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Understanding Traumatic Shock: Out-of-Hospital Hypotension With and Without Other Physiologic Compromise

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Abstract

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CONFLICTS OF INTEREST

No author has any financial or other conflicts of interest that could inappropriately bias this work. There are no conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

CDN conceived of and designed the study. ENM performed all database management and statistical analyses. BM provided key statistical input and oversight in the analysis. All authors helped refine the study plan, interpret preliminary results, and refine the analysis. CDN drafted the manuscript and all authors participated in critical revision of the manuscript. CDN and ENM take full responsibility for the data, results and manuscript as a whole.

Background—Among trauma patients with out-of-hospital hypotension, we evaluated the predictive value of systolic blood pressure (SBP) with and without other physiologic compromise for identifying trauma patients requiring early critical resources.

Methods—This was a secondary analysis of a prospective cohort of injured patients 13 years with out-of-hospital hypotension (SBP < 90 mmHg) who were transported by 114 EMS agencies to 56 Level I and II trauma centers in 11 regions of the U.S. and Canada from January 1, 2010 through June 30, 2011. The primary outcome was early critical resource use, defined as blood transfusion ≥ 6 units, major non-orthopedic surgery, interventional radiology or death within 24 hours.

Results—Of 3,337 injured patients with out-of-hospital hypotension, 1,094 (33%) required early critical resources and 1,334 (40%) had serious injury (Injury Severity Score ≥ 16). Patients with isolated hypotension required less early critical resources (14% vs. 52%), had less serious injury (20% vs. 61%) and lower mortality (24 hours, 1% vs. 26%; in-hospital, 3% vs. 34%). The standardized probability of requiring early critical resources was lowest among patients with blunt injury and isolated moderate hypotension (0.12, 95% CI 0.09 – 0.15) and steadily increased with additional physiologic compromise, more severe hypotension, and penetrating injury (0.94, 95% CI 0.90 – 0.98).

Conclusions—A minority of trauma patients with isolated out-of-hospital hypotension require early critical resuscitation resources. However, hypotension accompanied by additional physiologic compromise or penetrating injury markedly increases the probability of requiring time-sensitive interventions.

Level of evidence—Level II; Study type – prognostic and epidemiological.

Keywords

emergency medical services; shock; resuscitation

BACKGROUND

Previous research has demonstrated the association between out-of-hospital hypotension and serious injury, need for specialized trauma resources and mortality.^{1–6} Additional studies have shown similar associations with emergency department (ED) hypotension.^{7–10} However, several recent prospective studies have suggested that out-of-hospital hypotension may not be as strong a predictor of injury outcomes and resource need as once thought, particularly among patients with isolated hypotension.^{11–14} The true predictive value of out-of-hospital hypotension and the influence of additional physiologic abnormalities, remains unclear.

Providing clarity about the predictive value of hypotension as a marker of hemorrhagic shock and high-risk trauma patients is important for several reasons. Hypotension has been a national field triage criterion for transport directly to the highest level of trauma care since 1987.^{15,16} However, hypotension has proven less effective in identifying high-risk trauma patients for interventional trials.^{11–13} Finding more effective methods for identifying high-risk patients requiring early critical interventions may help guide out-of-hospital decision making, early resuscitation practices, appropriate enrollment in clinical trials, and our

understanding of “shock” following injury. While additional out-of-hospital tools (e.g., point-of-care lactate) may prove effective in these goals,^{17,18} better understanding the utility of commonly used field physiologic measures (e.g., Glasgow Coma Scale [GCS] score, heart rate, respiratory status) in the setting of hypotension offers the benefits of familiarity, generalizability and rapid implementation.

In this study of out-of-hospital hypotensive trauma patients (systolic blood pressure [SBP] 90 mmHg), we evaluated the predictive value of hypotension with versus without additional physiologic compromise for identifying patients requiring early critical resuscitation resources. We also derived out-of-hospital clinical decision rules to demonstrate how various out-of-hospital physiologic markers may be used in combination with hypotension to improve the identification of patients requiring early critical resources.

METHODS

Study Design

This was a secondary analysis of a prospective, out-of-hospital registry of consecutive trauma patients with out-of-hospital hypotension. Institutional review boards at 11 sites in the U.S. and Canada approved this protocol and waived the requirement for informed consent.

Study Setting

These data were collected as part of the Resuscitation Outcomes Consortium (ROC) Prospective Observational Prehospital and Hospital Registry for Trauma (PROPHET). Prospective data were collected from January 1, 2010 through June 30, 2011 by 114 emergency medical services (EMS) agencies transporting to 56 Level I and II trauma centers in 11 sites across the U.S. and Canada. The 11 participating sites included: Birmingham, AL; Dallas/Fort Worth, TX; Memphis, TN; Milwaukee, WI; Pittsburgh, PA; Portland, OR; San Diego, CA; Seattle/King County, WA; Ottawa, ON; Toronto, ON; and British Columbia. The sites vary in size, location, geographic diversity (urban, suburban, rural and frontier areas) and EMS system structure, as previously described.¹⁹

Selection of Participants

The PROPHET registry includes all trauma patients treated by participating 9-1-1 EMS agencies with hypotension (SBP < 90 mmHg) or depressed mentation (GCS score < 8) and direct transport to a Level I or II trauma center. The study cohort for this analysis (Figure 1) consisted of injured patients > 13 years with SBP < 90 mmHg at any point during the out-of-hospital evaluation; PROPHET patients with GCS < 8 and no hypotension were excluded. We included persons > 13 years of age to represent patients for whom SBP < 90 mmHg is considered hypotensive. Younger children were excluded due to differing values for normal blood pressure. We also excluded patients who died in the field, were not transported, or were transported without any signs of life (i.e., no pulse).

