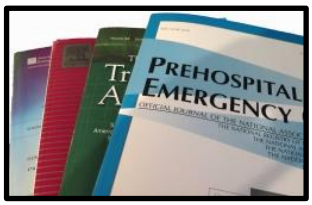
International Prehospital Medicine Institute



IPHMI Literature Review

Keeping You Up To Date with Current EMS Literature and Studies

Vol. 3.2

1. **Effect of Out-of-Hospital Tranexamic Acid vs Placebo on 6-Month Functional Neurologic Outcomes in Patients with Moderate or Severe Traumatic Brain Injury.** Rowell SE, Meier EN, McKnight B, et al. *JAMA* 2020;324(10):961-974.
2. **Paramedic utilization of Vision, Aphasia, Neglect (VAN) stroke severity scale in the prehospital setting predicts emergent large vessel occlusion stroke.** Birnbaum L, Wampler D, Shadman A, et al. *J NeuroIntervent Surg* Published online July 2020. doi:10.1136/neurintsurg-2020-016054
3. **Outcomes with the Use of Bag–Valve–Mask Ventilation during Out-of-hospital Cardiac Arrest in the Pragmatic Airway Resuscitation Trial.** Lupton JR, Schmicker RH, Stephens S, et al. *Acad Emerg Med*. 2020;27:366-374.
4. **Retrospective Analysis of Emergency Medical Services (EMS) Physician Medical Control Calls.** Rai B, Tennyson J, Marshall RT. *West J Emerg Med* 2020;21(3)665-670.

1. Effect of Out-of-Hospital Tranexamic Acid vs Placebo on 6-Month Functional Neurologic Outcomes in Patients with Moderate or Severe Traumatic Brain Injury.

Rowell SE, Meier EN, McKnight B, et al. *JAMA* 2020;324(10):961-974.

Traumatic Brain Injury (TBI) remains a leading cause of death and disability worldwide. Despite multiple trials, no drug has been approved by the U.S. Food and Drug Administration for the management of TBI. Popularized by the CRASH-2 trial, tranexamic acid (TXA) is a drug which has gained popularity over the last decade for treatment of hemorrhagic shock. It works by preventing the natural breakdown of clot by the body, thus reducing ongoing hemorrhage. Some have hypothesized that TXA may be beneficial in patients with TBI by reducing ongoing intracranial hemorrhage and improving long-term functional outcome and mortality. The CRASH-3 trial in 2019 examined the use of TXA in patients with TBI. . The study compared the standard dosing regimen of 1 gm initial bolus followed by a 1 gm infusion over 8 hours to placebo; however, there was no survival benefit.

The Prehospital TXA for TBI Trial was a randomized, double-blind, 3-group, multicenter trial examining the effect of prehospital TXA administration compared to placebo in patients with moderate to severe TBI who were not in shock. The TXA was administered within 2 hours of injury and treatment in the prehospital setting and trauma center was not otherwise altered. The study involved 39 EMS services and 20 trauma centers in the United States and Canada. Eligible patients were aged 15 years or older, had either a blunt or penetrating mechanism of injury, a Glasgow Coma Scale (GCS) score of 3-12, had at least one reactive pupil, and a systolic blood pressure greater than 90 mmHg. Patients were randomized to receive one of three prehospital dosing regimens:

- 1 gm IV TXA bolus followed by a 1 gm infusion over 8 hours (bolus-maintenance group) at the hospital
- 2 gm IV TXA bolus followed by an 8 hour placebo infusion (bolus only group) at the hospital
- IV placebo bolus followed by a placebo bolus at the hospital (placebo group)

The authors chose to study the single 2 gm IV bolus dose since it may be easier to administer in a military or austere environment. The primary outcome studied was 6-month neurologic status, as measured by the Glasgow Outcome Scale-Extended (GOSE) score: a GOSE score > 4 (moderate disability or good recovery) and a GOSE score ≤ 4 (severe disability, vegetative state, or death). Secondary outcomes studied were 28-day mortality, the 6-month Disability Rating Scale (DRS) score (range 0 – no disability to 30 – death), progression of intracranial hemorrhage (ICH), and safety related outcomes.

The study enrolled 966 patients, with a mean GCS 8. Most patients were male (74%), with a mean age of 42 years. The study groups were similar with respect to demographics and baseline physiologic characteristics. The median time from injury to prehospital study drug administration was estimated to be 40-43 minutes across the three groups.

