Emergency Medical Services Intervals and Survival in Trauma: Assessment of the "Golden Hour" in a North American Prospective Cohort

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Abstract

Study objective—The first hour after the onset of out-of-hospital traumatic injury is referred to as the "golden hour," yet the relationship between time and outcome remains unclear. We evaluate the association between emergency medical services (EMS) intervals and mortality among trauma patients with field-based physiologic abnormality.

Methods—This was a secondary analysis of an out-of-hospital, prospective cohort registry of adult (aged ≥15 years) trauma patients transported by 146 EMS agencies to 51 Level I and II trauma hospitals in 10 sites across North America from December 1, 2005, through March 31, 2007. Inclusion criteria were systolic blood pressure less than or equal to 90 mm Hg, respiratory rate less than 10 or greater than 29 breaths/min, Glasgow Coma Scale score less than or equal to 12, or advanced airway intervention. The outcome was inhospital mortality. We evaluated EMS intervals (activation, response, on-scene, transport, and total time) with logistic regression and 2-step instrumental variable models, adjusted for field-based confounders.

Results—There were 3,656 trauma patients available for analysis, of whom 806 (22.0%) died. In multivariable analyses, there was no significant association between time and mortality for any EMS interval: activation (odds ratio [OR] 1.00; 95% confidence interval [CI] 0.95 to 1.05), response (OR 1.00; 95% CI 9.97 to 1.04), on-scene (OR 1.00; 95% CI 0.99 to 1.01), transport (OR 1.00; 95% CI 0.98 to 1.01), or total EMS time (OR 1.00; 95% CI 0.99 to 1.01). Subgroup and instrumental variable analyses did not qualitatively change these findings.

Conclusion—In this North American sample, there was no association between EMS intervals and mortality among injured patients with physiologic abnormality in the field.

INTRODUCTION

Background

The first 60 minutes after traumatic injury has been termed the "golden hour."[1] The concept that definitive trauma care must be initiated within this 60-minute window has been promulgated, taught, and practiced for more than 3 decades; the belief that injury outcomes improve with a reduction in time to definitive care is a basic premise of trauma systems and emergency medical services (EMS) systems. However, there is little evidence to directly support this relationship.[1] Two studies from Quebec suggested that increased total out-of-hospital (ie, EMS) time was associated with increased mortality among seriously injured trauma patients,[2,3] yet this finding has not been replicated in other settings.[4-10] Additional studies suggesting a link between out-of-hospital time and outcome have been tempered by indirect comparisons,[11] small samples of highly selected surgical patients,[12-14] rural trauma patients with long EMS response times,[15] and mixed samples that included patients with nontraumatic cardiac arrest.[16,17]

Importance

To date, patients with out-of-hospital cardiac arrest remain the only field-based patient population with a consistent association between time (response interval) and survival.[18,19] Despite the paucity of outcome evidence supporting rapid out-of-hospital times for the broader population of patients activating the 911 system, EMS agencies in North America are generally held to strict standards about intervals, particularly the response interval. Meeting such expectations requires comprehensive emergency vehicle and personnel coverage throughout a community and travel at high speeds in risky traffic situations (eg, intersections) that occasionally result in crashes causing injury and death to emergency vehicle occupants and others.[20-22] Demonstrating the benefit of such time standards in noncardiac arrest patients is important in justifying the resources and risks inherent in meeting such goals in EMS systems. Previous studies assessing the time-outcome association in trauma have been limited by heterogeneous patient groups, single EMS agencies, small sample sizes, and the exclusion of patients who died in the field.

Goals of This Investigation

In this study, we tested the association between EMS intervals and mortality among trauma patients known to be at high risk of adverse outcomes (those with field-based physiologic abnormality) in 146 diverse EMS agencies across 10 North American sites. Patients who died in the field were also examined as a subset of this population.

MATERIALS AND METHODS

Study Design

This was a secondary analysis of an out-of-hospital, consecutive-patient, prospective cohort registry of injured persons with field-based physiologic abnormality.

Setting

These data were collected as part of the Resuscitation Outcomes Consortium epidemiologic out-of-hospital trauma registry (the Resuscitation Outcomes Consortium Epistry-Trauma).[23] The primary sample for this study was collected from December 1, 2005, through March 31, 2007. Eligible patients were identified from 146 EMS agencies (ground and air medical) transporting to 51 Level I and II trauma hospitals in 10 sites across the United States and Canada (Birmingham, AL; Dallas, TX; Iowa; Milwaukee, WI; Pittsburgh, PA; Portland, OR; King County, WA; Ottawa, ON; Toronto, ON; and Vancouver, BC). The sites vary in size, location, and EMS system structure and provide care to injured persons from diverse urban, suburban, rural, and frontier regions.[24] One hundred fifty-three institutional review boards/research ethics boards (127 hospital-based and 26 EMS agency-based) in both the United States and Canada reviewed and approved the Resuscitation Outcomes Consortium Epistry-Trauma project and waived the requirement for informed consent.

Selection of Participants

The primary study cohort consisted of consecutive injured adults (aged ≥15 years) requiring activation of the emergency 911 system within predefined geographic regions at each Resuscitation Outcomes Consortium site. For the primary sample, patients must have been evaluated by an EMS provider, had signs of physiologic abnormality at any point during out-of-hospital evaluation, and required EMS transport to a hospital. The definition for out-of-hospital physiologic abnormality was based on the American College of Surgeons Committee on Trauma Field Triage Decision Scheme "Step 1" criteria[25] that have been demonstrated to have high specificity for identifying patients with serious injury and need for specialized trauma resources.[26-34] Injured patients with one or more of the following

criteria were included: systolic blood pressure (SBP) less than or equal to 90 mm Hg, Glasgow Coma Scale (GCS) score less than or equal to 12, respiratory rate less than 10 or greater than 29 breaths/min, or advanced airway intervention (tracheal intubation, supraglottic airway, or cricothyrotomy). "Injury" was broadly defined as any blunt, penetrating, or burn mechanism for which the EMS provider(s) believed trauma to be the primary clinical insult.

