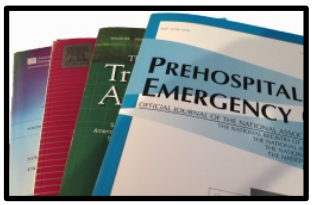
International Prehospital Medicine Institute



IPHMI Literature Review

Keeping You Up To Date with Current EMS Literature and Studies

Vol. 2.7

1. **Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomized, placebo-controlled trial.** The CRASH-3 trial collaborators. Lancet 2019;394:1713-1723.
2. **Death by Suicide—The EMS Profession Compared to the General Public.** Vigil NH, Grant AR, Perez O, et al. Prehosp Emerg Care 2019;23:340-345.
3. **Prehospital Plasma in Injured Patients is Associated With Survival Principally in Blunt Injury: Results From Two Randomized Prehospital Plasma Trials.** Reitz KM, Moore HB, Guyette FX, et al. J Trauma Acute Care Surg. 2020;88:33-41.
4. **Effectiveness of Prehospital Dual Sequential Defibrillation for Refractory Ventricular Fibrillation and Ventricular Tachycardia Cardiac Arrest.** Beck R, Ostermayer D, Ponce J, Srinivasan S, Wang H. Prehosp Emerg Care 2019;23:597-602.

1. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomized, placebo-controlled trial. The CRASH-3 trial collaborators. Lancet 2019;394:1713-1723

There are more than 60 million new cases of traumatic brain injury (TBI) worldwide each year. The most common causes are motor vehicle collisions and falls, and the incidence is increasing. Intracranial bleeding is a common complication of head trauma and can start from the moment of impact and continue for several hours after injury. Tranexamic acid (TXA) reduces bleeding and blood loss by inhibiting the breakdown of fibrin blood clots (fibrinolysis). Prior studies, including the CRASH-2 trial, have demonstrated a survival benefit in bleeding trauma patients who receive TXA within three hours of injury. While controversial, the CRASH-2 trial did set the groundwork for many future trials demonstrating possible benefit of TXA administration in trauma.

The CRASH-3 trial was an international, multicenter, randomized, placebo–controlled trial on the effects of TXA on death and disability in patients with TBI. Adults with TBI who were treated within three hours of injury, had a Glasgow Coma Scale (GCS) score of 12 or less or with intracranial bleeding noted on CT scan, and no major extracranial bleeding were eligible. The primary endpoint was death due to TBI within 28 days of injury. Of note, the authors amended the enrollment criteria midway through the trial. Their original criteria called for inclusion in any patient treated within eight hours of injury. This will be discussed again later, but has been a major criticism of the study. The authors also examined secondary outcomes such as the incidence of vascular events (myocardial infarction, stroke, deep vein thrombosis, and pulmonary embolism). Patients with a GCS of 3 or bilateral nonreactive pupils were excluded because they were unlikely to survive regardless of the treatment provided. Patients were randomized to receive either TXA or a matching placebo

(0.9% NaCl). The TXA dose consisted of an initial loading dose of 1 g over 10 minutes followed by a 1 gm intravenous infusion over eight hours.

This study randomized 12,787 patients from 175 hospitals in 29 countries to receive either TXA (n=6,406) or placebo (n=6,331). Of these, 9,202 (72.2%) were enrolled within three hours of injury. Overall, the authors did not find a clear improvement in survival in patients with TBI who received TXA. However, in patients who had bilateral reactive pupils and a mild-to-moderate head injury (GCS 9-15), the authors did note a potential reduction in the risk of injury related death with TXA compared to those who received placebo (18.5% vs 19.8%). The authors found no benefit of TXA administration in patients with a severe head injury (GCS 3-8). Early treatment of patients with mild to moderate head injury was more effective than later treatment but there was no obvious specific time specified. Of note, while there was a decrease in the risk of death, there was no difference in neurologic function between the two groups. The authors found no evidence that TXA increased the rate of deep venous thrombosis and pulmonary embolism, or myocardial infarction.

This study has some limitations as well as many good qualities. It is another large, international, randomized study showing potential benefit of TXA administration, this time in patients with mild to moderate TBI. However these results must be kept in the context of knowing the authors changed the primary outcome in the middle of the study (administration within 8 hours changed to 3 hours). The results trended towards an improved mortality from mild-to-moderate TBI in patients who received TXA within three hours of injury however the author's blanket statement that TXA is beneficial in mild-to-moderate head injury is inaccurate. There was no analysis of the blood clotting properties of these patients with a thromboelastogram (TEG) to see if fibrinolysis was actually occurring. If it was not occurring, TXA would not be indicated.