The primary outcome (6-month neurologic improvement) was measured in 85% (819/966) of the patients (15% were lost to follow-up, primarily due to withdrawing from the study or the study investigators were unable to locate them). As expected, the patients lost to follow-up were less severely injured and had better outcomes than the patients who remained in the study. There was no statistically significant difference in neurologic improvement in patients who received either prehospital TXA dose versus those who received placebo (65% vs 62%, p=0.16). The 28-day mortality was 17% in the placebo group (p=0.26), 12% for the bolus only group and 17% for the bolus maintenance group (p=0.98); combined TXA groups vs placebo 14% and 17% respectively, p=0.26. The mortality difference, although not statistically significant, was noted early after injury. This is noted later in the limitations on the study, as those who survived had a higher chance of complications. The difference in DRS score at 6 months and the progression of ICH also show similar non-significant results. Overall, there was a low (and non-significant) rate of adverse events, including thrombosis and seizures.

There are several limitations to the study, which the authors acknowledged. The early mortality difference between treatment groups could lead to survival bias, in which those patients who survived had a higher complication rate simply because they lived long enough to experience more complications. Second, determining exact time of injury can be difficult. Third, GCS measurements in the prehospital setting can be difficult and have been known to be inaccurate. In this study, 20% of participants enrolled had an initial EMS GCS of 13 or higher on admission, despite the enrollment criteria being a GCS < 13. Fifth, follow-up is always difficult in this patient population. The authors acknowledge this as a challenge. Overall, 15% of patients were lost to follow-up.

In conclusion, among patients with moderate or severe TBI, prehospital use of TXA within 2 hours of injury did not improve 6-month neurologic outcome or survival. This study adds to the CRASH-3 study conclusion in which there was no significant improvement in death from head injury among patients who received prehospital TXA versus placebo. EMS Medical Directors and agencies may need to reconsider the role of TXA usage among trauma patients with head injury, as to date it does not appear to be beneficial.

2. **Paramedic utilization of Vision, Aphasia, Neglect (VAN) stroke severity scale in the prehospital setting predicts emergent large vessel occlusion stroke.** Birnbaum L, Wampler D, Shadman A, et al. *J NeuroIntervent Surg* Published online July 2020. doi:10.1136/neurintsurg-2020-016054

There are multiple stroke prediction tools (Cincinnati Prehospital Stroke Scale [CPSS],Rapid Arterial oCclusion Evaluation [RACE], Field Assessment Stroke Triage for Emergency Destination [FAST-ED] and

the Cincinnati Prehospital Stroke Severity Scale [C-STAT]) currently being used by EMS systems. Many of these stroke tools require the provider to calculate a score in hopes of identifying Emergent Large Vessel Occlusion [ELVO] strokes, and in some cases, significant intracranial hemorrhage (ICH).

The Vision, Aphasia, Neglect (VAN) test has been used by nurses to predict ELVOC and ICH. It is simple to perform and does not require any calculations, but it has not been evaluated in the prehospital setting. To perform a VAN test, patients are first asked to raise their arms and hold them up for ten seconds. If they don't exhibit any signs of drift, weakness or paralysis from the arm raise and hold request, the test is considered negative and no further assessments are done. If the patient exhibits any signs of drift, severe weakness or paralysis, the test continues with evaluation for vision symptoms, any aphasia or neglect. The test is considered positive for ELVOC or ICH if the patient has an abnormal arm raise test along with any one or more of the vision, aphasia, or neglect components.

Depending on the patients last known well time (LKW), and if EMS protocols allow, patients with predictive ELVO and ICH exams may be transported directly to comprehensive stroke centers capable of intravenous thrombolysis (IVT) and / or mechanical thrombectomy (MT), bypassing lesser capable hospitals.

The purpose of this study was to evaluate the effectiveness of VAN as a prehospital predictor of ELVOC and ICH. The authors conducted a prospective, system wide, IRB approved study. They also evaluated the ability to easily educate and verify comprehension of VAN in a multi-delivery model EMS system. Both fire based and private EMS providers participated in either classroom, internet based or recorded presentations on how perform a VAN exam. Comprehension was evaluated by patient simulation and a brief ten question quiz.

Between June 2017 to December 2019, all regional paramedics were mandated to perform a VAN assessment on all stroke alert patients transported to any of the three regional Comprehensive Stroke Centers (CSCs). Stroke alerts were activated for all patients with an onset of symptoms within 6 hours of EMS contact, any abnormal finding on the CPSS, and point of care blood glucose levels between 60–600 mg/dL. Wake up strokes, where the time of symptom onset was unknown, were excluded. The authors then looked at the stroke alert criteria, prehospital CPSS and VAN assessments documented in the EMS patient care reports. They also looked at the corresponding patient outcome data from the receiving CSCs which included National Institutes of Health Stroke Scale (NIHSS), neuroimaging, MT and diagnosis. ELVO was determined by emergent advanced neuroimaging (CT angiography of the head looking for both anterior and posterior circulation intracranial occlusions).