The primary analysis included patients transported directly to trauma centers to minimize the effect of hospital type (trauma versus nontrauma hospitals) on outcome.[35] Injured persons who were not transported by EMS (ie, died in the field with or without resuscitative measures, refused transport, or were not otherwise transported by EMS) were excluded from the primary analysis because certain out-of-hospital intervals (on-scene, transport, total out-of-hospital) could not be calculated. Children (aged <15 years) were excluded because of different responses to injury, different "normal" physiologic ranges compared with those of adults, and age-based variability in EMS procedure use (eg, tracheal intubation). Although these patients groups were excluded from the primary analysis, information on such patients was collected during the same period and included in sensitivity analyses to better understand how the broader inclusion of such injury patients may affect study results.

Patients enrolled in a concurrent clinical trial with embargoed outcomes (Hypertonic Resuscitation Following Traumatic Injury, ClinicalTrials.gov identifiers NCT00316017 and NCT00316004) were also excluded from the Trauma Epistry database.

Data Collection and Processing

The process used for data collection in Resuscitation Outcomes Consortium Epistry-Trauma has been described in detail elsewhere.[23] In brief, each Resuscitation Outcomes Consortium site identified eligible out-of-hospital trauma patients from participating EMS agencies. Standardized data were collected from each agency, processed locally, entered into standardized data forms, matched to hospital outcomes, deidentified, and submitted to a central data coordinating center (Seattle, WA). Quality assurance processes included EMS provider data collection training, data element range and consistency checks, and annual site visits to review randomly selected study records, data capture processes, and local data quality efforts. Sites and agencies that had substantially higher or lower monthly case capture (relative to their average), as determined with a Poisson distribution with a 5% cutoff, were sent inquiries to reduce biased sampling. The dates for enrollment and resulting sample size were based on the initial inception of the Resuscitation Outcomes Consortium Epistry-Trauma database (December 1, 2005) through the most recent date demonstrating complete case capture and a high level of outcome completion (March 31, 2007).

Methods of Measurement

EMS intervals were calculated from dispatch records and all available out-of-hospital patient care reports. For patients with multiple sources of time records (eg, dispatch, 2 or more patient care reports from different EMS agencies), discrepancies were resolved between data sources to produce the most accurate representation of true times. Intervals were based on standard EMS definitions, including activation interval (time 911 call received at dispatch to alarm activation at EMS first response agency), response interval (time from alarm activation to arrival of first responding vehicle on scene), on-scene interval (time arrival of first EMS responding vehicle on scene until leaving the scene), and transport interval (time leaving the scene to vehicle arrival at the receiving hospital).[36] We defined the total EMS interval as time from 911 call received to arrival at the receiving hospital. This definition was used to approximate the interval from time of injury to time of definitive care and represents a slightly longer duration than the "total out-of-hospital interval" defined by

Spaite et al.[36] Time at patient's side and time of care transfer in the hospital were not consistently captured by all sites and were therefore not available in this study. We considered all intervals as continuous covariates but also evaluated categorical versions of total EMS time (≤60 versus >60 minutes) and response interval (<4, 4 to 8, and >8) according to previously defined response intervals for cardiac arrest.[18,19]

Fourteen additional out-of-hospital variables were considered in the analysis. Physiologic information included the initial (ie, preintervention) field values (SBP [mm Hg], GCS score, respiratory rate [breaths/min], shock index [pulse rate/SBP]) and use advanced airway procedures (tracheal intubation and "rescue" airways [supraglottic airway or cricothyrotomy]). SBP (<90, 150 to 179, and ≥180 mm Hg; reference 90 to 149 mm Hg) and respiratory rate (<10 and >29 breaths/min; reference 10 to 29 breaths/min) were categorized to allow for nonlinear associations with outcome. The "worst" physiologic values (eg, lowest GCS score) were also assessed to account for the portion of patients with repeated vital sign measurements that demonstrated physiologic decompensation after initial field assessment. Additional variables included age (years), sex, mechanism of injury (motor vehicle, motorcycle, pedal cyclist, pedestrian, other transport, fall, struck by/against, stabbing, firearm, machinery, burn, natural/environment, other), type of injury (blunt versus penetrating), trauma hospital level (I versus II), use of intravenous or intraosseous fluids, hemorrhage control (ie, compression), mode of transport (ground ambulance versus helicopter), EMS service level of first responding vehicle (advanced versus basic life support), and site. The primary outcome was inhospital mortality (whether in the emergency department [ED] or after hospital admission).

We also collected and geocoded census tract location of the injury event (ESRI ArcMap v. 9.1, Redlands, CA) and then identified the center of these locations by weighting on census block (United States) or dissemination areas (Canada). The straight-line distance from the weighted center of each census tract (the "centroid") to the receiving hospital was then calculated for each patient and used as an instrument in 2-step instrumental variable analyses (described below). We validated this distance measure against the "true" distance calculated from latitude/longitude coordinates for a subset of patients at 2 sites (n=498).

Primary Data Analysis

We used descriptive statistics to compare groups by quartile of total EMS time. We then used 2 types of multivariable regression models to test the association between EMS intervals and mortality. Multivariable logistic regression models were used for all analyses, and 2-step instrumental variable models were used for analyses in which distance fulfilled criteria as an "instrument." Instrumental variable analysis is an analytic strategy used in observational research to account for both measured and unmeasured confounders, allowing improved estimation of causal effect, provided an appropriate instrument is available and certain assumptions are met.[37-39] The instrumental variable analysis was proposed in our study as a potential analytic solution to the dilemma of unmeasured confounding (eg, injury severity, patient acuity) and because we believed EMS intervals were strongly influenced by paramedic perception of serious injury and acuity (ie, shorter times for sicker patients with inherently worse prognosis). Measures of distance have been used as instruments in previous trauma studies.[40,41] Additional details about the instrumental variable analysis are included in Appendix E1 (available online at http://www.annemergmed.com).