Variables

Several out-of-hospital variables, as obtained by EMS personnel, were collected for the PROPHET database. We used rigorous quality assurance processes for data collection and processing, identical to those described for a similar observational trauma cohort in ROC.²⁰ Variables included: SBP (mmHg), GCS, heart rate (beats/minute), respiratory compromise (bag-valve mask ventilation, attempted intubation, supraglottic airway or cricothyrotomy), demographics (age, sex), mechanism of injury (gunshot wound, stab/impalement, fall, motor vehicle occupant, motor vehicle vs. pedestrian/cyclist, motorcycle, struck, machinery or crushing injury, other), field disposition and transport mode. For SBP, we used the lowest recorded out-of-hospital value. For GCS, we used the initial value to avoid confounding by out-of-hospital interventions (e.g., sedatives, opiates and paralytic medications).

To facilitate analysis and interpretation of results, we categorized GCS, SBP and heart rate into commonly used clinical definitions for physiologic compromise. We stratified hypotension into three SBP categories (< 70 mmHg, 71 – 80 mmHg and 81 – 90 mmHg). Values for GCS were split into GCS 12 (moderate to severe) versus GCS 13–15 (near-normal). We categorized heart rate into bradycardia (1 – 49 beats/minute) and tachycardia (> 110 beats/minute), with 50 – 110 beats/minute used as the reference range.

Hospital variables included measures of injury severity (Abbreviated Injury Scale [AIS] score, Injury Severity Score [ISS]), surgical interventions, timing and volume of blood product transfusion, intensive care unit stay, length of hospital stay (LOS) and mortality (24 hours and in-hospital).

Outcomes

The primary outcome was early critical resource use, defined as any of the following within 24 hours of ED arrival: packed red blood cell transfusion ≥ 6 units, major non-orthopedic surgical procedures, interventional radiology procedures or death. This composite measure was intended to reflect high-risk trauma patients requiring early, aggressive, specialized trauma care and is similar to a recent consensus-based definition of patients requiring immediate transport to major trauma centers.²¹ Non-orthopedic surgical procedures were defined as any brain, spine, neck, thoracic, abdominal or pelvic surgical intervention. These procedures generally represent specialized surgical resources not available at non-trauma hospitals. We included patients who died within 24 hours of ED presentation to retain high-risk patients who may not have survived long enough to undergo critical interventions.

Because resource use and injury severity are not perfectly correlated,²² we evaluated Injury Severity Score ≥ 16 as a secondary outcome measure to reflect patients with serious anatomic injuries. This definition identifies the subset of patients at high risk of mortality,²³ most likely to benefit from care at major trauma centers^{24–26} and potentially benefiting from early resuscitation and therapeutic interventions.

Analysis

We used descriptive statistics to characterize the full sample, patients with isolated hypotension and patients with hypotension accompanied by additional physiologic

compromise. We then built multivariable regression models to evaluate the adjusted association between each physiologic measure and early critical resource use after accounting for other out-of-hospital variables. We included the primary physiologic variables (GCS, SBP, heart rate and respiratory failure), mechanism of injury, age, sex and site in each of the models. Model discrimination, fit and diagnostics were evaluated to further refine the final model. We used adjusted predicted probabilities from the model to compare physiologic scenarios for common injury mechanisms (motor vehicle occupant, stab/impalement and gunshot wound) and provide easier translation to clinical practice. For each injury mechanism, we standardized to the distribution of demographic characteristics (age, sex, and site) of all the patients with that mechanism to estimate the predicted probability for each physiologic scenario. This standardization removed confounding by demographics in comparisons between scenarios within a given mechanism.

To minimize bias in the analysis, we used multiple imputation²⁷ for missing values. Multiple imputation allowed the inclusion of subjects missing values for age (n = 36, 1% of sample), GCS (n = 126, 4%), heart rate (n = 29, 1%), and ISS (n = 136, 4%), in the regression models. The validity of multiple imputation for imputing missing out-of-hospital values and trauma data has been demonstrated under a variety of conditions.^{28,29} We generated 25 independently imputed datasets and analyzed each independently, then combined the results using Rubin's methods to appropriately account for variance within- and between-datasets.²⁷

Finally, we used binary recursive partitioning³⁰ to derive two clinical decision rules to demonstrate how various measures of out-of-hospital physiology could be used in combination with hypotension to improve the identification of patients requiring early critical resources. Recursive partitioning is an analytic method well suited for identifying complex, higher-level interactions among variables, finding appropriate cut-points in continuous and ordinal variables, and developing clinical decision rules.^{31,32} We used Gini splitting algorithms and selected misclassification costs to produce two decision trees with differing functions: (1) a high sensitivity (90%) tree to identify most hypotensive patients requiring early critical resources (e.g., a more efficient strategy for field triage) and (2) a high specificity (90%) tree that favors positive predictive value at the expense of sensitivity (e.g., for enrolling high-risk patients in clinical trials). We randomly selected 60% of patients from each outcome group to derive the rule and used the remaining 40% of patients for rule validation. We used physiologic measures, mechanism of injury and age for the recursive partitioning analysis.

