

Impact of Prehospital Exsanguinating Airway-Breathing-Circulation Resuscitation Sequence on Patients with Severe Hemorrhage

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- BACKGROUND:** At the 2023 ATLS symposium, the priority of circulation was emphasized through the “x-airway-breathing-circulation (ABC)” sequence, where “x” stands for exsanguinating hemorrhage control. With growing evidence from military and civilian studies supporting an x-ABC approach to trauma care, a prehospital advanced resuscitative care (ARC) bundle emphasizing early transfusion was developed in our emergency medical services (EMS) system. We hypothesized that prioritization of prehospital x-ABC through ARC would reduce in-hospital mortality.
- STUDY DESIGN:** This was a single-year prospective analysis of patients with severe hemorrhage. These patients were combined with our institution’s historic controls before prehospital blood implementation. Included were patients with systolic blood pressure (SBP) less than 90 mmHg. Excluded were patients with penetrating head trauma or prehospital cardiac arrest. Two-to-one propensity matching for x-ABC to ABC groups was conducted, and the primary outcome, in-hospital mortality, was compared between groups.
- RESULTS:** A total of 93 patients (x-ABC = 62, ABC = 31) met the inclusion criteria. There was no difference in patient age, sex, initial SBP, initial Glasgow Coma Score, and initial shock index between groups. When compared with the ABC group, x-ABC patients had significant improvement in vitals at emergency department admission. Overall mortality was lower in the x-ABC group (13% vs 47%, $p < 0.001$). Multivariable regression revealed that prehospital circulation-first prioritization was independently associated with decreased in-hospital mortality (odds ratio 0.15, 95% CI 0.04 to 0.54, $p = 0.004$).
- CONCLUSIONS:** This is the first analysis to demonstrate a prehospital survival benefit of x-ABC in this subset of patient with severe injury and hemorrhagic shock. Standardization of prehospital x-ABC management in this patient population warrants special consideration. (*J Am Coll Surg* 2024;238:367–373. © 2024 by the American College of Surgeons. Published by Wolters Kluwer Health, Inc. All rights reserved.)

The airway-breathing-circulation (ABC) sequence has been considered standard of care for CPR since the first guidelines were published in 1966 and championed by the American Heart Association.¹ The ATLS guidelines,

developed in the late 1970s, adopted a similar ABC approach to the initial evaluation and management of patients with traumatic injury.² As evidence emerged that cardiac arrest survival was improved among patients who

Members of the Damage Control Resuscitation Study Group who coauthored this article are listed in the Appendix.

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Abbreviations and Acronyms

ABC	=	airway breathing circulation
ARC	=	advanced resuscitative care
ED	=	emergency department
GCS	=	Glasgow coma scale
HR	=	heart rate
OR	=	odds ratio
SBP	=	systolic blood pressure
SI	=	shock index
TXA	=	tranexamic acid
x-ABC	=	exsanguinating hemorrhage control airway breathing circulation

received early chest compressions and defibrillation, the American Heart Association shifted to a "circulation first" approach and introduced the circulation-airway-breathing sequence into the 2010 CPR guidelines.³ Similar physiologic principles may explain improvement in trauma outcomes when hemorrhage control and restoration of circulating blood volume are prioritized over early advanced airway management. The ATLS guidelines, however, for the next 13 years continued to recommend an ABC sequence for the early management of injured patients.⁴

Based on physiologic principles and emerging clinical evidence that earlier hemorrhage control and hemostatic resuscitation improves outcomes after trauma, numerous authors have advocated a shift toward "circulation-first" resuscitation in trauma care, where control of hemorrhage and restoration of circulating blood volume are prioritized over an ABC sequence prioritizing early invasive airway management.⁵⁻⁷ At the recent 2023 Global ATLS Symposium, an "x-ABC" resuscitation concept was proposed to formalize this shift, where "x" signifies the priority of addressing exsanguinating hemorrhage before other interventions.⁷

The emerging recent trend toward prehospital transfusion offers an opportunity to study the real-world application of the x-ABC approach to severe traumatic injury since both hemorrhage control and early resuscitation with blood products can now be provided closer to the point of injury and before hospital arrival. We chose to evaluate the impact of an x-ABC resuscitation strategy in a busy urban emergency medical services (EMS) system where a prehospital advanced resuscitative care (ARC) bundle was recently implemented to address a rise in trauma mortality associated with an epidemic of gun violence. The objective of this study was to determine the impact of the ARC bundle on prioritization of a circulation-first, or x-ABC, approach to trauma patients with severe hemorrhage on in-hospital mortality.

