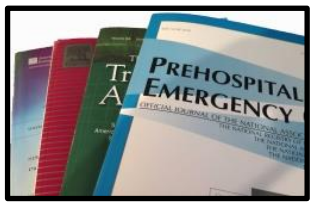
International Prehospital Medicine Institute



IPHMI Literature Review

Keeping You Up to Date with Current EMS Literature and Studies

Vol. 6.6

1. **Evaluating associations between level of trauma care and outcomes of patients with specific severe injuries: A systematic review and meta-analysis**. Van Ditshuizen JC, Rojer LA, Van Lieshout EMM, et al. *J Trauma Acute Care Surg* 2023;94:877-892.
2. **Getting patients to the right level of trauma center after motorcycle crashes in a rural trauma system.** Stamey HM, Brou LI, Meyers KR, et al. *Am J Em Med.* 2024;78:8-11.
3. **Intubation Rates following Prehospital Administration of Ketamine for Acute Agitation: A Systematic Review and Meta-Analysis**. Lipscombe C, Akhlaghi H, Groombridge C, Bernard S, Smith K, Olaussen A. *Prehosp Emerg Care* 2023;27:1016-1030.
4. **Etomidate as an induction agent for endotracheal intubation in critically ill patients: A meta-analysis of randomized trials**. Kotani. Y, Piersanti. G, Maiucci. G, et al. *J Crit Care* Published on-line: 2023;77: doi: 10.1016/j.jcrc.2023.154317.

1. **Evaluating associations between level of trauma care and outcomes of patients with specific severe injuries: A systematic review and meta-analysis.** Van Ditshuizen JC, Rojer LA, Van Lieshout EMM, et al. *J Trauma Acute Care Surg* 2023;94:877-892.

The injury severity system (ISS), used to define major trauma (MT) based on an anatomical injury scoring, might have limitations and underestimate the severity of injuries in the very heterogeneous population of major trauma patients. In this study, they sought to identify the beneficial effect of trauma center level on patient outcome from specific injuries.

Computer search engines were used to identify publications that looked at patient outcomes in relation to trauma level care. Studies that compared different levels of trauma centers caring for trauma patients in relation to fatal and non-fatal injuries were considered for inclusion. Studies that "examined specific severe injuries or severely injured body regions of all causes" with a study population of patients aged 14 years or older were included. Exclusions included studies that focused on burns, pediatrics, isolated hip fractures, and general major trauma as well studies that addressed general public health, economic evaluation, prediction, trauma system implementation, geography or volume-outcome. Conference abstracts, forums, panel discussions, and papers that did not result in full text articles were also excluded.

The review included 35 studies with a total patient population of 1,100,888 trauma patients. Twenty-five (25) of these studies compared survival benefits of Level one and level two trauma centers. Overall, they found a small survival benefit for severely injured patients admitted to a Level 1 Trauma Center compared to a Level II Center. Patients with traumatic brain injury, those with hemodynamic instability, and those with penetrating injury had a survival benefit when admitted to a level one trauma center. They also found that overall hospital length of stays were short while ICU stays were longer in level one trauma centers.

Limitations of this study included overall patient heterogeneity, inconsistent and missing data and the difficulty in determining the effect of level criteria, hospital volume, local EMS protocols, and use of helicopter emergency medical services had on outcomes of the patients included in this study. In addition, functional outcomes of patients could not be compared. They also cited the lack of randomized trials and the fact that they restricted their search to English language publications.

This systematic review and meta-analysis provides support that Level I trauma centers provide a survival benefit compared with non-level I trauma centers for severely injured patients.

2. Getting patients to the right level of trauma center after motorcycle crashes in a rural trauma system. Stamey HM, Brou LI, Meyers KR, et al. *Am J Em Med.* 2024;78:8-11.

Studies have demonstrated that rural trauma patients have a higher mortality compared to similar patients injured in an urban setting. This is due to a variety of factors, including EMS response time, time and distance to a trauma center, and challenges with roads and weather over those distances. Montana is a large state (over 145,000 square miles) with 44% of the population living in "rural" areas with fewer than 2,500 people. Only 53% of the population of Montana lives within 60 minutes of a higher-level trauma center, compared to the national average of 89%. Montana has four American College of Surgeons verified Level II trauma centers, 39 state-designated trauma facilities including 4 Area Trauma Hospitals (equivalent to a Level III), 11 Community Trauma Facilities (equivalent to a Level IV), and 24 Trauma Receiving Facilities. There are no Level 1 trauma centers in Montana.