Analyses were conducted using R v3.0.1 and the following R libraries: mice v2.16, epibasix v1.3, and rpart v4.1-1 (Free Software Foundation Inc., Boston MA, <http://www.r-project.org/>).³³

RESULTS

There were 3,337 injured patients with out-of-hospital hypotension transported by EMS to major trauma centers and included in the primary analysis. Of this sample, 1,094 (33%) required critical resources within 24 hours and 1,334 (40%) had ISS $\geq$ 16. Four hundred

forty-four (13%) patients died within 24 hours and 607 (18%) died during their hospital stay. Among the 1,094 patients requiring critical resources within 24 hours, 313 (29%) had major transfusion, 673 (62%) had major non-orthopedic surgery, 72 (7%) had interventional radiology procedures, and 444 (41%) died. Characteristics of the study sample, overall and stratified by isolated hypotension versus hypotension with other physiologic compromise, are described in Table 1.

In Figure 2, we demonstrate the standardized probabilities of early critical resource use among hypotensive trauma patients with versus without other physiologic compromise, categorized by the degree of hypotension and representative injury mechanisms. The need for early critical resources was lowest among patients with blunt injury and isolated hypotension, though increased with more severe hypotension (standardized probabilities: 0.12 for SBP 81–90 mmHg, 0.17 for SBP 71 – 80 mmHg, and 0.29 for SBP 70 mmHg). The predictive value of isolated hypotension was notably higher in the setting of penetrating injury (standardized probabilities for GSW: 0.40 for SBP 81 – 90 mmHg, 0.44 for 71 – 80 mmHg, and 0.57 for SBP 70 mmHg). The presence of additional physiologic compromise was associated with higher probabilities of early critical resource use, reaching the highest values among GSW patients with multiple physiologic derangements (standardized probabilities: 0.77 for SBP 81–90 mmHg, 0.81 for SBP 71 – 80 mmHg, and 0.94 for SBP 70 mmHg). Compared to blunt trauma patients with isolated hypotension, the presence of additional out-of-hospital physiologic compromise and/or penetrating injury had a cumulative effect on the probability of requiring early critical resources. The model used to generate the adjusted probabilities is shown in Appendix 2.

Figure 3 illustrates a similar analysis for the probability of ISS ≥ 16. Isolated hypotension identified a minority of patients with serious injury, with the lowest values occurring among patients with a stabbing mechanism (standardized probabilities: 0.13 for SBP 81–90 mmHg, 0.17 for SBP 71 – 80 mmHg, and 0.20 for SBP 70 mmHg). Injury as a MVC occupant or by GSW yielded similar probabilities for ISS ≥ 16. As in Figure 2, more severe hypotension and/or additional physiologic compromise was associated with notably higher estimates for the probability of ISS ≥ 16, with the highest values for MVC occupants who had multiple markers of physiologic compromise (standardized probabilities: 0.81 for SBP 81–90 mmHg, 0.86 for SBP 71 – 80 mmHg, and 0.88 for SBP 70 mmHg). The role of injury mechanism differed from the resource-based analysis, with MVC occupants and GSW patients having consistently higher association with serious injury than patients injured by stabbing

In Figure 4, we show two decision trees to demonstrate how different out-of-hospital physiologic measures and mechanism could be used in combination with hypotension to identify high-risk trauma patients. Accuracy measures for these trees are shown in Table 2. The first decision rule (Figure 4A) was derived as a highly sensitive tree and included (in order): respiratory compromise, injury type (penetrating vs. blunt) and tachycardia (heart rate ≥ 102 beats per minute). The high-sensitivity tree demonstrated sensitivity 90% (95% CI 87–93%) and specificity 57% (95% CI 54–60%) for identifying patients requiring early critical resources. This decision tree was less sensitive for identifying patients with ISS ≥ 16 (sensitivity 79% [95% CI 76 – 83%], specificity 56% [95% CI 52 – 59%]). The second decision rule (Figure 4B) was derived as a highly specific tree and included: respiratory

failure, severe hypotension (SBP < 70 mmHg) and low GCS (< 10). The high-specificity tree demonstrated sensitivity 50% (95% CI 46–55%) and specificity 92% (95% CI 90–94%) for identifying patients requiring early critical resources, with similar values for identifying patients with ISS ≥ 16 (sensitivity 47% [95% CI 42 – 51%], specificity 95% [95% CI 93 – 96%]).