METHODS**Study population**

This was a single-year prospective analysis of patients with severe hemorrhage who received a prehospital advanced resuscitative care (ARC) bundle after a penetrating injury. The ARC bundle consisted of 2 units of packed RBCs administered via a rapid transfusion device, 2 g of calcium chloride, and 2 g of tranexamic acid (TXA) administered at the scene and during transport to the trauma center. Patients who received the ARC bundle were considered the x-ABC cohort and were compared with patients in our institution's trauma registry from 2016 to 2019, before implementation of the prehospital blood transfusion program. These patients were deemed controls as they were eligible for ARC based off presenting physiology but did not receive blood products, calcium, or TXA in the prehospital setting. The controls were labeled as the "ABC" group since they were intubated prehospital. Patients with prehospital hypotension who sustained penetrating injuries were included for analysis. For the purposes of this study, patients with a prehospital SBP listed as "unable to obtain" at initial EMS triage were presumed to have an SBP of 90 mmHg or less and were included in the analysis. Patients with blunt injuries, isolated head injuries, prehospital cardiac arrest, or missing prehospital vital signs were excluded. Once grouped, 2-to-1 propensity matching for x-ABC to ABC groups was conducted using vital signs collected at EMS arrival including SBP, heart rate (HR), and Glasgow Coma Scale (GCS) as predictors with a match tolerance of 0.01.

Data sources

Variables included patient demographics, vitals, injury type (penetrating), SBP, HR, shock index (SI), and GCS for both EMS and emergency department (ED) characteristics, total prehospital interval, and in-hospital mortality. Prehospital interval was defined as the total time from activation of EMS to ED arrival in minutes. Hypotension was defined as an initial EMS SBP 90 mmHg or less.

Statistical analysis

The primary outcome of interest was in-hospital mortality. Secondary outcomes of interest included EMS transport times, EMS interventions, vital sign changes from EMS to ED destination, ED interventions, total blood transfused and mortality location. The distribution of continuous variables was tested and reported as median (interquartile range [IQR]). These variables were then tested using independent sample Mann-Whitney U analysis. Categorical variables were expressed as frequencies and percentages

and compared using 2-sided chi-square analysis. Sensitivity analysis was conducted on univariate statistics to assess the impact of missingness on p values and conclusions drawn from the analysis. Median, highest, and lowest values were independently imputed for missing data, and univariate analysis was repeated for each outcome. This analysis showed no impact on reported p values, and therefore, all variables were included in univariate analysis.

Multivariate analysis began by independently assessing each variable’s impact on in-hospital mortality through univariate logistic regression. Patients with missing data were automatically excluded during this phase of analysis. A multivariate logistic model was then constructed using each variable identified as an independent predictor of in-hospital mortality.

All data analysis was conducted using SPSS version 29 (IBM, Armonk, NY). In this analysis, a p value of less than 0.05 was considered statistically significant. We sought to adhere to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines to ensure all necessary components of the study design were included and discussed. This study obtained IRB approval before commencement.

RESULTS

Figure 1 details patient inclusion criteria. During the study period, a total of 2,024 patients with an EMS or ED triage SBP of 90 mmHg or less were evaluated. Among these patients, 1,149 were excluded due to nonpenetrating injuries, 111 due to prehospital cardiac arrest, 15 due to isolated head injuries, and 539 due to missing data. The remaining

cohort of 210 patients was divided into the ABC group (n = 53) and x-ABC group (n = 153). Two-to-one propensity matching for x-ABC (n = 62) to ABC (n = 31) groups was conducted using scene SBP, HR, and GCS as predictors with a match tolerance of 0.01. Patients were predominately Black (97%) and men (91%) with a median (IQR) age of 32 (24 to 41) years. Prehospital vitals, interventions, timing intervals, hospital characteristics, and new injury severity scores for the cohort can be found in Table 1.