In conclusion, TXA may offer a survival benefit in patients with mild-to-moderate TBI who receive their initial dose within three hours of injury, although neurologic function appears to be similar when comparing TXA to placebo. Further studies must be done to validate the claims made in this study. Additionally, further research must be done to see if TXA is beneficial in the prehospital setting.

2. **Death by Suicide—The EMS Profession Compared to the General Public.** Vigil NH, Grant AR, Perez O, et al. Prehosp Emerg Care 2019;23:340-345.

Suicide is the second leading cause of death for people aged 15-34 and is the tenth leading in all age groups in the USA. This has increased over fifteen (15) percent in the eight years from 2008 to 2016. Public safety personel have been identified in many studies to have a significantly higher suicide rate than the general population.

The authors of this study analyzed data compiled from the Arizona Bureau of Vial Records with the permission of the Arizona Department of Health. This retrospective study was conducted analyzing mortality data from the AZ-Electronic Death Registry data base between January 1, 2009 and December 31, 2015. During the study period there were 350,998 deaths in the adult population (over the age of 18). Non-EMTs accounted for 349,793 of the reports and EMTs (included EMTs and Paramedics) accounted for 1205 of the deaths. In the non-EMT group, suicide was listed as the cause of death in 7755 (2.2%) of cases. Of the 1205 cases identified as EMTs, sixty-three (63) deaths were directly identified as suicides. This represents 5.2% off all deaths in the EMT cohort. The EMT group had a higher percentage of males 93.5% vs. 52.8% and were younger that the non-EMT cohort. The mechanism of suicide were similar between the EMT and non-EMT cohorts in the study data set. Firearms were the most prevalent method of suicide (57.6% in the non-EMT group and 66.7% in the EMT cohort) followed by suffocation and poisoning. After adjusting for age, race and ethnicity, EMTs still had a significantly higher suicide rate than those in the non-EMT group.

The national epidemic of suicide has substantially increased to this day. As this study has identified, suicide is even more prevalent amongst EMTs and Paramedics. Programs must be developed to help managers and supervisory staff identify risk factors for suicide and the various stressors in EMS providers that can lead to suicidal ideation and attempt and institute these programs to provide critical evaluation and counseling for the EMS providers who provide vital emergency services to our communities.

3. **Prehospital Plasma in Injured Patients is Associated With Survival Principally in Blunt Injury: Results From Two Randomized Prehospital Plasma Trials.** Reitz KM, Moore HB, Guyette FX, et al. J Trauma Acute Care Surg. 2020;88:33-41

We previously reviewed two major articles analyzing the effect of prehospital plasma transfusion in seriously injured trauma patients. Both studies had a similar design but took place in very different environments. The Control of Major Bleeding After Trauma (COMBAT) Trial was a single center trial in an urban ground ambulance environment. Patients were randomized to either two units of plasma or standard ground transport care involving crystalloid resuscitation. The Prehospital Air Medical Plasma (PAMPer) Trial was a helicopter based study of multiple different aeromedical teams in which patients either received plasma or standard care which involved crystalloid and in some cases packed red blood cell transfusion. Inclusion criteria for both studies were similar and enrolled trauma patients who were hypotensive and tachycardic (SBP < 90 mmHg and HR > 108) or patients who were severely hypotensive without tachycardia (SBP < 70 mmHg). Results varied among the studies. The PAMPer Trial showed a survival benefit to prehospital plasma transfusion in the aeromedical setting while the COMBAT Trial was stopped early as showed no benefit to prehospital plasma transfusion in the urban ground ambulance environment.

In this study the authors combined data from both the COMBAT and PAMPer Trials to further analyze whether there is a benefit to prehospital plasma in severely injured trauma patients. The primary outcome measured was 28-day mortality with secondary outcome analysis including 24 hour mortality, prehospital transport time, and blood transfusion requirements.

A total of 626 patients were in the combined studies. The mean prehospital systolic blood pressure was 80 mmHg, mean Injury Severity Score 22 (major trauma = ISS score>15), and an overall mortality of 24.8%. Blunt mechanism of injury was the most common (75%), with nearly all being from motor vehicle collisions. The 25% who injured due to penetrating trauma were equally divided among gunshot wounds and stab wounds. As expected, the majority of patients in the PAMPer study were blunt and the majority of patients in the COMBAT trial were penetrating.