The purpose of this study is to compare outcomes between motorcycle crash (MCC) patients transported directly to a Level II trauma center versus those initially transported to a lower-level trauma center and subsequently transferred to a Level II. This was a retrospective study of the State of Montana trauma registry over a 2-year period. The two study groups being compared were those transported directly to a Level II (L2TC) and those transported to a lower-level trauma center (LLTC) and transferred to a L2TC. Patients were excluded if they were not transfer to a L2TC, meaning they received all their care at a LLTC, or were transferred out of state to a Level 1 trauma center.

The study included 377 MCC patients. Of these, 186 (55%) were transported to a LLTC and later transferred, while 151 (45%) were transported directly to a L2TC. There were no statistically significant differences between the groups in terms of age, sex, type of crash, helmet use, or having protective clothing. The initial EMS response was slightly longer for the LLTC group (11 minutes vs 8 minutes which was statistically significant), but on-scene time, transport time, and total EMS time did not differ significantly. Those transported initially to a LLTC then transferred to a L2TC had a slightly higher mortality rate than those transported directly to a L2TC (12% vs 8%), but it was not statistically significant. There was no statistically significant difference among the groups in terms of total hospital days, ICU days, or ventilator days.

There were several limitations to this study. This was a retrospective study of a database, with the inherent limitations associated with such a study. The level of EMS care (BLS vs ALS) could not be determined from the database. Patients were not included in the database if they died on scene or were transported directly from the scene to an out of state Level 1 trauma center.

This is a unique study in that it shows no significant difference in mortality between patients transported directly to a Level 2 trauma center compared to those transferred after initial treatment at a lower-level facility, which is not consistent with many other studies which show a survival benefit following direct transport to a Level 1 or II trauma center. This study should not change EMS practice of direct transport to a higher level trauma center whenever possible.

3. Intubation Rates following Prehospital Administration of Ketamine for Acute Agitation: A Systematic Review and Meta-Analysis. Lipscombe C, Akhlaghi H, Groombridge C, Bernard S, Smith K, Olaussen A. *Prehosp Emerg Care* 2023;27:1016-1030.

Prehospital providers frequently encounter patients exhibiting severe agitation for various reasons, and their challenge is to provide safe care and transportation to Emergency Departments. The incorporation of ketamine into prehospital protocols has offered providers a tool to address highly agitated or combative patients. The use of ketamine for managing severe agitation in the prehospital setting has recently sparked controversy. Despite notable incidents that have gained significant public attention, this study focuses on one specific complication: the occurrence of intubation in patients who have received ketamine from prehospital providers.

The authors of this systemic review article searched the medical literature for the use of ketamine as a sedative agent in the prehospital setting for patients experiencing acute, undifferentiated agitation. The primary focus is on determining the rates and settings of intubations following prehospital administration of ketamine, as well as assessing the indications for intubation and any associated adverse events.

Eighteen (18) studies (15 retrospective and 3 prospective) were included in the final analysis. There was significant heterogeneity among the included studies. Of 3,476 patients who received ketamine, 341 (9.8%) were intubated, resulting in an overall intubation rate of 16%. Only 65 patients (1.9%) were intubated in the prehospital setting. In the emergency department (ED), the overall intubation rate was 7.9% (ED intubation rate varied from 0% to 60%). The most common indication for intubation was airway protection (40.4%), followed by respiratory depression/failure (15.8%) and agitation (15.5%). Airway-related issues were the predominant reasons for intubation after prehospital ketamine use for agitation. Limited data were available regarding adverse events, however when present, hypoxia was the most common adverse event, occurring in 11.6% of patients, followed by respiratory distress/depression/apnea (6.7%).

The main limitation of this study was the low grade of evidence produced by most studies reviewed. This in turn produces a lower grade of evidence for this study. A more robust prospective clinical study is needed.