Study site was included in all models as a fixed-effects term to account for the potential clustering of cases within sites.[42] We used an indicator of missingness to handle covariates with missing data because more sophisticated methods of handling missing values (eg, multiple imputation) present problems for combining results across 2-step instrumental variable models. The final models were generated according to a priori understanding of

known confounders. Potential interactions between intervals and clinical covariates were tested, and the presence of effect modification was noted if such terms demonstrated statistical significance at *P*<.05. Model fit was assessed with the Hosmer-Lemeshow goodness of fit test and examination of diagnostic plots for change in coefficients (Δ-*β*) when individual episodes were excluded from the analysis.

Several important strata and subgroups were identified a priori for the analysis. These groups included mode of transport (ground ambulance versus air medical), level of first responding EMS vehicle on scene (advanced life support versus basic life support), injury type (blunt versus penetrating), traumatic brain injury (GCS score ≤8), shock (SBP ≤70 mm Hg or SBP 71 to 90 mm Hg, with pulse rate >108 beats/min[43]), advanced airway intervention, and country (United States versus Canada). Two additional subgroups (aged ≥65 years and Revised Trauma Score ≤2) were evaluated in post hoc analyses.

Regression analyses were performed using SPlus (version 6.2; Seattle, WA), and 2-step instrumental variable analyses were done with Stata (version 9.1; StataCorp, College Station, TX).

Sensitivity Analyses

To further explore the potential for correlated data to alter our results, we analyzed 2 additional cluster-adjusted analyses: a hierarchical linear probability model that allowed for non-nested multilevel clustering (up to 2 EMS agencies and hospital) and a random-effects model with sites as clusters. To better understand the relationship between time and outcome, sensitivity analyses also included injured adults transported by participating EMS agencies to all types of hospitals (trauma centers and nontrauma centers), children (aged <15 years), and patients who died in the field (activation and response intervals only).

RESULTS

Characteristics of Study Subjects

Of the 7,555 patients meeting Epistry inclusion criteria and transported to a hospital, there were 4,276 adult trauma patients transported by 146 EMS agencies to 51 Level I or II trauma centers during the 16-month period (Figure 1). After exclusion of patients with missing survival status (n=152), coenrollment in a concurrent clinical trial with embargoed outcomes (n=130), and missing or erroneous out-of-hospital times, locations, or other incomplete data (n=338), 3,656 adults with complete information were retained for the primary analysis (Figure 1). Eight hundred six (22.0%) patients died after EMS transport to a hospital, including 504 (62.5% of deaths) on the same day as EMS evaluation. Among hospitalized patients, median length of stay was 2 days (interquartile range [IQR] 0 to 8), though this was substantially different between survivors (median 3 days) and patients who died (median 0 days). When excluded patients (adults transported to major trauma centers; n=620) were compared with the study sample (n=3,656) for important demographic, physiologic, and mechanism measures, the excluded population was younger (median age 34 years; IQR 24 to 49 years), with slightly lower GCS scores (median 8; IQR 3 to 13), lower rate of penetrating injury (16.8%), and a higher rate of air medical transport (36.2%).

There was substantial variation between sites and countries in all intervals (Table 1). Across the 10 sites, the median (IQR) intervals were activation 0.98 minutes (0.27 to 1.62 minutes), response 4.28 minutes (3.00 to 6.30 minutes), on-scene 19.0 minutes (13.4 to 26.0 minutes), transport 10.0 minutes (6.37 to 15.30 minutes), and total EMS time 36.3 minutes (28.4 to 47.0 minutes). Distribution of total EMS time is illustrated in Figure 2. Descriptive characteristics of the cohort, by quartiles of total time, are listed in Table 2. Depressed GCS score and hypotension (SBP ≤90 mm Hg) appeared more common among patients with the

shortest EMS times, though other physiologic measures were similar across quartiles. The proportion of tracheal intubations attempted, median age, women, air medical transport, blunt injury, and unadjusted survival all increased with increasing total EMS times.

Main Results

In the multivariable logistic regression model, total EMS time was not associated with mortality (odds ratio [OR] for every minute of total time 1.00; 95% confidence interval [CI] 0.99 to 1.01) (Table 3). When the sample was assessed with 10-minute increments for total EMS time, there was no evidence of increased mortality with increasing field times (OR 0.90; 95% CI 0.80 to 1.02). Similar results were obtained when total times were grouped by quartile (OR 0.95; 95% CI 0.83 to 1.08). We were also unable to demonstrate independent associations between mortality and any other EMS interval for the overall sample (Table 4). When total EMS time was dichotomized to compare patients with greater than 60 minutes to those with less than or equal to 60 minutes, there was no association with mortality (OR 1.11; 95% CI 0.70 to 1.77). Categorization of total EMS time into quartiles did not suggest a threshold effect between time and mortality (quartile 1=reference; quartile 2=OR 0.69, 95% CI 0.47 to 1.00; quartile 3=OR 0.77, 95% CI 0.53 to 1.13; quartile 4=OR 0.81, 95% CI 0.54 to 1.21). For categorized response interval, there was no association with mortality for patients with a 4- to 8-minute interval (OR 0.95; 95% CI 0.71 to 1.25) or greater than 8-minute interval (OR 1.22; 95% CI 0.80 to 1.85) compared with patients with a response less than 4 minutes. Two-step instrumental variable analyses were used only in subgroup analyses (described below) because the correlation between distance and time was low (F test <10) for all intervals using the primary sample. These results did not qualitatively change when the "worst" physiologic values were used in place of initial values (data not shown). The primary model was well fit (Hosmer-Lemeshow goodness of fit statistic P=. 80). There was no evidence of effect modification between any interval and clinical variables (all interactions P>.05).