When comparing x-ABC with the ABC cohort, no demographic differences between patient groups were observed. Additionally, no differences were noted in median prehospital SBP, HR, SI, or GCS. Total prehospital time interval and median new injury severity scores were also similar between groups (Table 1). En route to the hospital, only 1 (1.6%) patient in the x-ABC cohort required prehospital intubation. All 31 (100%) patients of the ABC group arrived in the ED intubated. During evaluation in the ED, the ABC group had lower ED SBP (66 vs 110, p = 0.02), higher ED SI (1.31 vs 0.85, p < 0.01), and lower GCS (15 vs 3, p < 0.01) when compared with the x-ABC group. When comparing ED disposition between the cohorts, patients in the ABC group died more frequently in the ED (Table 1). In-hospital mortality was significantly lower in the x-ABC cohort (13% vs 47%, respectively, p < 0.001). Figure 2 is a presentation of the prehospital timing intervals, including time to first blood transfusion. For patients in the x-ABC cohort, blood transfusion was initiated 12 minutes earlier than in the ABC group, and most x-ABC patients received 2 units of packed RBCs, as well as calcium and TXA, before trauma center arrival.

Univariate logistic regression showed that prehospital GCS, patient age, male sex, total prehospital time interval, and the x-ABC sequence were all independently associated with in-hospital mortality. When combined in a multivariate model, an increase in prehospital GCS was associated with lower odds of in-hospital mortality (odds ratio [OR] 0.74, 95% CI 0.61 to 0.90, p = 0.002; Table 2). The x-ABC sequence was also found to be protective and linked to lower odds of in-hospital mortality (OR 0.15, 95% CI 0.04 to 0.54, p = 0.004; Table 2). Age, male sex, and total prehospital time were not found to be significantly impact in-hospital mortality.

DISCUSSION

Definitive airway management has been a cornerstone of emergency care for critically ill patients since the ABC resuscitation sequence was first introduced in the 1960s and has remained a priority within the ATLS guidelines. Although basic maneuvers to open the airway, provide supplemental oxygen, and if necessary deliver rescue

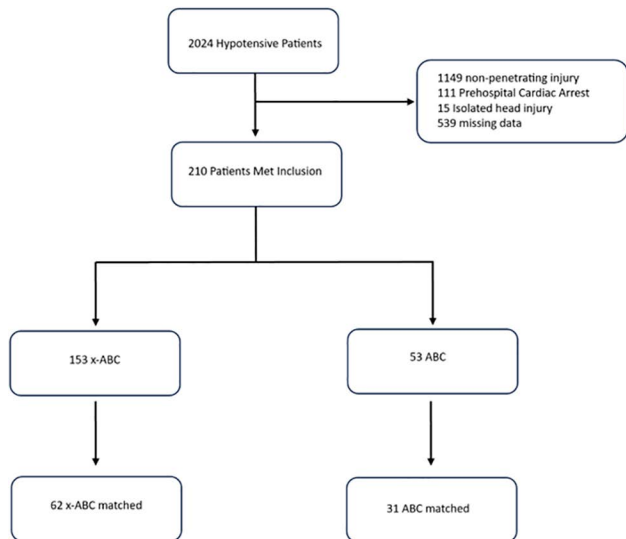


Figure 1. Patient selection flow diagram. x-ABC, exsanguinating hemorrhage control airway breathing circulation.

Table 1. Demographic, Vitals, and Outcome Univariate Comparison Between Advanced Resuscitative Care and Airway Breathing Circulation

