Lead-Time Bias and Interhospital Transfer after Injury: Trauma Center Admission Vital Signs Underpredict Mortality in Transferred Trauma Patients

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BACKGROUND: Admission physiology predicts mortality after injury, but may be improved by resuscitation before transfer. This phenomenon, which has been termed *lead-time bias*, may lead to underprediction of mortality in transferred patients and inaccurate benchmarking in centers receiving large numbers of transfer patients. We sought to determine the impact of using vital signs on arrival at the referring center vs on arrival at the trauma center in mortality prediction models for transferred trauma patients.

STUDY DESIGN: We performed a retrospective cohort study using a state-wide trauma registry including all patients age 16 years or older, with Abbreviated Injury Scale scores ≥ 3, admitted to level I and II trauma centers in Pennsylvania, from 2011 to 2014. The primary outcomes measure was the risk-adjusted association between mortality and interhospital transfer (IHT) when adjusting for physiology (as measured by Revised Trauma Score [RTS]) using the referring hospital arrival vital signs (model 1) compared with trauma center arrival vital signs (model 2).

RESULTS: After adjusting for patient and injury factors, IHT was associated with reduced mortality (odds ratio [OR] 0.85; 95% CI 0.77 to 0.93) using the RTS from trauma center admission, but with increased mortality (OR 1.15; 95% CI 1.05 to 1.27) using RTS from the referring hospital. The greater the number of transfer patients seen by a center, the greater the difference in center-level mortality predicted by the 2 models (β -0.044; 95% CI -0.044 to -0.0043; $p \leq 0.001$).

CONCLUSIONS: Trauma center vital signs underestimate mortality in transfer patients and may lead to incorrect estimates of expected mortality. Where possible, benchmarking efforts should use referring hospital vital signs to risk-adjust IHT patients. (J Am Coll Surg 2017;224:255–263.

The validity of efforts to benchmark trauma center mortality is dependent on the validity of the underlying risk-adjustment models, which, in turn, are a function of the variables used to construct them. Mortality prediction models such as the Trauma Injury Severity Score[1] and A Severity Characterization of Trauma,[2] include factors to control for presenting physiology, patient reserve (as measured by age), and injury severity. Unlike injury severity and age, which are fixed at the time of presentation to a trauma center, vital signs are dynamic and are

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Abbreviations and Acronyms

AIS = Abbreviated Injury Scale
AUC = area under the curve
CEM = coarsened exact matching
GCS = Glasgow Coma Scale
ICC = intraclass correlation
IHT = interhospital transfer
IQR = interquartile range
ISS = Injury Severity Score
OR = odds ratio
RTS = Revised Trauma Score

subject to modification by interventions before trauma center admission. Because vital signs themselves are a proxy of cellular shock (ie patients are not dying because they are hypotensive, but rather hypotensive because they are dying), correction of vital signs may be accomplished without resolving the underlying cause of derangement. Measurements of patient physiology may therefore be influenced by the time from injury at which they are taken as well as the interventions undertaken to correct them. All other factors held equal, patients who have been resuscitated may present with less deranged vital signs than those who have not, leading to lower predicted mortality using these "corrected" vitals relative to patients presenting with less resuscitation.

This phenomenon, known as "lead-time bias," has been previously demonstrated in transferred critical care patients,[3,4] but the degree to which it affects injured patients undergoing transfer from nontrauma centers to trauma centers is not well described. Although nontrauma centers may not have the capacity to definitively manage injured patients, they may resuscitate and stabilize patients in the hours before transfer. This may, in turn, result in arrival vital signs at the trauma center that belie the initial physiologic derangement of the patient. Measures of presenting physiology have long been known to be associated with mortality in injured patients,[1,5,6] but risk of mortality may be underpredicted in patients who have been resuscitated at a referring hospital before transfer.

The influence of lead-time bias on estimated center level mortality would be expected to be small at centers that receive few transfer patients and larger in centers that receive greater proportions of transfer patients. Pennsylvania is a largely rural state, with 95% to 99.3% of the land area meeting a census definition of rurality,[7] and is home to 30 level I and II trauma centers. The percentage of admissions derived from interhospital transfer at these centers ranges from 0% to 63%,[8] making this a promising environment to investigate the effects of lead-time bias. We hypothesized that in transfer patients, risk-adjustment using presenting vital signs from the referring hospital would result in higher predicted probability of mortality than would using vital signs from the receiving trauma center, and differences in center-level expected mortality would be a function of the number of transfers. As a secondary goal, we sought to characterize the impact of changing physiology over the course of transfer on mortality in transfer patients.

METHODS

We performed a retrospective cohort study using the Pennsylvania Trauma Outcomes Study registry of injured adult patients admitted to level I and II trauma centers in Pennsylvania from 2011 to 2014. Patients presenting to level III or IV centers in Pennsylvania were excluded because the number of centers was small (n = 4) and varied over the study period. To ensure the quality of data collection at the center level, specially trained registrars at each trauma center prospectively abstract detailed data from the medical chart of each patient meeting inclusion criteria into the Pennsylvania Trauma Outcomes Study registry. These data are collected according to standardized definitions[9] put forth by the Pennsylvania Trauma Systems Foundation (Mechanicsburg, PA), and a subset of charts is re-reviewed to ensure inter-rater reliability by registrars. Additionally, subsets of submitted data are reabstracted by the Pennsylvania Trauma Systems Foundation during site accreditation visits to verify accuracy. Because data quality is linked to accreditation, centers are strongly incentivized to accurately report data, and rates of missing data are low. Data for this work were provided by the Pennsylvania Trauma Systems Foundation, which specifically disclaims responsibility for any analyses, interpretations, or conclusions presented herein. This study was conducted after approval of our institutional IRB.

Patients with moderate or severe injuries (minimum Abbreviated Injury Scale [AIS] $\geq$ 3) and age 16 years or older, were considered for inclusion. Patients who were transferred between trauma centers or who had a primary mechanism of injury of burn were excluded. Because a prerequisite of transfer is survival to the point of transfer, to allow for fair comparison between transfer and nontransfer patients, deaths in the emergency department (in both transferred and nontransferred patients) were excluded from analyses. The primary outcomes measure was in-hospital mortality, and the primary exposure of interest was interhospital transfer (IHT) status. To build multivariable logistic regression models on mortality, we first examined patient factors including age, Injury Severity Score (ISS), mechanism of injury (blunt vs penetrating), sex, and presenting physiology known or suspected to be associated with mortality.