Adjusted ORs for mortality among the subgroups are presented in Table 4. In multivariable logistic regression models, there was no demonstrable association between time and mortality for any subgroup. The only subgroup that met criteria for using instrumental variable analyses to assess total EMS time was trauma patients transported in the United States (F statistic 46.4), and these results were not qualitatively different (OR 1.00; 95% CI 0.997 to 1.001).

Sensitivity Analysis

Using a random-effects model with sites as clusters, the lack of association between total EMS time and mortality persisted (OR 0.99; 95% CI 0.999 to 1.0003). In a hierarchical, non-nested linear probability model integrating EMS agencies (up to 2) and hospital as clusters, there remained no association between total EMS time and mortality (linear probability estimate −0.0004; 95% CI −.001 to 0.0003).

When the sample was expanded to include injured adults transported to all types of hospitals (restricted to those with outcomes available; n=5,356), there remained no association between total EMS time and mortality (OR 1.00 per minute; 95% CI 0.99 to 1.00), or between other intervals and mortality (data not shown). Among the 460 children transported to Level I or II trauma centers with outcome information available, there was no association between mortality and total EMS time or other intervals (data not shown).

Of the 1,385 patients who died at the scene after injury, there were 914 adults with interval data available for analysis. Of these patients, 722 (79%) were declared dead without attempted resuscitation, 130 (14%) had attempted resuscitation with no documented vital

signs, and 62 (7%) had attempted resuscitation with documented initial vital signs. The median (IQR) activation and response intervals for patients who died in the field were 1.00 minute (0.43 to 1.67 minutes) and 4.92 minutes (3.27 to 7.38 minutes) for those without resuscitation; 1.03 minutes (0.58 to 1.67 minutes) and 5.00 minutes (3.62 to 7.69 minutes) for patients with resuscitation attempted and no vital signs; and 1.00 minute (0.32 to 1.57 minutes) and 4.58 minutes (3.40 to 7.33 minutes) for patients with resuscitation attempted and initial measurable vital signs. These intervals were slightly longer than the median activation interval (0.98 minutes; IQR 0.27 to 1.62 minutes) and response interval (4.28 minutes; IQR 3.00 to 6.30 minutes) for patients transported to a hospital (*P*<.001). When we reevaluated the multivariable models with both the primary sample *and* patients who died in the field after attempted resuscitation, there remained no statistical association between time and mortality for activation (OR 1.00; 95% CI 0.97 to 1.04) or response (OR 1.00; 95% CI 0.99 to 1.04) intervals. These results persisted when all patients who died in the field (with or without a resuscitation attempt) were included in the models (data not shown).

LIMITATIONS

Previous studies have demonstrated an apparent association between increasing out-of-hospital time and decreased mortality (ie, the appearance that longer times decrease mortality),[7-10,16] even after accounting for injury severity. This phenomenon is at least partly explained by EMS providers moving and driving faster for patients believed to have serious injury and spending more time on calls with patients recognized as having minor injury (ie, less urgency to get such patients to a hospital). The association between increasing injury severity and decreased on-scene and transport intervals has been previously demonstrated.[6,7,44] This type of confounding, which is unlikely to be fully accounted for with available variables (ie, unmeasured confounding), was the primary reason we considered instrumental variable models in addition to logistic regression. Although the instrumental variables strategy ultimately could not be used for most analyses, the subgroup analysis that met criteria for such analysis generated results similar to those of logistic regression models.

Detailed hospital-based information, including measures of injury severity (eg, Injury Severity Score), was not available in the Resuscitation Outcomes Consortium Epistry-Trauma database. We used field-based information to adjust for confounding by injury severity, though it is possible that these measures did not fully account for such relationships. We also did not have longer term (eg, 30-day survival) or functional outcomes for these patients, either of which may have altered the results. In addition, the exclusion of patients enrolled in the concurrent clinical trial and those with missing data could have introduced bias to the results.

There was substantial variability in intervals between sites and heterogeneity in our patient population. Such differences likely reflect geographic variation (eg, rural land mass), variability in EMS agencies, EMS system differences, population variation in injury mechanisms (eg, penetrating trauma), and response to injury, plus other factors. A large meta-analysis similarly demonstrated time differences among trauma patients cared for by urban/suburban versus rural ground ambulance crews, especially for activation, response, and transport intervals.[45] Although the inclusion criteria were designed to reduce heterogeneity and isolate a field-identified high-risk trauma population, some variability between patients and sites was unavoidable. This variability may have further reduced our ability to demonstrate an association between time and outcome, though we believe inclusion of such a broad and heterogeneous group of sites increased the generalizability of our findings.

In addition to variation in intervals, there was also likely variation in field care, hospital care, and injury characteristics between sites, EMS agencies, and hospitals. We attempted to account for this possibility by using fixed-effects models, with sites as clusters. There was likely clustering present on many levels (eg, EMS agencies, hospitals, providers), with overlap between clusters (non-nested), which produced challenges in fully accounting for such potentially correlated data. However, different model specification (ie, hierarchical) to account for non-nested multilevel clustering (ie, EMS agency, hospital) and using random-effects models did not qualitatively change our study results. It is also possible that addressing the study question using sites with mature EMS systems and relatively short EMS intervals could have suppressed a demonstrable association between time and outcome. That is, most patients had a total EMS time well below 60 minutes, which may have precluded the ability to fully test the "golden hour" premise based on a 60-minute cut point. A nonlinear relationship between time and outcome could also exist, though categorical terms for the total EMS interval and response interval did not suggest such a relationship.

The duration of time from EMS dispatch through delivery to the receiving hospital represents only a portion of the time from actual injury event to definitive care. We did not know the time of injury and were therefore unable to measure the interval from injury onset to hospital arrival, which may represent a critical window for a small portion of patients (eg, those who die in the field). Our definition for total EMS time and the "golden hour" in this study was based on the assumption that the time between injury onset and 911 notification was short, though this may not have been the case with all patients (eg, unwitnessed injury events, rural areas, lack of immediate telephone access, or call coverage). Time to hospital arrival may also be different from the time to definitive care (eg, for patients requiring operative intervention or other important hospital-based interventions), which may also have affected the ability to demonstrate an association between time and outcome.