Variable	All (n = 93)	x-ABC (n = 62)	ABC (n = 31)	p Value
Age, y, median (IQR)	32 (24–41)	35 (24–43)	31 (25–40)	0.90
Sex, m, n (%)	90 (97)	60 (97)	30 (97)	0.93
Black, n (%)	85 (91)	57 (92)	28 (91)	0.89
Emergency medical services characteristic, median (IQR)				
SBP, mmHg	74 (0–82)	78 (66–88)	70 (0–80)	0.79
HR, bpm	114 (73–135)	114 (84–136)	116 (55–140)	0.05
Shock index	1.51 (1.01–1.76)	1.48 (0.94–1.77)	1.57 (1.36–2.05)	0.09
GCS	6 (3–15)	8 (3–15)	5 (3–15)	0.43
Prehospital intubation, n (%)	32 (34)	1 (1.6)	31 (100)	<0.01
Total prehospital interval, median (IQR)	20 (15–26)	22 (16–26)	20 (15–25)	0.176
Hospital characteristic, median (IQR)				
ED SBP, mmHg	86 (0–118)	110 (84–136)	66 (0–93)	0.02
ED HR, bpm	93 (68–118)	92 (69–121)	95 (0–129)	0.12
ED shock index	1.08 (0.85–1.39)	0.85 (0.60–1.27)	1.31 (1.09–1.63)	<0.01
ED GCS	3 (3–15)	15 (14–15)	3 (3–12)	<0.01
ED disposition, n (%)				<0.01
Intensive care	28 (30)	22 (35)	6 (19)	
Operating room	47 (51)	32 (52)	15 (48)	
Floor	8 (9)	8 (13)	0 (0)	
Death	10 (10)	0 (0)	10 (33)	
Packed RBCs in 24 h, n, median (IQR)	2 (0–4)	3 (2–4)	1 (0–6)	0.01
New injury severity score, median (IQR)	20 (14–35)	20 (14–34)	21 (15–36)	0.11
In-hospital mortality, n (%)	23 (37)	8 (13)	15 (47)	<0.01
Mortality location, n (%)				<0.01
ED	10 (11)	0 (0)	10 (33)	
Operating room	5 (5)	3 (5)	2 (6)	
ICU	7 (8)	5 (8)	3 (10)	

bpm, beats per minute; ED, emergency department; HR, heart rate; IQR, interquartile range; GCS, Glasgow Coma Scale; SBP, systolic blood pressure; x-ABC, exsanguinating hemorrhage control airway breathing circulation.

breaths are still essential in the early management of a severely injured patient, advanced airway management before effective hemorrhage control and resuscitation may actually cause harm by worsening hypotension and leading to cardiovascular collapse.

In our analysis of patients with penetrating trauma and hemorrhagic shock who received x-ABC care through the delivery of a prehospital ARC bundle, mortality reduced to 13% compared with 47% among patients who were treated with a traditional ABC approach. Although all patients in the ABC cohort received advanced airway management before delivery of in-hospital blood products, endotracheal intubation was performed in only 1 x-ABC patient, or 1.6% of the total cohort.

These results may have important potential implications for the management of severely injured trauma patients. First, the early delivery of blood products targeted at the

reversal of hemorrhagic shock, coupled with hemostatic adjuncts including TXA and calcium, can begin to reverse the cascade of organ injury and traumatic coagulopathy resulting from injury. Second, delivery of sufficient volume of blood products to result in hemodynamic stability at trauma center arrival may help streamline the diagnostic and therapeutic interventions provided by the hospital trauma team. Third, and perhaps most importantly, the x-ABC sequence prioritizing hemorrhage control and resuscitation with blood products may decrease or delay the need for early advanced airway management by improving cerebral perfusion and the patient's control of airway and breathing. Because endotracheal intubation in the setting of hypovolemic shock can increase mortality, this procedure is ideally performed only after replacement of adequate intravascular volume.^{7,8} Before effective resuscitation, advanced airway placement can further diminish

