Comparison of a Trauma Comorbidity Index with Other Measures of Comorbidities to Estimate Risk of Trauma Mortality

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ACEM.14270

Running title: Development of a Trauma Comorbidity Index

Presented at the 78th Annual Meeting of American Association for the Surgery of Trauma, September 06-08, 2019 in Dallas, TX.

Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR002529 and the Indiana State Department of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Indiana State Department of Health.

Authorship contributions: study concept and design (PJ, SS, LT), acquisition of the data (PJ, LT), analysis and interpretation of the data (PJ, LT), drafting of the manuscript (PJ), critical revisions (BD, AC, MH, CN, CT), statistical expertise (LT, CT, CN), and acquisition of funding (PJ).

No conflict of interest

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Article type : Original Contribution

ABSTRACT

Background Comorbidities influence the outcomes of injured patients, yet a lack of consensus exists regarding how to quantify that association. This study details the development and internal validation of a trauma comorbidity index (TCI) designed for use with trauma registry data and compares its performance to other existing measures to estimate the association between comorbidities and mortality.

Methods Indiana state trauma registry data (2013-2015) was used to compare the TCI with the Charlson and Elixhauser comorbidity indices, a count of comorbidities, and comorbidities as separate variables. The TCI approach utilized a randomly selected training cohort and was internally validated in a distinct testing cohort. The C-statistic of the adjusted models was tested using each comorbidity measure in the testing cohort to assess model discrimination. C-statistics were compared using a Wald test, and stratified analyses were performed based on predicted risk of mortality. Multiple imputation was used to address missing data.

Results The study included 84,903 patients (50% each in training and testing cohorts). The Indiana TCI model demonstrated no significant difference between testing and training cohorts ($p = 0.33$). It produced a C-statistic of 0.924 in the testing cohort, which was significantly greater than that of models using the other indices ($p < 0.05$). The C-statistics of models using the Indiana TCI and the inclusion of comorbidities as separate variables – the method used by the American College of Surgeons Trauma Quality Improvement Program – were comparable ($p = 0.11$) but use of the TCI approach reduced the number of comorbidity-related variables in the mortality model from 19 to one.

Conclusions When examining trauma mortality, the TCI approach using Indiana state trauma registry data demonstrated superior model discrimination and/or parsimony compared to other measures of comorbidities.

INTRODUCTION

Comorbidities influence the detection, prognosis, treatment, and outcomes of disease.[1, 2] As the U.S. population continues to age and cases of geriatric trauma become more prevalent, the influence of comorbidities on the outcomes of the trauma population is likely to grow.[3] Studies of trauma patient outcomes have long advocated for specific clinical practices, such as the transfer of certain patients to highly specialized trauma centers based on the presence of comorbid conditions.[4, 5] Moreover, quality improvement efforts, such as those of the American College of Surgeons Trauma Quality Improvement Program (ACS TQIP), routinely include comorbidities in the risk-adjusted models used to report patient outcomes and evaluate hospital quality.[6]

Despite widespread recognition that comorbidities influence trauma care and outcomes, a lack of consensus exists regarding how best to measure that influence. Virtually all U.S. trauma centers and many non-trauma hospitals maintain detailed clinical registries, which are the predominant data source for trauma quality improvement initiatives.[6, 7] Yet neither of the two most prevalent composite indices of comorbidities, the Charlson and Elixhauser comorbidity indices, were designed to leverage trauma registry data; the former was developed using clinical registry data from patients with non-trauma diagnoses, while the latter employed administrative data. Current statistical models employed by ACS TQIP include each comorbidity as a separate variable, an approach that requires considerable statistical power and consumes valuable degrees of freedom when investigating low prevalence outcomes such as mortality.[6]

We postulate that a comorbidity index specifically developed for use with trauma registry data would improve the predictive modelling of trauma mortality, particularly for hospitals and patient cohorts whose case volumes cannot support the statistical demands of the ACS TQIP approach. To test that hypothesis, in this study, we describe an approach to develop and internally validate such an index, and we compare the model discrimination of that measure with other, existing comorbidities measures when evaluating the mortality of injured patients.