Finally, the use of instrumental variable analysis is predicated on having an available instrument that fulfills all the required criteria and assumptions. Unfortunately, after geocoding of all injury census tracts to generate the distance measure in this sample, distance did not ultimately have a strong correlation with EMS intervals. There was only one subgroup that met our predefined criteria to use distance as an instrument (F test >10), and this analysis produced similar results to those from logistic regression models. Despite the fact that we could use instrumental variable methods in only a small portion of the analysis, we believe these results support our overall findings of no demonstrable association between time and outcome.

DISCUSSION

In this study, we were unable to support the contention that shorter out-of-hospital times (as measured from receipt of 911 call to hospital arrival) improve survival among injured adults with field-based physiologic abnormality. This finding persisted across many subgroups, including level of first responding EMS provider, mode of transport, country, age, injury type, and more severe physiologic derangement. Our findings are consistent with those of previous studies that similarly have failed to demonstrate a relationship between out-of-hospital time and outcome using different patient populations, trauma and EMS systems, regions, data sources, and confounders.[4-10] However, we believe our findings are unique because of the field-based inclusion criteria for a recognized high-risk subset of injured patients, the sampling design of Epistry (population-based data from a large number of EMS agencies and sites across North America), sensitivity analyses that included deaths in the field and non–trauma center patients, and rigorous data collection for EMS times that accounted for multiple EMS agencies caring for the same patient.

It is possible that other factors, such as unmeasured confounders, selection bias, statistical approach, inclusion criteria, intervals assessed, or heterogeneity in the sample (variance), precluded our ability to show such an association. Although it is likely that minutes do affect outcome for certain severely injured individuals, demonstrating this relationship across a field-defined population of injured persons using EMS intervals has generally produced inconclusive results. The 2 previous studies from Quebec suggesting an association between total out-of-hospital time and mortality were conducted with retrospectively defined samples of seriously injured patients[2,3] and have not been replicated in other settings. Although a cornerstone of trauma systems, the "golden hour" premise has proven challenging to consistently demonstrate across larger samples of trauma patients and specific EMS intervals. One must also consider the possibility that assessing the influence of EMS time on outcome is not feasible through an observational study design because of inherent forms of bias and unmeasured confounding. Because more rigorous study designs (ie, randomized controlled trials or quasi-experimental designs) are generally not practical, feasible, or ethical for addressing this study question, adequately testing the hypothesis that shorter intervals improve outcomes may not be possible.

The only condition in which rapid EMS response has been shown to consistently improve survival is nontraumatic cardiac arrest.[18,19] Although several studies have demonstrated the survival benefit of trauma systems and trauma centers,[2,35,46-49] the benefit of advanced out-of-hospital trauma care (eg, advanced airway intervention and intravenous fluid resuscitation) remains unclear. Further, there is a growing body of literature questioning the benefit of out-of-hospital advanced life support practices in trauma patients.[4,50-54] Although some seriously injured individuals may require time-dependent EMS interventions to survive (eg, airway obstruction, respiratory arrest, external hemorrhage at a compressible site), faster application of such interventions may not have a measureable effect on outcomes for most trauma patients. It is also plausible that the "golden hour" is primarily dependent on the timeliness of hospital-based interventions (ie, initiation of definitive care after arrival at an ED), rather than out-of-hospital care. Although the relationship between hospital time and outcome among seriously injured patients also remains unproven, such a possibility would lend credence to the "golden hour" concept and be consistent with the previously demonstrated hospital-based effect on survival.[35]

The relationship between duration of on-scene time and outcomes in trauma also remains unclear. In this study, we were unable to demonstrate a significant relationship between time on-scene and mortality. Previous studies have suggested that on-scene time is affected by injury severity, plus the number and type of EMS interventions.[44,55,56] As with response intervals, many urban EMS systems are held to specific standards for the acceptable duration of on-scene care. As the scope of practice among EMS providers increases (eg, rapid sequence tracheal intubation, advanced airway management, use of additional medications), such standards may help to contain the opportunity for very long on-scene times. However, our results do not suggest an important association between shorter scene times and improved survival.

Similarly, there has been little information to evaluate the potential effect of transport times on outcomes in trauma. Patients perceived by EMS providers to have serious injury are frequently transported to the hospital by "lights and siren" to facilitate rapid arrival at a trauma center. The demonstrated survival benefit of treating seriously injured patients in trauma centers[2,35,46-49] suggests that time lost bypassing nontrauma hospitals is recouped by the benefits of specialized care provided for injured persons at major trauma centers. One previous study found that although transport times to trauma centers were higher for patients bypassing other local facilities, longer transport times were not associated with adverse outcomes.[57] Our findings support this conclusion and further substantiate the practice of

transporting patients presumed to have serious injury to trauma centers, despite longer transport times.

Although the association between out-of-hospital time and outcome remains unsubstantiated beyond persons in cardiac arrest, there is a public expectation of rapid EMS response and care after activation of the 911 system. In the setting of a perceived "emergency," the public may not necessarily value whether faster EMS time and expeditious care have been shown to save lives for the majority of clinical conditions. However, meeting these expectations costs money (eg, establishment of fire houses and positioning of EMS crews to achieve predefined response intervals), can place EMS providers, patients, and the nearby public at risk,[20-22] and is a common reason (ie, emergency vehicle crashes) for tort claims against EMS agencies.[58] In an increasingly costly and competitive health care environment, these factors must be contemplated when seeking to further "optimize" EMS systems.

Among injured patients with physiologic abnormality prospectively sampled from a diverse group of sites and EMS systems across North America, there was no association between EMS intervals and mortality.

Editor's Capsule Summary

What is already known on this topic

The "golden hour" concept in trauma is pervasive despite little evidence to support it.

What question this study addressed

Is there an association between various emergency medical services (EMS) intervals and inhospital mortality in seriously injured adults?