DISCUSSION

In this study, we demonstrate that only a minority of trauma patients with isolated out-of-hospital hypotension required critical early resources or had serious injuries, particularly among patients with a blunt mechanism. However, when hypotension was accompanied by at least one additional physiologic abnormality (or a penetrating mechanism), the likelihood of requiring critical early resources was approximately doubled. While these findings may seem intuitive, the results refine our understanding of traumatic shock. We used a resource-based definition of traumatic shock, indicative of hypotensive patients with severe injuries requiring early recognition and time-dependent intervention for survival. The compounding effect of additional physiologic derangement on the predictive value of hypotension has implications for resuscitation strategies and future clinical trials.

The finding that isolated out-of-hospital hypotension is a relatively weak predictor of early resource use is contrary to many previous studies and traditional clinical teaching for trauma. While previous studies have demonstrated the high-risk nature of hypotension following injury,^{1–10} most of these studies did not discriminate between hypotension with or without other physiologic compromise. Although more severe isolated hypotension increased the probability of requiring early resources in our sample, the predictive value remained relatively low compared to hypotensive patients with other physiologic compromise. Importantly, our findings do not refute previous research demonstrating that hypotensive trauma patients are higher risk than normotensive patients. Rather, we show that a minority of patients with isolated hypotension require early critical interventions, have serious injuries or die from their injuries.

The utility of our findings differs depending on the application. For field triage, our findings do not necessarily support modifying the current SBP < 90 mmHg field triage criterion for transport to a major trauma center. However, the presence of more severe hypotension, additional physiologic abnormality or penetrating injury should be recognized as increasing the urgency for immediate transport to a high-resource hospital. Regarding inclusion criteria for future out-of-hospital trauma trials and identifying patients for resource-intensive interventions (e.g., direct to operating room protocols, air transport, and specialized field resuscitation protocols), our findings suggest that isolated hypotension may not be enough to pass the threshold required to initiate such actions.

Our results support the coupling of non-SBP physiologic measures with hypotension to increase specificity in identifying high-risk trauma patients. This is particularly true for clinical trials seeking to both identify high-risk patients likely to benefit from early interventions and to minimize harm (especially for low-risk patients); high-specificity inclusion criteria may provide a better balance for these competing interests. For example,

the presence of tachycardia *and* hypotension almost doubled the probability of requiring early critical resources compared to that of isolated hypotension, which is similar to findings from a previous trauma trial seeking to better identify patients with hemorrhagic shock.^{12,13} Although we did not directly evaluate the shock index (heart rate ÷ SBP), our findings are similar in concept – hypotension accompanied by tachycardia (or other physiologic derangement) increases the probability of requiring early intervention. These findings illustrate that the predictive value of hypotension should be considered in the context of other physiologic measures and type of injury.

Our conclusions differed when predicting serious anatomic injury (ISS). While the probability of serious injury increased when hypotension was accompanied by other physiologic compromise, the influence of injury type was different. Blunt injury (i.e., motor vehicle crash) was identical to GSW in estimating the probability of serious injury and both these mechanisms produced notably higher estimates than stabbing. These findings may be partially explained by ISS underestimating injury severity in penetrating trauma³³ and the more lethal nature of firearm injuries. Thus, the role of hypotension and mechanism should be considered with respect to how high-risk trauma patients are defined (i.e., early critical resource need versus serious anatomic injury).

There are limitations to consider when interpreting this study. The study was observational and excluded patients transported to non-trauma hospitals. These exclusions yielded a higher acuity sample and may have introduced selection bias. Based on the focus of and requisite resources required to complete PROPHET, we also intentionally excluded all normotensive patients, so the analysis was not structured to compare the predictive value of hypotension to normotension. Although higher values of SBP (e.g., 91 – 110 mmHg) have been associated with increased mortality,¹⁰ the PROPHET database was designed using SBP ≥ 90 mmHg as the inclusion criterion to balance the capture of high-risk trauma patients with the resources required to collect detailed prehospital and hospital data on these patients. It is likely that when compared to normotensive patients, those with isolated hypotension remain at higher risk,⁹ even if the absolute risk is relatively small. Our definition of hypotension is consistent with the SBP criterion used for ROC interventional trials,^{12,13} the long-standing trauma triage SBP criterion listed in the Field Triage Decision Scheme^{15,16} and is a familiar cut-point recognized as “hypotension” by EMS providers.

We did not evaluate persistent out-of-hospital hypotension. While persistent hypotension can be an important prognostic marker, there is large variability in the use of repeat vital signs by EMS. Factors such as transport time, patient acuity, availability of extra personnel and need for additional interventions can determine whether repeat vital signs are taken. Therefore, any analysis that relies on a definition of “persistent hypotension” will risk significant bias from other factors affecting the availability of these values. To reduce this potential bias, we used a single SBP value.

The primary outcome of need for early critical resources was limited by how time was collected for each component of the outcome. Because blood transfusions in PROPHET were collected in 24-hour increments, we were unable to use an hourly rate of transfusion or number of units transfused over a smaller time period (e.g., the first 6 hours). Similarly,

operative interventions were collected by date of procedure and separated into 24-hour increments. While we had detailed information on time of death, the composite definition required a common time reference for all components of the definition. Therefore, we used the first 24 hours to indicate the “early” period of resource need and critical interventions. The use of shorter time intervals (0–6 hours or 0–12 hours) may have produced different results.