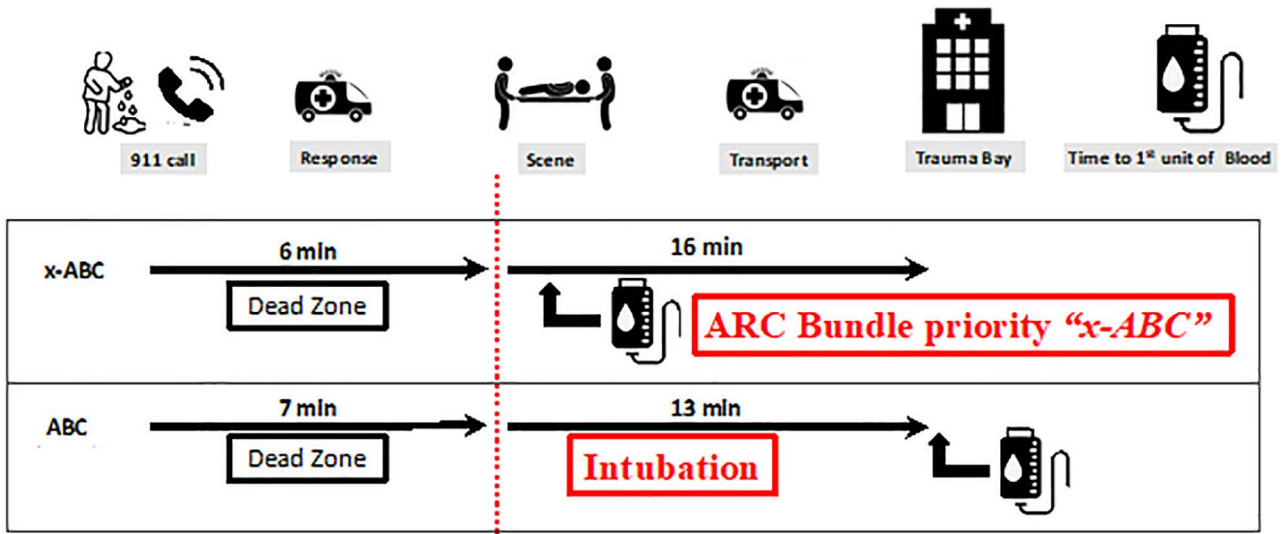


Figure 2. Prehospital and blood transfusion timing intervals. Patients in the ABC cohort received their first unit of blood 12 minutes later when compared to the x-ABC cohort. ABC, airway-breathing-circulation; ARC, advanced resuscitative care; x-ABC, exsanguinating hemorrhage control airway breathing circulation.

Table 2. Logistic Regression Analysis Examining Variable Impact on the Odds of Mortality

Variable	Odds ratio	95% CI	p Value
Age	1.01	0.96–1.05	0.78
Male sex	0.91	0.18–7.02	0.93
Prehospital Glasgow coma scale	0.74	0.61–0.90	0.002
Total prehospital time	1.05	1.00–1.12	0.05
Prehospital x-ABC	0.15	0.04–0.54	0.004

x-ABC, exsanguinating hemorrhage control airway breathing circulation.

cardiac output by increasing positive intrathoracic pressure and blunt the augmentation of venous return provided by spontaneous respiration, leading to worsening hypotension or cardiac arrest.

Numerous studies, including a large meta-analysis, have demonstrated that prehospital endotracheal intubation can lead to increased mortality among patients with hemorrhagic shock.⁹⁻¹⁵ In the largest single-center series evaluating this question, among 1,615 patients with penetrating trauma, prehospital intubation was associated with significantly higher mortality (HR 8.3).⁹ Recently, a large Eastern Association for the Surgery of Trauma multicenter study evaluating the effect of EMS trauma interventions demonstrated that prehospital intubation was the intervention associated with the highest risk of death (OR 10.76).¹¹ It is important to note that in neither of these large studies were EMS agencies carrying blood products.

The potential benefits of an x-ABC resuscitation strategy have been demonstrated in a growing body of literature. A meta-analysis of published studies on

circulation-first resuscitation found that trauma patients with hemorrhagic shock who received blood before endotracheal intervention had significantly lower mortality than those for whom advanced airway management was performed first.¹⁶ Similarly, a recent analysis of an American Association for the Surgery of Trauma registry evaluated the impact of ED intubation among patients with noncompressible torso trauma and hypotension. This study showed that endotracheal intubation before effective resuscitation was associated with more than twice the risk of hospital mortality compared to patients who received early transfusion.¹⁰ In an analysis of hypotensive trauma patients who received blood products or TXA during air medical transport, every minute of delay in receiving either therapy resulted in a 2% increase in 30-day mortality, suggesting that every minute of delay in resuscitation really does matter.¹⁷

Our data suggest that circulation-first care focused on restoring perfusion through the early delivery of blood products improves patient outcomes in urban prehospital trauma care. The observed mortality reduction is likely due to a

combination of early shock reversal and a reduction in the need for the potentially harmful intervention of endotracheal intubation before trauma center arrival. Our data also demonstrate that effective resuscitation blood products are possible in a busy urban EMS environment with minimal increase in already very short transport times, thereby avoiding the "dead zones" in prehospital care where no resuscitation is provided.

CONCLUSIONS

In this prospective analysis of trauma patients with hemorrhagic shock who were treated with a prehospital x-ABC resuscitation strategy, we observed decreased mortality compared with historical controls who received a standard ABC approach, even after controlling for injury type, severity, and physiological derangement. These results suggest a survival benefit in patients with penetrating injury managed with a circulation-first approach before advanced airway management. Early prioritization of hemorrhage control and resuscitation with blood products improves patient physiology and may prevent the need for immediate advance airway management. This is the first analysis to the best of our knowledge to demonstrate a survival benefit of an x-ABC sequence in patients with severe hemorrhage. Ongoing prospective observational studies will continue to add to this body of knowledge, and future randomized trials of this strategy are necessary.