METHODS

Study design

We conducted a retrospective cohort study of trauma patients using data from the Indiana state trauma registry. Primary exposure variables included four different measures of comorbid disease burden, and the outcome of interest was in-hospital mortality. The study consisted of three stages: first, we developed and internally validated the trauma comorbidity index (TCI) in "training" and "testing" cohorts, respectively; second, we compared the predictive value of the TCI with other comorbidity measures using the testing cohort; and third, we compared model specification attributable to the TCI and two other comorbidity indices using the testing cohort, stratified by predicted risk of mortality.

Data Source and Study Population

The study cohort consisted of all patient data (ages ≥16 years) collected in the state trauma registry by the Indiana State Department of Health (ISDH) from 2013 through 2015. All diagnoses are encoded using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, because ICD-10-CM codes were not included in the Indiana trauma registry until 2016.[8] The registry includes all data fields of the National Trauma Data Standards set by the ACS Committee on Trauma, and it consists of data from all hospitals that submit data in compliance with state rule 410 IAC 34 of the ISDH Trauma Care Committee.[9, 10] The Indiana trauma registry is inclusive, since the rule applies to all hospitals, including both trauma centers and non-trauma hospitals. To populate the registry, hospital personnel collect detailed prehospital, emergency department, operative, intensive care, and hospital data for all patients with diagnoses encoded as injury and poisoning.[8] These data are provided in an encrypted fashion through collaboration with ISDH to ensure compliance with the Health Insurance Portability and Accountability Act.

We excluded patients who presented to emergency departments without signs of life, defined as an initial systolic blood pressure of 0 mmHg, heart rate of 0 beats/min, and Glasgow Coma Scale motor score of 1.[11]

We supplemented the data from the trauma registry with hospital-level data – number of hospital beds, teaching status, and profit status – obtained from the American Hospital Association (AHA) by linking the datasets using the name of each hospital identified in both

datasets.[12] For hospitals that lacked AHA data, ISDH conducted a hospital survey to directly acquire that information so that we had comprehensive hospital data from all hospitals included in the study.

Pre-existing Comorbid Conditions and Comorbidity Indices

The ISDH trauma registry provides a list of comorbid factors defined by ICD-9-CM/ ICD-10-CM codes consistent with the National Trauma Data Standards.[13] To conduct this study, we used four different measures of pre-existing comorbid conditions to model trauma outcomes: the Charlson comorbidity index,[14] the Elixhauser comorbidity index,[15] a count of comorbidities, all comorbidities included as separate variables (the method used by ACS TQIP),[6] and the TCI. We accounted for changes that occurred to the comorbidity data collected during the study period with the following two steps: 1) "pulmonary disease" was changed to "chronic obstructive pulmonary disease," so we classified both diseases as "chronic obstructive pulmonary disease;" and 2) the ACS COT omitted the variable "pre-hospital cardiac arrest" from the National Trauma Data Standard as a pre-existing comorbid condition in 2015, so we omitted that variable from the analyses."[16, 17]

Charlson Comorbidity Index (CCI)

First described in 1987, the CCI was developed in a training cohort of 559 patients admitted to the medical service of a single hospital and externally validated in a testing cohort of 685 patients admitted to the medical service in another hospital.[14] The CCI consists of 16 diagnoses that are weighted (1, 2, 3, and 6) based on association of the comorbidity with 1-year mortality. Greater weights, therefore, represent an increased association with mortality. In order to generate CCI scores using trauma registry data, we identified all available comorbidity diagnoses included in the CCI and weighted them accordingly. Five comorbidities included in the CCI were not present in the trauma registry, and those diagnoses are listed in the Supplement, eTable 2. The missing comorbidities were assigned with zero weights to compute CCI.

Elixhauser Comorbidity Index (ECI)

The ECI was first described in 1998, and it was developed using administrative data from 439 hospitals in California.[15] The ECI consists of 30 diagnoses associated with increased hospital

length of stay, charges, and in-patient mortality. In the scoring system, all diagnoses are weighted equally and tabulated to determine a single score.[18] We identified all available comorbidity diagnoses in the trauma registry that are included in the ECI. Fourteen variables included in the ECI were not included in trauma registry, and those diagnoses are listed in the Supplement, eTable 2. The missing comorbidities were assigned with zero weights to compute ECI.