Finally, the decision rules have not been prospectively validated. We developed the decision trees to illustrate how non-SBP physiologic measures and mechanism of injury might be combined with hypotension to better identify high-risk trauma patients. The decision trees serve as a complement to the standardized probability figures in understanding how these results might translate to a clinical setting or a future clinical trial.

In summary, a minority of patients with isolated out-of-hospital hypotension required early critical resources. When hypotension was accompanied by additional physiologic compromise or penetrating injury, the probability of requiring time-sensitive interventions was much higher. These findings suggest that coupling physiologic measures may refine the early identification process for hypotensive patients requiring time-sensitive interventions and better balance the potential benefits and harms of enrollment in clinical trials.

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REFERENCES

1. Henry MC, Hollander JE, Alicandro JM, Cassara G, O'Malley S, Thode HC Jr. Incremental benefit of individual American College of Surgeons trauma triage criteria. *Acad Emerg Med*. 1996 Nov; 3(11):992–1000. [PubMed: 8922003]
2. Franklin GA, Boaz PW, Spain DA, Lukan JK, Carrillo EH, Richardson JD. Prehospital hypotension as a valid indicator of trauma team activation. *J Trauma*. 2000 Jun; 48(6):1034–1039. [PubMed: 10866247]
3. Lipsky AM, Gausche-Hill M, Henneman PL, Loffredo AJ, Eckhardt PB, Cryer HG, de Virgilio C, Klein SL, Bongard FS, Lewis RJ. Prehospital hypotension is a predictor of the need for an emergent, therapeutic operation in trauma patients with normal systolic blood pressure in the emergency department. *J Trauma*. 2006 Nov; 61(5):1228–1233. [PubMed: 17099534]

4. Idris AH, Meier E, Minei J, Brasel K, Daya M, Egan D, Kannas D, Kerby JD, Lin S, McCleod B, et al. Prehospital hypotension is associated with emergent in-hospital procedures and mortality in trauma patients. [Abstract] *Circulation*. 2012; 126:A5.
5. Chan L, Bartfield JM, Reilly KM. The significance of out-of-hospital hypotension in blunt trauma patients. *Acad Emerg Med*. 1997; 4:785–788. [PubMed: 9262696]
6. Bruns B, Gentiello L, Elliott A, Shafi S. Prehospital hypotension redefined. *J Trauma*. 2008; 65:1217–1221. [PubMed: 19077604]
7. Hasler RM, Nuesch E, Jüni P, Bouamra O, Exadaktylos AK, Lecky F. Systolic blood pressure below 110 mm Hg is associated with increased mortality in blunt major trauma patients: multicentre cohort study. *Resuscitation*. 2011 Sep; 82(9):1202–1207. [PubMed: 21632168]
8. Hasler RM, Nüesch E, Jüni P, Bouamra O, Exadaktylos AK, Lecky F. Systolic blood pressure below 110 mmHg is associated with increased mortality in penetrating major trauma patients: Multicentre cohort study. *Resuscitation*. 2012 Apr; 83(4):476–481. [PubMed: 22056618]
9. Seamon MJ, Feather C, Smith BP, Kulp H, Gaughan JP, Goldberg AJ. Just one drop: the significance of a single hypotensive blood pressure reading during trauma resuscitations. *J Trauma*. 2010 Jun; 68(6):1289–1294. [PubMed: 20539171]
10. Eastridge BJ, Salinas J, McManus JG, Blackburn L, Bulger EM, Cooke WH, Concertino VA, Wade CE, Holcomb JB. Hypotension begins at 110 mm Hg: redefining “hypotension” with data. *J Trauma*. 2007; 63:291–299. [PubMed: 17693826]
11. Bulger EM, Jurkovich GJ, Nathens AB, Copass MK, Hanson S, Cooper C, Liu PY, Neff M, Awan AB, Warner K, et al. Hypertonic resuscitation of hypovolemic shock after blunt trauma. *Arch Surg*. 2008; 143:139–148. [PubMed: 18283138]
12. Brasel KJ, Bulger E, Cook AJ, Morrison LJ, Newgard CD, Tisherman SA, Kerby JD, Coimbra R, Hata JS, Hoyt DB. Hypertonic resuscitation: design and implementation of a prehospital intervention trial. *J Am Coll Surg*. 2008 Feb; 206(2):220–232. [PubMed: 18222373]
13. Bulger EM, May S, Brasel KJ, Schreiber M, Kerby JD, Tisherman SA, Newgard C, Slutsky A, Coimbra R, Emerson S, et al. Out-of-hospital hypertonic resuscitation following severe traumatic brain injury: a randomized controlled trial. *JAMA*. 2010; 304(13):1455–1464. [PubMed: 20924011]
14. Newgard CD, Rudser K, Hedges JR, Kerby JD, Stiell IG, Davis DP, Morrison LJ, Bulger E, Terndrup T, Minei JP, et al. A critical assessment of the out-of-hospital trauma triage guidelines for physiologic abnormality. *J Trauma*. 2010; 68(2):452–462. [PubMed: 20154558]
15. Mackersie RC. History of trauma field triage development and the American College of Surgeons criteria. *Prehospital Emergency Care*. 2006; 10:287–294. [PubMed: 16801263]
16. Sasser SM, Hunt RC, Faul M, Sugerman D, Pearson WS, Dulski T, Wald MM, Jurkovich GJ, Newgard CD, Lerner EB. Guidelines for Field Triage of Injured Patients: Recommendations of the National Expert Panel on Field Triage, 2011. *MMWR*. 2012; 61:1–20. [PubMed: 22237112]
17. Vandromme MJ, Griffin RL, Weinberg JA, Rue LW 3rd, Kerby JD. Lactate is a better predictor than systolic blood pressure for determining blood requirement and mortality: could prehospital measures improve trauma triage? *J Am Coll Surg*. 2010 May; 210(5):861–867. 867–869. [PubMed: 20421067]
18. Guyette F, Meier E, McKnight B, Powell J, Bulger E, Klotz P, Fabian T, Daya M, Newgard C, Weinberg J, et al. Prehospital Lactate is Superior to Systolic Blood Pressure for Predicting the Need for Resuscitative Care in Trauma. [Abstract]. *Circulation*. 2012; 126:2776–2799.
19. Davis DP, Garberson LA, Andrusiek DL, Hostler D, Daya M, Pirrallo R, Craig A, Stephens S, Larsen J, Drum AF, et al. A descriptive analysis of Emergency Medical Service Systems participating in the Resuscitation Outcomes Consortium (ROC) network. *Prehosp Emerg Care*. 2007; 11:369–382. [PubMed: 17907019]
20. Newgard CD, Sears GK, Rea TD, Davis DP, Pirrallo RG, Callaway CW, Atkins DL, Stiell IG, Christenson J, Minei JP, et al. The Resuscitation Outcomes Consortium Epistery-Trauma: Design, Development, and Implementation of a North American Epidemiologic Prehospital Trauma Registry. *Resuscitation*. 2008; 78:170–178. [PubMed: 18482792]