What this study adds to our knowledge

In 3,656 injured patients with substantial perturbations of vital signs or mental status, transported by 146 EMS agencies to 51 trauma centers across North America, no association was found among any EMS interval and mortality.

How this might change clinical practice

This study suggests that in our current out-of-hospital and emergency care system time may be less crucial than once thought. Routine lights-and-sirens transport for trauma patients, with its inherent risks, may not be warranted.

Acknowledgments

APPENDIX E1

Instrumental variables analysis

Instrumental variable analysis is an analytic strategy used in observational research to account for both measured and unmeasured confounders, allowing improved estimation of causal effect, provided an appropriate instrument is available and certain assumptions are met.[37-39] Instrumental variable analysis was proposed in our study as a potential analytic solution to the dilemma of unmeasured confounding (eg, injury severity, patient acuity, and the phenomenon of shorter times for sicker patients with inherently worse prognosis) that may not have been fully accounted for in measured predictor variables. Martens et al[37] observed that through certain assumptions, the causal effect of the exposure (in this case, time) on the outcome can be captured through the relationship between the exposure and the instrumental variable. Specifically, McClellan et al[38] observed that it is possible to mimic randomization of patients to the likelihood of receiving a certain treatment according to the association between treatment and the instrumental variable. This process eliminates unmeasured confounders and allows for the estimation of causal effect in terms of the likelihood. A Hausman test is also generally used to determine whether a single equation model is sufficient versus use of a 2-step instrumental variable analysis to remove bias associated with unobserved confounders.

In essence, 2 relevant equations are estimated:

$$Y = \alpha + \beta T + \theta X + E \tag{1}$$

$$T = \gamma + \delta Z + \theta X + F \tag{2}$$

where Y is the outcome of interest, T is the predictor of interest (eg, time), X represents other confounders, Z is the instrumental variable, and E and F are error terms. The key assumptions in instrumental variable analyses are (1) Z and T are highly correlated such that T can be predicted from Z; (2) there is no confounding of the Z and T association; and (3) Z and Y are uncorrelated (except through Z's influence on T).

We proposed using distance as an instrumental variable because of its perceived correlation with time, lack of correlation with survival (except through time), and demonstrated success in previous trauma research with instrumental variable analyses.[40,41] In this situation, if we assume distance to be Z and time T, we then use the instrumental variable model to estimate the likelihood of different intervals according to distance; this likelihood is then used to estimate the causal effect of time on outcome. Because a weak instrument can introduce bias to an analysis, the F statistic is typically used to assess adequate correlation between T (time) and Z (distance) after accounting for X (important confounders), with F greater than 10 indicating an adequate instrument.[39] In this study, we tested the appropriateness of distance as an instrument for all intervals in the primary sample and for total EMS time in all subgroups. Only the subgroup of trauma patients treated in the United States fulfilled criteria for using distance as an instrument (F test >10), which restricted our use of instrumental variable analysis to this subgroup of patients.

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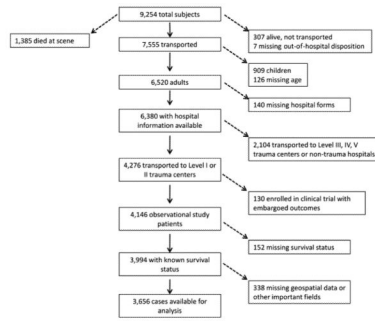
Figure 1.
Flow diagram of patients included in the primary analysis.
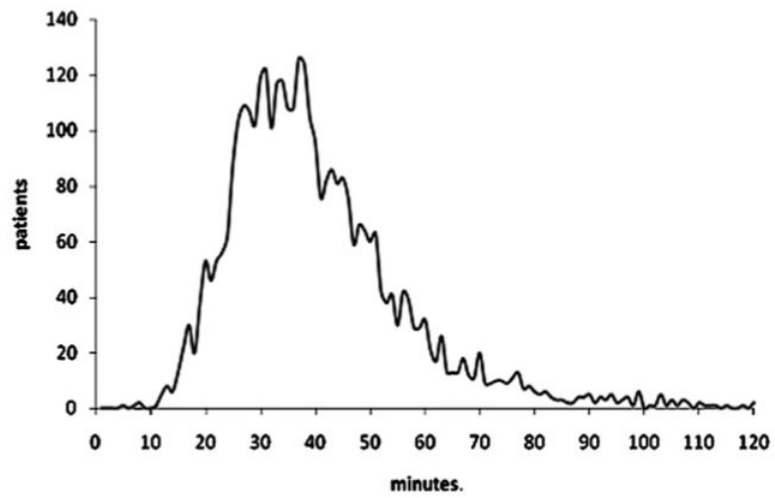
Figure 2.
Distribution of the total EMS times for 10 sites across North America (n=3656).

Table 1

EMS intervals among trauma patients with physiologic abnormality, by site (n=3,656)