This systematic review reports a significant number of emergency department (ED) intubations following the administration of ketamine for agitation in the prehospital setting. There is no clear explanation for this elevated rate in the existing literature. Interestingly, when ketamine is directly administered in the ED for agitation, the intubation rates are much lower, suggesting that the phenomenon is linked primarily to prehospital ketamine administration. Several factors may contribute to the high ED intubation rate, with individual practice variation among physicians being a notable factor. Some studies indicate that a small number of physicians are responsible for a significant portion of intubations. The reasons for intubation after ketamine use often center on airway and breathing issues, despite ketamine's properties that are supposed to maintain airway reflexes and respiration. This raises questions about the necessity of some of the ED intubations and points towards potential influencing factors such as additional drugs taken by the patient prior to EMS arrival or variations in underlying conditions.

Prehospital providers often encounter patients displaying significant agitation or combativeness. In cases where de-escalation techniques prove ineffective, many protocols permit the administration of ketamine. While this study indicates only a 1% requirement for airway protective procedures before reaching the Emergency Department, prehospital providers must be ready to monitor and promptly address airway and breathing concerns before administering ketamine.

4. **Etomidate as an induction agent for endotracheal intubation in critically ill patients: A meta-analysis of randomized trials.** Kotani. Y, Piersanti. G, Maiucci. G, et al. *J Crit Care* Published on-line: 2023;77: doi: 10.1016/j.jcrc.2023.154317.

Rapid Sequence Intubation (RSI) or Medication Assisted Intubation (MAI) has become an increasingly popular procedure to intubate critically ill patients. The use of medications to optimally prepare a patient for intubation, once limited to operating rooms and intensive care units, is now a common occurrence in emergency rooms and the prehospital environment. Providers have a number of options when it comes to which medication is used to induce / sedate patients prior to using a paralytic agent and placing the endotracheal tube. The use of benzodiazepines for initial induction has progressed to medications such as propofol, etomidate, ketamine and thiopental. Etomidate had been recommended as a preferred option, as it can be rapidly prepared and given via the IV bolus route. However, one of the well-known side effects of etomidate is adrenal suppression.

The authors of this meta-analysis paper looked at published randomized trials that compared fixed interval mortality rates of other induction agents to etomidate to determine if giving etomidate to critically ill patients (patients with organ dysfunction, ill health and a high risk of imminent death without immediate interventions), who are often hemodynamically unstable, increases mortality. Their study was a registered systematic review and meta-analysis limited to patients equal to or greater than 15 years of age.

Database searches initially returned 4,399 papers which were culled accordingly: 1,903 were duplicates, 2,331 were excluded by title / abstract as not relevant, 136 excluded for not being randomized in nature or having no mortality outcome, 18 excluded for not having critically ill patients or not looking at etomidate resulting in 11 papers included in this meta-analysis.

The 11 randomized trials that were included represented 2,704 critically ill adult patients. Countries of origin for the included trials were the United States, France, the United Kingdom and the Netherlands. All trials used an etomidate dose of 0.2 to 0.3 mg/kg. Ketamine alone or with another medication was the most common comparator medication. The primary outcome measure was mortality and the secondary measure was development of adrenal insufficiency.

The authors determined that etomidate was associated with increased mortality when compared to ketamine. Earlier deaths were seen in patients being treated for sepsis. The calculated number needed to harm was 31 (meaning treating 31 patients would result in harm to 1). In addition, etomidate led to a higher incidence of adrenal insufficiency.

Limitations of this work include the potential for providers violating treatment protocols, co-mingling of induction medications to achieve the desired level of sedation, and the possibility heterogeneity by including papers studying induction agents and not using etomidate as the control.

Although this was not directly an EMS study, this paper raises some important concerns about the use of etomidate for induction prior to intubation. Prior analyses have provided conflicting results as to the dangers of etomidate. The authors of this paper believe that the evidence shows that etomidate does cause harm and that another RSI / MAI induction agent should be used for RSI / MAI induction when treating critically ill patients. All providers should always attempt to optimize blood pressure and SpO2 of patients undergoing RSI / MAI before any induction medication is administered. Underlying patient conditions and disease progression must be considered when choosing the best medication to administer to a patient.