APPENDIX

Members of the Damage Control Resuscitation Study Group are as follows: Sharven Taghavi, MD, MPH, Patrick McGrew, MD, Kevin Harrell, MD, and Olan Jackson-Weaver, PhD, Department of Surgery, Tulane University School of Medicine, New Orleans, LA; Alison Smith, MD, PhD, Department of Surgery, Louisiana State University Health Science Center, New Orleans, LA; and Meg Marino, MD, and Tom Dransfield, CCEMT-P, New Orleans Emergency Medical Services, New Orleans, LA.

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Software: Broome

Validation: Tatum

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Discussion

DR LAWRENCE LOTTENBERG (Boca Raton, FL): In my 43-year career, I have seen trauma care evolve from blood pouring out of extremities and body cavities onto the street, in the emergency department (ED), and the operating room, and futile attempts to correct derangements morph into damage-control surgery, damage-control resuscitation, REBOA, hybrid EDs and now what appears to be the first major change in ATLS and resuscitation.

This study gets us closer to a national trauma system integrating military and civilian trauma systems to achieve zero preventable deaths after injury.

I am a little curious about how the patients were selected. There seem to be 91 patients who did not match. Can you elaborate?

What has changed in your ED? The ED mortality in your exsanguinating airway-breathing-circulation (xABC) group was a remarkable 0% compared with 33% in the ABC group.

Has REBOA, resuscitative thoracotomy, ED laparotomy, hybrid ED (which I know you are working on very extensively), changed as well? Does this potentially cloud the earlier time to transfusion?

Do you think that tranexamic acid (TXA) is making a difference? Are you looking at thromboelastography in all these patients and looking at the clot lysis at 30 minutes? Are you also looking at serum calcium? Finally, what about whole blood vs packed cells in your cohorts?

Do you think that whole blood would make a difference? When these patients are coming in, are you providing them with prothrombin complex concentrate? Are you providing them with plasma? Are you providing them with platelets?

We looked at our cohort of whole blood use in penetrating trauma in Palm Beach County. We started this about 18 months ago, and we have shown that patients do not need to be intubated first with positive pressure ventilation when they are resuscitated with whole blood. We have also noted that the mortality is lower.

I think, in your cohort of very short transport times, this is extremely significant. I would also be remiss in not pointing out the very, very hard work of the emergency medical services (EMS) providers, and the fact that we now have trauma surgeons involved.

This is a remarkable study with remarkable results. Dr McSwain would be so proud of this work.

DR BRYAN A COTTON (Houston, TX): I want to congratulate the authors on a fantastic effort in examining the increasing enthusiasm of the CAB, or circulation before airway and breathing sequence. The authors have a new name for this: xABC.

Can you provide a brief description of some of the changes in that advanced resuscitative care (ARC) bundle? Were they all rolled at the same time or were they rolled out in sequence? In other words, did you roll out the blood, then TXA, then calcium sequentially, or was there truly a simultaneous bundle?

Are we really looking at avoiding the rapid sequence intubation (RSI) positive pressure intubation as the saving grace? Or is it because we are getting blood in earlier?

Could you explain why the Glasgow coma scale (GCS) scores were so low? Were you getting RSI; pushing medication before you intubated the patients, and then intubating them, which can give a sympathectomy, and losing some of that sympathetic tone that people advocated for on top of the preload reduction of positive pressure?

Is that what you are looking at, or are these really obtunded patients and your EMS folks are just inserting a king airway or a pharyngeal airway and making it to the hospital really quickly?

Could you explain where the signal was in your study between extremity hemorrhage that can easily be downgraded (put a tourniquet on and take your time) vs a non-compressible torso hemorrhage?

Finally, what is your recommendation going forward? Should we avoid intubation altogether? I do not know if your data really shows that. Or, if you have good blood, can you just intubate the patient and be okay? If you do not have whole blood, should you avoid all that and just scoop and run and get to the hospital? Please just provide some recommendations for the global trauma community and where to go next.