Site	Activation Interval*		Response Interval*		On-Scene Interval		Transport Interval		Total EMS Interval	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Birmingham, AL	0.00	0.00–0.50	5.00	4.00–7.00	14.0	11.0–18.0	9.76	6.00–15.0	30.0	24.0–41.0
Dallas, TX	0.98	0.63–1.40	3.82	2.58–5.53	15.7	10.9–21.4	8.58	5.24–13.2	31.5	25.0–39.6
Iowa	0.86	0.02–1.53	4.00	3.00–5.55	15.4	11.9–20.0	7.98	4.93–10.2	28.1	23.3–37.2
Milwaukee, WI	0.00	0.00–1.00	3.00	3.00–4.00	22.0	16.0–27.0	12.0	9.00–15.0	38.0	32.0–45.0
Ottawa	0.60	0.37–1.00	5.44	3.88–8.19	21.2	15.9–27.5	9.67	6.45–16.0	39.3	31.2–49.1
Pittsburgh, PA	1.13	0.65–2.00	5.60	3.62–9.10	13.9	8.41–25.5	10.0	6.73–13.5	33.4	24.2–53.1
Portland, OR	0.18	0.10–0.72	4.28	3.10–5.94	16.8	12.4–23.0	13.5	9.60–18.1	36.3	29.6–45.9
Seattle/King County, WA	1.08	0.60–1.68	3.94	3.05–5.18	24.1	18.6–30.5	10.3	6.52–17.9	42.1	32.8–53.1
Toronto	1.62	1.00–2.38	4.78	3.52–7.45	19.1	14.4–25.0	9.45	5.00–15.1	37.0	29.6–48.1
Vancouver	1.70	1.12–2.68	4.99	3.16–8.18	20.3	14.8–29.3	10.1	6.24–15.5	39.0	31.1–54.5
United States	0.82	0.08–1.32	4.00	3.00–5.87	18.2	13.0–25.5	10.2	6.66–15.2	35.7	27.8–45.7
Canada	1.28	0.67–2.15	5.00	3.53–8.00	20.2	14.9–27.0	9.75	5.85–15.4	38.1	30.5–49.9
Overall	0.98	0.27–1.62	4.28	3.00–6.30	19.0	13.4–26.0	10.0	6.37–15.3	36.3	28.4–47.0

*
Calculation of activation and response intervals include patients who died in the field and had nonmissing values for times (n=914).

Table 2

Characteristics of injured persons with field physiologic abnormality, by quartile of total EMS time[*]

Characteristics	Lowest (First) Quartile EMS Time (n=917)	Second Quartile EMS Time (n=913)	Third Quartile EMS Time (n=927)	Highest (Fourth Quartile EMS Time (n=899)
Initial physiologic measures				
GCS score ≤12 (%)	652 (71.1)	602 (65.9)	615 (66.3)	535 (59.5)
Median GCS score (IQR)	9 (3–14)	10 (4–15)	10 (3–15)	11 (4–15)
SBP ≤90 mm Hg (%)	418 (45.6)	353 (38.7)	361 (38.9)	351 (39.0)
Median SBP (IQR)	100 (70.5–134)	110 (83–136)	110 (81.5–140)	110 (80–140)
RR <10 or >29 breaths/min (%)	162 (17.7)	167 (18.3)	146 (15.7)	167 (18.6)
Median low RR (IQR)	18 (16–24)	20 (16–24)	20 (16–24)	20 (16–24)
Pulse (beats/min)				
Median low pulse (IQR)	94 (75–110)	94 (80–110)	92 (77.5–110)	92 (76–110)
Median shock index, pulse/SBP (IQR)	0.75 (0.55–1.00)	0.78 (0.62–1.00)	0.77 (0.60–1.00)	0.78 (0.57–1.05)
Tracheal intubation attempt (%)	194 (21.1)	200 (21.9)	237 (25.6)	314 (34.9)
Rescue airway (%)	22 (2.4)	14 (1.5)	14 (1.5)	15 (1.7)
Median pulse oximetry (IQR)	98 (94–99)	97 (94–99)	98 (95–100)	98 (94–99)
Demographics				
Median age, y (IQR)	34 (24–49)	37 (25–50)	38 (25–53)	39 (25–54)
Male (%)	697 (76.0)	682 (74.7)	669 (72.2)	621 (69.1)
Type of injury (%)				
Blunt	593 (64.7)	667 (73.1)	712 (76.8)	744 (82.8)
Penetrating	298 (32.5)	228 (25.0)	175 (18.9)	106 (11.8)
Burn	9 (1.0)	10 (1.1)	13 (1.4)	12 (1.3)
Other	7 (0.8)	6 (0.7)	16 (1.7)	12 (1.3)
Unknown	9 (1.0)	2 (0.2)	11 (1.2)	23 (2.6)
Injury mechanism (%)				
Motor vehicle occupant	163 (17.8)	201 (22.0)	209 (22.5)	322 (35.8)
Motorcyclist	38 (4.1)	41 (4.5)	29 (3.1)	42 (4.6)
Pedal cyclist	23 (2.5)	29 (3.2)	17 (1.8)	16 (1.7)
Pedestrian	126 (13.7)	86 (9.4)	75 (8.1)	43 (4.8)

Characteristics	Lowest (First) Quartile EMS Time (n=917)	Second Quartile EMS Time (n=913)	Third Quartile EMS Time (n=927)	Highest (Fourth Quartile EMS Time (n=899)
Other transport	3 (0.3)	6 (0.7)	10 (1.1)	20 (2.2)
Fall	160 (17.4)	212 (23.2)	267 (28.8)	231 (25.7)
Stuck by/against or crushed	65 (7.1)	80 (8.8)	91 (9.8)	82 (9.1)
Cut/pierce stab	102 (11.1)	78 (8.5)	72 (7.8)	38 (4.2)
Fire/burn	10 (1.1)	12 (1.3)	10 (1.1)	10 (1.1)
Machinery	5 (0.5)	2 (0.2)	4 (0.4)	5 (0.6)
Firearm gunshot	183 (20.0)	139 (15.2)	98 (10.6)	57 (6.3)
Natural/environment	1 (0.1)	0	0	0
Other	17 (1.9)	23 (2.5)	29 (3.1)	23 (2.6)
Unknown	19 (2.1)	4 (0.4)	16 (1.7)	9 (1.0)
Scene information				
Time of day				
Morning (%)	100 (10.9)	112 (12.3)	143 (15.4)	144 (16.0)
Day (%)	194 (21.1)	219 (24.0)	229 (24.7)	244 (27.1)
Evening (%)	302 (32.9)	286 (31.3)	269 (29.0)	267 (29.7)
Night (%)	321 (35.0)	296 (32.4)	286 (30.9)	244 (27.1)
Weekend (%)	324 (35.3)	315 (34.5)	336 (36.2)	313 (34.8)
Air medical transport	2 (0.2)	7 (0.8)	20 (2.2)	133 (14.8)
Hospitals receiving patients	40	43	47	44
Outcomes				
Mortality (%)	268 (29.2)	189 (20.7)	181 (19.5)	168 (18.7)
Median hospital length of stay (days)	1 (0-8)	2 (0-8)	2 (0-8)	3 (0-11)

RR, Respiratory rate.