21. Lerner EB, Willenbring B, Pirrallo RG, Brasel KJ, Cady CE, Colella MR, Cooper A, Cushman JT, Gourlay DM, Jurkovich GJ, et al. A Consensus-Based Gold Standard for Trauma Center Need. *J Trauma and Acute Care Surgery*. (In Press).
22. Newgard CD, Hedges JR, Diggs B, Mullins RJ. Establishing the need for trauma center care: anatomic injury or resource use? *Prehosp Emerg Care*. 2008 Oct-Dec;12(4):451–458. [PubMed: 18924008]
23. Baker SP, O'Neill B, Haddon W, Long WB. The Injury Severity Score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma*. 1974; 14:187–196. [PubMed: 4814394]
24. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, Salkever DS, Scharfstein DO. A national evaluation of the effect of trauma-center care on mortality. *NEJM*. 2006; 354:366–378. [PubMed: 16436768]
25. Mullins RJ, Veum-Stone J, Helfand M, Zimmer-Gembeck M, Hedges JR, Southard PA, Trunkey DD. Outcome of hospitalized injured patients after institution of a trauma system in an urban area. *JAMA*. 1994; 271:1919–1924. [PubMed: 8201736]
26. Sampalis JS, Denis R, Lavoie A, Fréchette P, Boukas S, Nikolis A, Benoit D, Fleiszer D, Brown R, Churchill-Smith M, Mulder D. Trauma care regionalization: a process-outcome evaluation. *J Trauma*. 1999; 46:565–581. [PubMed: 10217218]
27. Rubin, DB. *Multiple Imputation for Nonresponse in Surveys*. New York: John Wiley & Sons, Inc.; 1987.
28. Newgard CD. The validity of using multiple imputation for missing prehospital data in a state trauma registry. *Acad Emerg Med*. 2006; 13:314–324. [PubMed: 16495420]
29. Newgard CD, Haukoos J. Missing data in clinical research – part 2: Multiple imputation. *Acad Emerg Med*. 2007; 14:669–678. [PubMed: 17595237]
30. Breiman, L.; Friedman, JH.; Olshen, RA., et al. *Classification and regression trees*. New York: Chapman & Hall; 1984.
31. McConnochie KM, Roghmann KJ, Pasternack J. Developing prediction rules and evaluating observation patterns using categorical clinical markers: two complimentary procedures. *Medical Decision Making*. 1993; 13(1):30–42. [PubMed: 8433634]
32. Stiell IG, Wells GA. Methodologic standard for the development of clinical decision rules in emergency medicine. *Ann Emerg Med*. 1999; 33:437–447. [PubMed: 10092723]
33. R Core Team. *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing; 2013. URL <http://www.R-project.org/>
34. Lavoie A, Moore L, LeSage N, Liberman M, Sampalis JS. The New Injury Severity Score: a more accurate predictor of in-hospital mortality than the Injury Severity Score. *J Trauma*. 2004; 56:1312–1320. [PubMed: 15211142]

Appendix 1

The Resuscitation Outcomes Consortium investigators involved with development of the Prospective Observational Prehospital and Hospital Registry for Trauma (PROPHET).

