours.

5. Patients taking clopidogrel or warfarin have an elevated risk of immediate or delayed intracranial bleed. A protocolled approach involving an immediate head CT followed by a repeat scan after 24 hours of observation will improve sensitivity of detection.

References


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Cite this article: Updates in ED Management of Trauma Patients. Medscape. Jul 01, 2013.