*
Values were calculated according to available (ie, nonmissing) data. Rescue airways included supraglottic airway (eg, esophageal-tracheal twin-lumen airway device [Combitube; Kendall-Sheridan Catheter Corp, Argyle, NY]) or cricothyrotomy.

Table 3

Multivariable logistic regression model evaluating the association between total EMS time and mortality (n=3,656)[*]

Covariates	OR	95% CI
Total EMS time (by minute)	1.00	(0.99-1.01)
Ln (age)	4.63	(3.34-6.42)
Sex	0.87	(0.65-1.16)
Air transport	0.71	(0.34-1.48)
GCS score obtained	5.42	(3.17-9.26)
Total GCS score (by increasing score)	0.81	(0.78-0.84)
SBP obtained	0.10	(0.04-0.23)
SBP <90 mm Hg	1.62	(1.10-2.38)
180>SBP≥150 mm Hg	1.06	(0.71-1.58)
SBP ≥180 mm Hg	1.57	(0.93-2.65)
150>SBP≥90 mm Hg	Reference	
Respiratory rate obtained	0.39	(0.21-0.75)
Respiratory rate <10 breaths/min	3.87	(2.45-6.12)
Respiratory rate >29 breaths/min	1.42	(0.93-2.19)
29≥RR≥10	Reference	
Shock index ≥1.0	1.32	(0.93-1.88)
Shock index <1.0	Reference	
Firearm or stabbing	1.06	(0.57-1.96)
Burn	2.02	(1.37-2.99)
Struck by/against crushed or fall	0.79	(0.22-2.82)
Other injury mechanism	0.93	(0.67-1.28)
Motor vehicle related	Reference	
Intravenous or intraosseous line placed	1.03	(0.69-1.56)
Hemorrhage control	0.72	(0.50-1.03)
Tracheal intubation attempt	3.76	(2.65-5.34)
Rescue airway	2.60	(1.10-6.15)
Hospital level	1.13	(0.72-1.77)

[*] Site was included in the model as a fixed-effects term to account for clustering.

Table 4

Adjusted ORs for mortality, using EMS intervals (in minutes) among injury subgroups[*]

Subgroup/Strata	n	Total EMS Interval	Activation Interval	Response Interval	On-Scene Interval	Transport Interval
Ground	3,498	1.00 (0.99-1.01)	1.00 (0.95-1.05)	1.00 (0.96-1.04)	1.00 (0.98-1.01)	1.00 (0.99-1.01)
Air	158	0.97 (0.91-1.02)	0.67 (0.25-1.79)	1.00 (0.87-1.16)	1.03 (0.97-1.09)	0.93 (0.86-1.02)
Blunt	2,716	1.00 (0.99-1.005)	1.00 (0.95-1.05)	1.01 (0.97-1.06)	0.99 (0.98-1.01)	0.99 (0.98-1.01)
Penetrating	807	1.01 (0.99-1.04)	1.01 (0.73-1.39)	1.03 (0.94-1.13)	1.02 (0.99-1.05)	1.01 (0.96-1.06)
TBI (GCS score ≤8)	1,145	0.99 (0.98-1.003)	0.92 (0.82-1.03)	0.98 (0.93-1.04)	0.99 (0.98-1.01)	0.99 (0.97-1.01)
Shock (SBP ≤70, or SBP 71-90 with pulse rate ≥108 beats/min)	1,483	0.99 (0.98-1.01)	0.86 (0.68-1.10)	1.02 (0.95-1.09)	1.00 (0.98-1.03)	0.97 (0.94-1.001)
Advanced airway management	945	0.99 (0.98-1.01)	1.05 (0.95-1.16)	0.97 (0.89-1.05)	1.00 (0.98-1.02)	0.98 (0.96-1.01)
Revised Trauma Score ≤2	79	1.01 (0.94-1.09)	1.79 (0.49-6.50)	1.32 (0.51-3.44)	1.00 (0.93-1.08)	1.09 (0.87-1.36)
BLS first arriving	1,803	1.01 (0.99-1.02)	1.03 (0.97-1.10)	0.99 (0.94-1.05)	1.01 (0.99-1.03)	1.00 (0.997-1.003)
ALS first arriving	1,853	0.99 (0.98-1.002)	0.76 (0.60-0.96)	1.01 (0.96-1.06)	0.99 (0.97-1.01)	0.99 (0.97-1.001)
Elders (≥65 y)	472	1.00 (0.99-1.02)	1.02 (0.96-1.07)	0.98 (0.89-1.07)	1.00 (0.97-1.03)	1.03 (0.996-1.06)
United States	2,610	0.99 (0.98-1.004)[†]	1.04 (0.97-1.11)	1.04 (0.98-1.09)	0.99 (0.97-1.01)	0.99 (0.97-1.01)
Canada	1,046	1.00 (0.99-1.01)	0.94 (0.85-1.04)	0.97 (0.91-1.03)	1.00 (0.98-1.02)	1.00 (0.98-1.02)
Overall	3,656	1.00 (0.99-1.01)	1.00 (0.95-1.05)	1.00 (0.97-1.04)	1.00 (0.99-1.01)	1.00 (0.98-1.01)

TBI, Traumatic brain injury; *BLS*, basic life support; *ALS*, advanced life support.

[*] In addition to interval, multivariable logistic regression models included the following covariates: age, sex, mode of transport, site, GCS score, SBP, respiratory rate, shock index, mechanism of injury, field intravenous or intraosseous fluid administration, tracheal intubation attempt, use of a rescue airway, field hemorrhage control, and hospital level. For each time interval point estimate, 95% confidence intervals are listed in parentheses.

[†] Results for 2-step instrumental variable analyses for US trauma patients: OR 1.00 (95% CI 0.997 to 1.001).