Appendix 2

The multivariable regression models used to generate predicted probabilities for Figures 2 and 3 (n = 3,337).

	Early critical resource use		ISS 16	
Predictors of Outcomes*	Estimate	95% CI	Estimate	95% CI
Age: [†]				
per 5-year increment for age < 45 years	0.003	(-0.004, 0.011)	0.007	(-0.002, 0.015)
per 5-year increment for age ≥ 45 years	0.004	(-0.003, 0.010)	-0.003	(-0.011, 0.004)
Male	0.035	(0.007, 0.064)	0.050	(0.020, 0.081)
Mechanism of injury:				
Fall	reference		reference	
Motor vehicle crash	0.124	(0.084, 0.165)	0.245	(0.202, 0.289)
Pedestrian or bicycle	0.146	(0.095, 0.196)	0.194	(0.141, 0.248)
Motorcycle crash	0.120	(0.060, 0.179)	0.275	(0.212, 0.339)
Assault/struck	0.009	(-0.043, 0.061)	-0.049	(-0.105, 0.006)
Gunshot wound	0.375	(0.324, 0.427)	0.210	(0.154, 0.265)
Stabbing/impalement	0.312	(0.262, 0.361)	0.023	(-0.030, 0.076)
Other	0.122	(0.028, 0.215)	0.052	(-0.048, 0.152)
Lowest systolic blood pressure, mmHg:				
70	0.170	(0.137, 0.203)	0.071	(0.035, 0.106)
71–80	0.045	(0.013, 0.077)	0.046	(0.011, 0.080)
81–90	reference		reference	
Heart rate, beats/min:				
1–49	0.088	(0.015, 0.162)	-0.054	(-0.137, 0.029)
50–110	reference		reference	
>110	0.106	(0.075, 0.138)	0.073	(0.039, 0.107)
GCS 12	0.135	(0.098, 0.172)	0.207	(0.167, 0.247)
Any airway attempted	0.236	(0.197, 0.275)	0.275	(0.234, 0.316)

* Site adjusted for but not presented above.

[†] Age modeled as spline with one knot at 45 years.

Figure 1.

Schematic of the sample construction.*

*PROPHECT = Prospective Observational Prehospital and Hospital Registry for Trauma;
GCS = Glasgow Coma Scale score; SBP = systolic blood pressure.

[†]"No other signs of life" was defined as GCS missing or 3, SBP missing or not detectable, and respiratory rate of zero or missing. Of 309 patients meeting this definition, 264 (85%) had a heart rate of 0.

Figure 2.

Standardized probability of *early critical resource use* among hypotensive patients with and without other physiologic compromise across different mechanisms of injury (n = 3,337).*

*Critical early resource need was defined as any of the following within 24 hours of hospital arrival: packed red blood cell transfusion ≥ 6 units, major non-orthopedic surgical procedures, interventional radiology or death. Each injury mechanism is standardized to the distribution of demographic characteristics (age, sex, and site) of all patients with that mechanism to estimate the predicted probability for each physiologic scenario. Covariates in the model included: physiologic predictors (SBP categories, airway intervention, GCS ≤ 12, HR categories), age, sex and site.

Figure 3.

Adjusted probability of *Injury Severity Score* ≥ 16 among hypotensive patients with and without other physiologic compromise across different mechanisms of injury (n = 3,337).*

*Each injury mechanism is standardized to the distribution of demographic characteristics (age, sex, and site) of all patients with that mechanism to estimate the predicted probability for each physiologic scenario. Covariates in the model included: physiologic predictors (SBP categories, airway intervention, GCS ≤ 12 , HR > 110), age, sex and site.

Figure 4.

Sample out-of-hospital decision trees for injured patients with hypotension to identify patients requiring *early critical resource use* (derivation sample n = 2,003; validation sample n = 1,334).

A. High sensitivity tree.*

B. High specificity tree.†

*Derivation of the high-sensitivity tree demonstrated sensitivity of 89.6% and specificity 54.7%; validation testing yielded sensitivity 89.9% (95% confidence interval [CI] –7.1 – 92.8%) and specificity of 57.1 (95% CI 53.8 – 60.3%). The numbers presented in the decision tree represent the validation sample.

†Derivation of the high-specificity tree demonstrated sensitivity of 51.2% and specificity of 89.1%; validation testing yielded sensitivity 50.3% (95% CI 45.6 – 55.1%) and specificity 92.3% (95% CI 90.4 – 94.0%). The numbers presented in the decision tree represent the validation sample.