Trauma Count of Comorbidities (TCC)

We calculated a TCC by testing the unadjusted association between each comorbidity included in the trauma registry and mortality through bivariate logistic regression. We then tabulated all comorbidities with a $p \leq 0.25$. We based this cutoff on previously published methods for the development of forward stepwise regression models.[19-21]

Comorbidities Included Separately

We identified comorbidities that met a minimum threshold association with mortality ($p \leq 0.25$) through bivariate analysis, and we included each variable separately in the mortality model, an approach consistent with the method used by ACS TQIP.[6]

Trauma Comorbidity Index (TCI)

The TCI approach used a 3-step process:

1. Identify comorbidities associated with mortality ($p \leq 0.25$) based on bivariate analysis
2. Obtain coefficients for each comorbidity through multivariable regression models
3. Sum the comorbidity coefficients to create coefficient weighted TCI for each patient

Details of the multivariable model are provided below in "Risk Adjustment." Positive coefficients derived in Step 2 denote that a comorbidity has an association with increased mortality, and negative values denote an association with decreased mortality.

Risk Adjustment

When modeling the association between comorbidities and trauma outcomes (in-hospital mortality and LOS), we included the following patient-level covariates: Injury Severity Score (ISS), Glasgow coma scale (GCS), age, gender, race, initial systolic blood pressure and pulse

rate in the emergency department, mechanism of injury, payer type, and transfer status. Additionally, we controlled for the following hospital-level covariates: American College of Surgeons trauma verification level, number of hospital beds, teaching status, and profit status. We directly selected the variables listed above to develop the risk-adjusted mortality models for this study, since they have been used previously by ACS TQIP as part of its established practice for risk-adjustment.[6]

Analysis

We began by inspecting the graphic distribution of continuous variables (patient age, systolic blood pressure, and heart rate) and found no skewness of the data. Additionally, we checked for statistically significant outlying observations and influential datapoints using the Pregibon's dbeta test and found no evidence of influential observations or datapoints that may significantly alter our conclusions.[22] To reduce bias and preserve statistical power to compare the comorbidity indices, we performed multiple imputation using chained equation algorithm (20 iterations) to address missing values.[23] We evaluated the results of imputation by examining trace plots of the imputed values (means and standard deviations) and found no evidence of violation of convergence.

In order to develop and internally validate the Trauma Comorbidity Index (TCI), we randomly divided the entire 2013-2015 cohort into training (50%) and testing cohorts (50%), We performed descriptive statistics to characterize the study cohort using Chi-square and t-test to calculate p-values for categorical and continuous variables, respectively. We elected to use this split-sample approach to validation, because the size of our training and testing cohorts was large enough (> 42,000 patients in each cohort) so the model would not suffer from unmeasured biases.[24]

In the first stage of analysis, we established a baseline estimate of the mortality model by performing multivariable logistic regression – omitting any comorbidity measure – using both training and testing cohorts. We clustered at the hospital level to account for any hospital-level association with mortality and to derive robust standard errors, and we calculated the C-statistic for the mortality model in each cohort. We tested for difference between the C-statistics of the two cohorts using the Wald test.[25] Then, we examined how the inclusion of the comorbidity measures impacted the predictive value of the mortality model. We calculated the TCI using the method detailed above using the training cohort, included it in the adjusted model, and calculated

the C-statistic. We evaluated the internal validity of the TCI by calculating it in the testing cohort, taking care to apply the coefficients derived from the training cohort, and we tested for difference between the C-statistics of the two cohorts using the Wald test. Next, we repeated these steps, substituting the TCI for each of the other measures of comorbidities. In the second stage of analysis, we used the Wald test to compare the C-statistics of the respective mortality models with each comorbidity measure in the testing cohort.

In the third stage of analysis, we compared the model specification attributable to the CCI, ECI, and TCI in two different ways, given the prevalence of the two former indices in existing literature. First, using the testing cohort, we calculated the number of deaths accurately predicted by each mortality model by 1) calculating the sensitivity of the mortality models for each dataset (the original and imputed ones) using a posterior predictive command that defines "sensitivity" as true positives (accurately predicted deaths) divided by all positives; 2) deriving the mean sensitivity of the datasets; and 3) multiplying that mean value by the total number of deaths in the unimputed testing cohort. Second, we examined how closely each comorbidity index score corresponded to observed and expected mortality. We did so by 1) calculating the predicted (i.e., expected) mortality for each patient using the three mortality models; 2) dividing patients into deciles of predicted risk; 3) calculating the percentage of actual (i.e., observed) deaths per decile; and 4) calculating the mean comorbidity index score within each decile.