In the defined time period, 386 stroke alert patients that were transported, of which 290 (75%) had complete data and were included in the final analysis. VAN assessments were scored positive in 193 (66.6%), NIHSS score was ≥6 in 168 (57.9%), with a mean NIHSS score of 10 (NIHSS score of 0 is completely normal; the higher the score, up to a maximum of 42, the more severe the stroke). In this study, VAN had an 81% sensitivity (true positive) but only a 38% specificity (true negative) for ELVO.

VAN is a simple stroke scale that is easy to teach and implement. While it is able to reliably predict patients with ELVO and ICH it does not necessarily help exclude patients with stroke like symptoms from diseases that mimic stroke. The authors suggest that VAN, with its easily taught and implemented characteristics, may make a good option for some prehospital systems to use to predict which patients with stroke like symptoms should bypass local community hospitals for comprehensive stroke centers.

The study was limited by the fact the stroke patients who did not have a VAN documented were excluded. In addition, the CPSS was used as the initial scoring system to determine whether or not to proceed to a comprehensive stroke center with the VAN being determined only after that decision was already made. The authors did not take the opportunity to directly compare the CPSS to the VAN in terms of sensitivity and specificity.

Unfortunately, this study shows that the ideal prehospital stroke prediction tool has yet to be identified. Based on this study, VAN seems to perform similarly to other prehospital stroke prediction tools and cannot be considered preferable to any of the others.

3. **Outcomes with the Use of Bag–Valve–Mask Ventilation during Out-of-hospital Cardiac Arrest in the Pragmatic Airway Resuscitation Trial.** Lupton JR, Schmicker RH, Stephens S, et al. *Acad Emerg Med*. 2020;27:366-374.

Management of and survival from Out of Hospital Cardiac Arrest (OHCA) has long been a benchmark when assessing EMS performance. Few things have been as controversial as the use of advanced airways. In the early days of OHCA management, bag mask ventilation (BVM) was the standard of care in the prehospital arena. With the advent of advanced prehospital providers and more invasive airways including blind insertion devices (BID) and endotracheal intubation, BVM-only techniques are rarely used. While many studies have been conducted on the use of these various devices, but there has been no definitive consensus as to the preferred method of airway management to optimize patient outcome.

The authors of this study examined the use of BMV-only resuscitation versus resuscitations that employed advanced airways. Data for this study was obtained from the Pragmatic Airway Resuscitation Trial (PART). The PART study was conducted by twenty-seven (27) EMS agencies in larger metropolitan areas of the United States. Patients eligible for enrollment were adults over the age of eighteen (18) with non-traumatic out of hospital cardiac arrest (OHCA). Patients excluded from the study include those with do not enroll bracelets, tracheostomy or advanced airways in place prior to EMS arrival, patients with LVADS, major bleeding or obvious trauma. The terminal outcomes were ROSC, survival to 72 hours, discharge from hospital and neurologically intact survival.

There were a total of 3004 patients enrolled in the PART study. Of these, 352 were managed with BVM-only while 2463 had an advanced airway placed, defined as either an endotracheal intubation or a supra-glottic airway device. One hundred eighty-nine (189) had BVM -rescue after failed intubation attempts. Complete data were available for 282 of the BVM-only patients, 2129 of the advanced airway patients, and 156 of the BVM rescue cases. Response time to the scene, intravenous line success rate, and defibrillation rates were the same for all groups. BVM-only patients had a higher percentage of initial shockable rhythms (34% vs. 18.6%). BVM patients also had a lower proportion of epinephrine administered; twice as many witnessed arrests, and a shorter total resuscitation time. The BVM-only group had greater ROSC (38% vs. 35%), higher survival to hospital admission (36% vs. 25%), and greater neurologically intact survival (21.6% vs. 3.6%). After multivariate regression analysis, the BMV-only patients had similar ROSC to the AAM group, but greater 72 hour survival, hospital discharge rate and neurologically intact survival. The authors conclude that “compared with advanced airway management, bag-valve-mask-only ventilation is associated with improved out-of-hospital cardiac arrest outcomes.

This study suggests that the use of advanced airways should be deferred in favor of BVM-only resuscitation. However, the major limitation to this study, as pointed out by the authors, was that the data used were secondary data gleaned from the PART study that was examining supra-glottic devices vs. endotracheal intubation and was not a randomized, controlled study of the various airway management modalities evaluated as part of this study. It is logical to expect that given early ROSC, the need for advanced airways would be less and survival to discharge is improved. This study clearly suggests the need for a randomized study comparing BVM only to advanced airway management with separate groups for intubation and supraglottic airways.