In those who suffered blunt injury, prehospital plasma transfusion was associated with a 24% reduction in the risk of blood transfusion as compared to those who received standard care. Most significantly, prehospital plasma transfusion was associated with a survival benefit in both short-term (24 hours) and long-term (28 day) mortality in blunt injured patients. The authors specifically noted a 32% improvement in long-term survival in severely blunt injured patients who received prehospital plasma. There was no survival benefit noted among penetrating trauma patients who received a prehospital plasma transfusion.

There are several theories as to why blunt injured patients may benefit from prehospital plasma transfusion while those with penetrating injury do not. In these studies, the blunt injured patients were older, had more significant injuries including traumatic brain injury, and longer overall prehospital transit times, and overall higher mortality. The systemic inflammatory changes associated from blunt injury may be different than those in penetrating injury. Penetrating trauma has a higher rate of bleeding amendable to rapid surgical control versus blunt trauma. Additionally,

most penetrating trauma occurs in an urban environment with shorter transport times which may limit the relative benefit of prehospital plasma transfusion.

Unfortunately, there remain significant logistic challenges and obstacles to the widespread implementation of prehospital plasma administration including the fact that, at least in the United States, plasma is a frozen product which has strict storage requirements and must be thawed prior to use.

4. **Effectiveness of Prehospital Dual Sequential Defibrillation for Refractory Ventricular Fibrillation and Ventricular Tachycardia Cardiac Arrest.** Beck R, Ostermayer D, Ponce J, Srinivasan S, Wang H. Prehosp Emerg Care 2019;23:597-602.

Improving survival from out of hospital cardiac arrest (OHCA) remains a challenge for many, if not most, EMS systems. Early recognition, bystander CPR and early defibrillation are key factors for successful out of hospital resuscitation and survivability of the patient. Occasionally, patents remain in ventricular fibrillation (VF) or ventricular tachycardia (VT) despite repeated shocks from a defibrillator. Dual sequence defibrillation (DSD) has been advocated as an intervention to convert refractory VF/VT, although the literature as to its success is conflicting. DSD is typically attempted by placing two sets of defibrillation pads from two separate manual defibrillators in opposing positions on the torso, anterior-lateral and anterior-posterior, followed by sequential biphasic defibrillations at 360 joules each. This study is an effort to determine if DSD is a reliable treatment option for patients in refractory ventricular fibrillation (RVF).

The authors conducted a four-year, IRB consent waived, retrospective study of all patients treated for OHCA by the Houston, TX Fire Department (HFD) EMS service. They looked at patient outcomes including return of spontaneous circulation (ROSC), survival to hospital admission, survival at 72 hours, and survival to hospital discharge. They defined RVF as patients who remained in VF following three defibrillations. The HFD DSD protocol requires on-line medical control consultation for two defibrillators to deliver simultaneous, 360 joules, biphasic shocks.

The study group was divided into two subsets, patients who received DSD and those that were treated with standard defibrillation. During the four year study period ending December 2016, 314 patients were identified as OHCA presenting with RVF. After excluding four patients for missing data or being underage for the study, 310 patients remained. The average age for all patients was 62 years of age. Seventy-one patients received at least one attempt at DSD. The remaining 239 patients received standard defibrillation. Bystander CPR was performed on 54% of the DSD group and on 49% of the standard defibrillation group.

ROSC occurred in 39% of the DSD group and in 60% of the standard defibrillation group. There was no statistical difference between the two groups in survival to hospital admission, 72-hour survival or survival to discharge, although DSD trended to be lower in all survival categories.

In this study, RVF patients were less likely to gain ROSC with DSD than standard defibrillation. The authors observed no difference in discharge outcomes and concluded that DSD may not be beneficial for patients in RVF.

HFD is an urban EMS system with many resources and the ability to bring multiple defibrillators and personnel quickly to the scene of an OHCA. Even with that depth of resources, DSD failed to improve the occurrence of ROSC, or survival to discharge, in OHCA patients in RVF. Systems with

fewer resources may have challenges implementing a DSD protocol, which may or may not have a patient survival benefit. Additional research is needed to determine if, and when, DSD is beneficial in the treatment of RVF in OHCA.