The study was approved by the Indiana University Institutional Review Board, and all analyses were performed using Stata 15 software (StataCorp LLC, College Station, TX).

RESULTS

The cohort consisted of 84,903 patients admitted to 109 hospitals over the study period. The hospitals included three Level 1 trauma centers, six Level 2 trauma centers, ten Level 3 trauma centers, and ninety non-trauma centers. All trauma centers had ACS verification for their respective levels. Patients were predominantly elderly, white, and male, and the most commonly identified mechanism of injury was falls. Patient data – demographics and injury characteristics – are summarized in Table 1. Approximately 65% of the patient cohort had at least one comorbidity, including conditions such as "drug abuse disorder" and "current smoker," and the maximum number of comorbidities was 9 (median = 1, interquartile range [IQR] = 0-2). Table 2 summarizes patient comorbidities. The incidence of in-hospital mortality was 2.8%.

When divided into training and testing cohorts, demographic, injury, and comorbidity characteristics were evenly distributed between the two groups ($p > 0.05$).[26] The distribution of demographic and injury characteristics between the cohorts is summarized in Table 1, and Table 2 summarizes the distribution of comorbid conditions used to develop the TCI. Of note, mortality was also evenly distributed between the training and testing cohorts (2.9% and 2.8% respectively, $p = 0.82$).

In the training cohort, we identified 19 comorbidities that met the minimum threshold association with mortality using bivariate analysis ($p \leq 0.25$), and the coefficients derived from the multivariable models ranged from -1.0 (drug use disorder) to 1.2 (presence of an advanced directive limiting care). The TCI ranged from -1.8 to 5.1, with negative values representing a decreased association with risk-adjusted mortality, relative to a TCI of zero. The p-values and coefficients for each comorbidity used to develop the TCI, along with the corresponding coefficient in the CCI and ECI are summarized in Table 3. Comorbidities included in the trauma registry but not incorporated in the TCI are listed in Supplement, eTable 2.

Regarding internal validation of the TCI, we found no significant difference ($p = 0.33$) between the C-statistics of the training (0.918) and testing (0.924) cohorts when we included the TCI in the mortality model. Similarly, we found no significant difference between cohorts when using no measure of comorbidities and the alternative comorbidity measures (Table 4).

In the testing cohort, all methods of comorbidity measurement significantly increased the C-statistic above a mortality model that lack any comorbidity measure (0.915). Inclusion of the CCI and ECI produced C-statistics of 0.921 and 0.920, respectively, which were statistically comparable to each other ($p = 0.27$). The C-statistic of the TCI model was significantly greater than models with the CCI and ECI ($p < 0.05$). Models that included the TCI and all nineteen comorbidities included separately (CIS) yielded the greatest C-statistics, 0.924 and 0.925 respectively. Those C-statistics were comparable ($p = 0.11$), but the CIS model included eighteen more variables than the TCI model. A summary of the C-statistics for mortality models with each of the comorbidity measures is summarized in Table 5.

When comparing the model specification attributable to the comorbidity indices – CCI, ECI, and TCI – in the testing cohort, sensitivity was greatest for the model with the TCI (91.1%); whereas the models with the CCI and ECI had sensitivities of 90.9% and 90.8%, respectively; and the model that lacked any measure of comorbidity had a sensitivity of 90.3%. Accordingly,

out of 1,201 deaths in the testing cohort, the TCI model accurately predicted 1,094; the CCI and ECI models predicted 1,091 and 1,090 deaths, respectively; and the model without a comorbidity measure predicted 1,084 deaths. When risk-stratified, each mortality model demonstrated that observed mortality progressively increased across decile of expected mortality (Figure 1). However, only the TCI score peaked in the tenth decile (that with the greatest mortality), whereas the CCI and ECI scores peaked in the ninth decide and decreased in the tenth decile.