4. **Retrospective Analysis of Emergency Medical Services (EMS) Physician Medical Control Calls.** Rai B, Tennyson J, Marshall RT. *West J Emerg Med* 2020;21(3)665-670.

In the developmental days of Emergency Medical Services (EMS) with providers, both basic and advanced, acting as the eyes, ears, and hands of the physician, it was not uncommon, if not mandated, for field providers to speak directly with an Emergency Medicine (EM) physician, acting as on-line medical control (OLMC), before performing any invasive procedure, medication administration or allowing the patient to refuse transport against medical advice. As EMS systems matured and, in many cases, as time constraints on EM physicians increased, many systems instituted standing order protocols, allowing field providers to perform authorized bundles of care for patients before speaking with an EM physician. In some systems, one exception has been in interfacility transports (IFT) and critical care transports (CCT). Field providers are often required to speak with OLMC before accepting IFT and CCT calls and to establish unique patient guidelines for adjusting ventilator settings and adjusting medication doses based on the patient's ongoing physiological response to treatment and the added stress of transport.

This study set out to explore the reasons why field providers still seek out OLMC in an EMS system with well-established standing order protocols. They also looked at how much time was spent by physicians delivering OLMC when they could otherwise have been taking care of patients in their emergency department. In their EMS system, any prehospital provider can ask to speak to an EM physician at the patient's receiving facility or they may contact a central medical direction service to speak with the on-call EMS physician or EMS Fellow. This service is provided using a 24/7, HIPAA compliant, recorded phone number. The authors obtained IRB approval to perform a retrospective analysis of OLMC calls to their dedicated EMS physician OLMC telephone line during the calendar year ending December 31, 2016.

Using the recorded medical control phone, the authors replayed and documented data points from all OLMC calls for calendar year 1 January 2016 to 31 December 2016. In addition to patient demographics, OLMC calls were categorized into one of seven reasons, or categories, for the call: refusal of transport, medication orders, level of care, ventilator management, termination of resuscitation, ventilator sedation and other,. They also documented the duration for each of these OLMC phone calls, representing the amount of time an EM physician would be away from direct patient care if they were taking OLMC calls while on-duty in the Emergency Room.

The authors listened to 519 recordings with zero exclusions. The total time for the all 519 calls was 1,594 minutes (26.6) hours that year. The average number of OLMC calls per day was 2.04 lasting on average 3.06 minutes; the maximum number of calls in a day was seven. Most of the calls took place between 16:00 and 08:00 (62.4%). The patient population comprised medical (68.5%), cardiac (16.1%), trauma (13.6%), and obstetrics (9.4%).

The most common reason for OMLC was for assistance with refusal of transport issues (32%). These calls often involved questions regarding the patient's capacity to refuse care and transport. The next most frequent reason was calls grouped into the "other" category (31%). This group was poorly defined and included calls with operational issues such as permission to move a helicopter EMS crew into a ground-based ambulance during times of local inclement weather or for a critical care transport, alteration of destination, and field pronouncement of death. Medication orders were the third most common reason for calls (23.5%). Level of care questions (12%) typically involved interfacility transfers and the ability of the patient to be transported by an ALS interfacility transfer ambulance as opposed to needing critical care transport by a helicopter service nurse/ paramedic team. Ventilator management and settings discussions were next (5%). Termination of resuscitation, a statewide protocol requirement to contact OLMC prior to terminating care in out of hospital cardiac arrest was sixth (4%). Lastly, requests for ventilator related sedation (2.5%).

This study is limited by the fact that it was conducted at a single academic medical center with EMS physicians. Many institutions do not have access to this specific sub-specialty physician group. In addition, these findings may not be generalizable to other EMS systems and emergency departments. It would have helpful to see the second largest group of calls for OLMC (Other) be further characterized for a better understanding of why field providers are calling for OLMC. Finally, this study involved only calls on the central medical direction call service and not those calls that were directed to the destination facility.

This study demonstrates the need to train physicians to provide OMLC for field providers while treating a diverse patient population during difficult field and transport circumstances. The EMS subgroup of EM physicians should be intimately familiar with EMS treatment protocols and the challenges EMS provider face when dealing with complicated patient transfers and refusals of care. It further raises the concept of using EMS trained physicians answering calls for OLMC who are not necessarily actively involved in emergency department patient care while being available for EMS responsibilities. Using EMS physicians may free up valuable patient care time allowing EM physicians to solely concentrate on Emergency Room patients without additional interruptions to take OLMC calls, particularly in busy EMS systems.