Table 1

Characteristics of hypotensive trauma patients transported by EMS, overall and stratified by hypotension with versus without other physiologic compromise.*

	Full Sample n = 3,337		Isolated hypotension (SBP < 90 mmHg) n = 1,679		Hypotension with other physiologic compromise n = 1,658	
Demographics:						
Age in years, mean (SD)	43.1	(20.2)	46.0	(20.9)	40.1	(18.9)
13–18 years (%)	211	(6.3)	90	(5.4)	121	(7.3)
19–54 years (%)	2,223	(66.6)	1,044	(62.2)	1,179	(71.1)
55 years (%)	903	(27.1)	545	(32.5)	358	(21.6)
Men (%)	2,225	(66.7)	1,045	(62.2)	1,180	(71.2)
Out-of-hospital physiology, procedures and transport:						
GCS, mean (SD)	11.9	(4.6)	14.7	(0.7)	9.1	(5.0)
GCS 13–15 (%)	2,300	(68.9)	1,679	(100.0)	621	(37.5)
GCS 9–12 (%)	249	(7.5)	0	(0.0)	249	(15.0)
GCS 8 (%)	788	(23.6)	0	(0.0)	788	(47.5)
Advanced airway attempted (%)	921	(27.6)	0	(0.0)	921	(55.5)
Intravenous line placement (%)	2,770	(83.0)	1,245	(74.2)	1,525	(92.0)
Helicopter transport (%)	425	(12.7)	103	(6.1)	322	(19.4)
Mechanism of injury:						
Gunshot wound (%)	407	(12.2)	134	(8.0)	273	(16.5)
Stabbing/impalement (%)	369	(11.1)	178	(10.6)	191	(11.5)
Assault/struck (%)	287	(8.6)	164	(9.8)	123	(7.4)
Fall (%)	933	(28.0)	620	(36.9)	313	(18.9)
Motor vehicle crash (%)	751	(22.5)	308	(18.3)	443	(26.7)
Motorcycle crash (%)	208	(6.2)	92	(5.5)	116	(7.0)
Pedestrian or bicycle (%)	314	(9.4)	135	(8.0)	179	(10.8)
Other (%)	68	(2.0)	48	(2.9)	20	(1.2)

	Full Sample n = 3,337	Isolated hypotension (SBP < 90 mmHg) n = 1,679	Hypotension with other physiologic compromise n = 1,658
Injury severity:			
ISS, mean (SD)	15.0 (15.2)	8.7 (10.1)	21.4 (16.8)
ISS 16 (%)	1,334 (40.0)	330 (19.7)	1,004 (60.6)
Head AIS 3 (%)	631 (18.9)	94 (5.6)	537 (32.4)
Chest AIS 3 (%)	958 (28.7)	270 (16.1)	688 (41.5)
Abdominal AIS 3 (%)	460 (13.8)	146 (8.7)	314 (18.9)
Early resource utilization:			
Early critical resource utilization (%)	1,094 (32.8)	239 (14.2)	855 (51.6)
PRBC 6 units in 1 st 24 hours (%)	313 (9.4)	49 (2.9)	264 (15.9)
Major non-orthopedic surgery in 1 st 24 hours (%)	673 (20.2)	206 (12.3)	467 (28.2)
Interventional radiology in 1 st 24 hours (%)	72 (2.2)	15 (0.9)	57 (3.4)
Mortality:			
In 1 st 24 hours (%)	444 (13.3)	14 (0.8)	430 (25.9)
In-hospital (%)	607 (18.2)	49 (2.9)	558 (33.7)

* AIS = Abbreviated Injury Scale; GCS = Glasgow Coma Scale; ISS = Injury Severity Score; PRBC = packed red blood cells; SBP = systolic blood pressure. The following measures had values multiply imputed: Age (n = 36), GCS (n = 126), ISS (n = 136), head AIS (n = 109), chest AIS (n = 87), and abdomen AIS (n = 82).

Table 2

Accuracy metrics for the decision trees among injured patients with out-of-hospital hypotension.

	Any hypotension (full sample) n = 3,337	High-sensitivity decision tree (validation cohort) n = 1,334	High-specificity decision tree (validation cohort) n = 1,334
Outcome: critical early resource need			
Sensitivity	100.0%	89.9% (86.7, 92.6)	50.3% (45.6, 55.1)
Specificity	0.0%	57.1% (53.8, 60.3)	92.3% (90.4, 94.0)
Positive predictive value	32.8%	50.5% (46.9, 54.1)	76.1% (70.8, 80.9)
Negative predictive value	0.0%	92.1% (89.5, 94.2)	79.2% (76.6, 81.7)
Positive likelihood ratio	1.00	2.10 (1.93, 2.27)	6.54 (5.12, 8.36)
Negative likelihood ratio	--	0.18 (0.13, 0.23)	0.54 (0.49, 0.59)
Outcome: ISS 16			
Sensitivity	100.0%	79.3% (75.7, 82.7)	46.7% (42.4, 51.1)
Specificity	0.0%	55.7% (52.2, 59.2)	95.0% (93.3, 96.4)
Positive predictive value	40.0%	54.4% (50.8, 57.9)	86.2% (81.6, 89.9)
Negative predictive value	0.0%	80.2% (76.7, 83.4)	72.8% (70.0, 75.5)
Positive likelihood ratio	1.00	1.79 (1.64, 1.96)	9.36 (6.82, 12.82)
Negative likelihood ratio	--	0.37 (0.31, 0.44)	0.56 (0.52, 0.61)

* Critical early resource need was defined as any of the following within 24 hours of hospital arrival: packed red blood cell transfusion 6 units, major non-orthopedic surgical procedures, interventional radiology or death.