DISCUSSION

In this study of Indiana state adult trauma patients, we found that comorbidities, as defined by the ACS National Trauma Data Standard, were exceedingly prevalent (65%), and the measurement of comorbidities using any method significantly improved the statistical modelling of in-hospital mortality. Inclusion of the TCI increased calibration of the mortality model in a manner similar to the CCI and ECI, providing concurrent validity to the TCI approach. Although the previously developed indices accounted for mortality-risk associated with comorbidities, the TCI improved the model discrimination of that relationship, albeit slightly. That improvement was evidenced by the increased number of deaths accurately predicted by the TCI model in comparison to models with the other indices. Moreover, although the benefit of using the TCI approach over other comorbidity indices was slight, it is notable that only the TCI score corresponded directly with mortality among patients with the greatest risk, whereas the mean scores of other comorbidity indices actually decreased from the ninth to the tenth decile of expected mortality (Figure 1). This finding indicates that the TCI is calibrated so its score reflects risk of mortality more closely than those of CCI and ECI. Therefore, we submit that at the very least, investigators should consider the TCI approach to be a viable alternative to develop a trauma-specific comorbidity index, rather than use more general comorbidity indices when performing risk-adjustment to examine trauma mortality.

The TCI and CIS (the method currently employed by ACS TQIP) estimated the mortality-risk associated with comorbidities comparably, but the TCI afforded substantially more parsimony, reducing the required number of comorbidity-related variables from 19 to one. These findings have notable implications for risk-adjustment when examining both rare outcomes and small patient cohorts, instances when degrees of freedom must be used sparingly to preserve statistical power. Whereas in this study, we divided the overall study cohort into training and

testing cohorts, future studies need not perform this separate step of internal validation if the Indiana weights for TCI externally validate in a national dataset. Therefore, future studies that incorporate the TCI approach could retain all of the statistical power imparted by the full size of their study cohort.

Unlike previously described comorbidity indices, the TCI uses comorbidity selection specific to trauma registry datasets. As a result, the TCI potentially identifies pre-existing conditions that one may not consider to be comorbidities in a conventional sense, such as the presence of an advanced directive limiting care. However, we submit that such diagnoses are both clinically relevant and designated as comorbidities by the ACS National Trauma Data Standard. Conversely, the TCI does not include certain well-recognized comorbidities, such as human immunodeficiency virus (HIV), if they are not included in the data or do not meet a minimum threshold association with mortality. Specifically, regarding missing comorbidities, the Charlson and Elixhauser comorbidity indices are widely used for risk-adjustment in trauma outcomes research, however, those indices include diagnoses such as HIV that are not included in the ACS National Trauma Data Standard. This discrepancy between the scoring systems and trauma registry data inherently limits the performance of the scoring systems themselves as they were originally derived and validated.

The flexibility of comorbidity selection of the TCI approach is particularly advantageous for the study of clinical registry data, which is subject to change over time or vary depending on whether or not an institution adheres to the ACS National Trauma Data Standard. Moreover, the TCI approach accounts for potential lapses in data quality, since it would exclude variables with fields that are consistently omitted, as they would be unlikely to meet the minimum statistical threshold of association with an outcome. As with other indices, the TCI approach achieves parsimony by estimating the cumulative effect of multiple factors – comorbidities, in this case – as a single value. The combination of these attributes (model flexibility and parsimony) make the TCI approach uniquely well-suited for the study of trauma subpopulations such as patients with specific mechanisms of injury or hospitals that treat small numbers of injured patients, such as non-trauma hospitals.

Although the TCI has certain advantages over other comorbidity indices, it also has limitations. Like other comorbidity indices, the TCI has no role in prospectively determining the expected outcomes of a given patient. Rather, the TCI was designed to enhance risk-adjusted

models used to examine trauma mortality retrospectively using clinical registry data. If the Indiana-derived weights for TCI externally validate on a national dataset, then the Indiana TCI can be used for future trauma registry risk-adjusted modeling.

If the Indiana TCI does not externally validate, we provide detailed methods of how to conduct the TCI approach to either derive and validate more generalizable TCI weights using a national dataset or use the TCI approach for project-specific derivation and internal validation. Compared with other fixed-weight comorbidity indices, the TCI approach requires additional steps for its calculation, specifically, the identification of statistically relevant comorbidities and the estimated association between those comorbidities and mortality. As a result, the TCI approach does not assign fixed coefficients to comorbidities. Instead, the coefficients can be derived from the particular dataset. Further, the TCI does not test for interaction effects or collinearity between comorbidities and assumes a cumulative relationship between comorbidities and mortality. Alternative methods, such as random forest regression, may address those shortcoming but would also add complexity to the calculation of a comorbidity index.[27] Despite the limitations of the TCI, it is notable for its improved predictive modelling compared with previously described comorbidity indices.

The results of this study should be interpreted in the context of its limitations. First, the trauma population in Indiana may not be representative of the national trauma population. As stated above, we do not propose to apply the coefficients for comorbidities reported in this study to other populations without external validation. Instead, the purpose of this study is to detail the approach for deriving the TCI. Further study, using national data, is necessary to externally validate the Indiana-derived TCI weights, or derive nationally representative TCI coefficients for comorbidities that can be applied more broadly. Second, the analyses are limited to in-hospital mortality, a short-term outcome. In the process of deriving the TCI, we found that certain comorbidities – current smoker, dementia, drug abuse disorder, and major psychiatric illness – were actually associated with decreased mortality. Since this study is retrospective, the results do not connote mechanisms for these relationships, and we do not intend to suggest that smoking, for example, is protective overall, but simply associated with lower in-hospital mortality after traumatic injury. The cumulative, long-term sequelae of smoking (e.g., peripheral vascular disease, respiratory disease, and myocardial infarction) are clearly associated with an increased risk of mortality.[28, 29] Regarding the association between psychiatric illnesses and decreased

mortality, our findings are consistent with other previously published work, but the influence of psychiatric illnesses on long-term mortality following trauma is still unclear.[30]

In conclusion, this study provides a critical analysis of several methods previously used to measure the association of comorbidities and trauma outcomes, and it identifies limitations of those methods when applied to trauma registry data. In response to those shortcomings, this study details the development of the TCI approach, a method of measurement specifically designed for use with clinical registry data. When compared with other methods of measuring the clinical impact of comorbidities, the TCI approach demonstrated superior model discrimination and/or parsimony for estimating the risk of trauma mortality using Indiana state trauma registry data.

ACKNOWLEDGEMENTS

The Indiana State Department of Health, Division of Trauma and Injury Prevention generously provided access to data in support of this study.

REFERENCES

1. de Groot V, Beckerman H, Lankhorst GJ, Bouter LM. How to measure comorbidity. a critical review of available methods. J Clin Epidemiol. 2003 Mar;56(3):221-9. PubMed PMID: 12725876. Epub 2003/05/03.

2. Feinstein AR. The Pre-Therapeutic Classification of Co-Morbidity in Chronic Disease. J Chronic Dis. 1970 Dec;23(7):455-68. PubMed PMID: 26309916. Epub 1970/12/01.

3. Hospital resources for optimal care of the injured patient. Prepared by a Task force of the Committee on Trauma of the American College of Surgeons. Bull Am Coll Surg. 1979 Aug;64(8):43-8. PubMed PMID: 10243405. Epub 1979/07/11.

4. Morris JA, Jr., MacKenzie EJ, Edelstein SL. The effect of preexisting conditions on mortality in trauma patients. JAMA. 1990 Apr 11;263(14):1942-6. PubMed PMID: 2313871. Epub 1990/04/11.

5. Ohmori T, Kitamura T, Ishihara J, Onishi H, Nojima T, Yamamoto K, Tamura R, Muranishi K, Matsumoto T, Tokioka T. Early predictors for massive transfusion in older adult severe trauma patients. Injury. 2017 May;48(5):1006-12. PubMed PMID: 28063676. Epub 2017/01/09.

6. Newgard CD, Fildes JJ, Wu L, Hemmila MR, Burd RS, Neal M, Mann NC, Shafi S, Clark DE, Goble S, et al. Methodology and analytic rationale for the American College of Surgeons Trauma Quality Improvement Program. J Am Coll Surg. 2013 Jan;216(1):147-57. PubMed PMID: 23062519. Epub 2012/10/16.

7. MacKenzie EJ, Hoyt DB, Sacra JC, Jurkovich GJ, Carlini AR, Teitelbaum SD, Teter H, Jr. National inventory of hospital trauma centers. JAMA. 2003 Mar 26;289(12):1515-22. PubMed PMID: 12672768. Epub 2003/04/04.

8. Statistics NCfH. International Classification of Diseases,Ninth Revision, Clinical Modification (ICD-9-CM) [cited 2018]. Available from: https://www.cdc.gov/nchs/icd/icd9cm.htm.

9. Health ISDo. ARTICLE 34. STATE TRAUMA REGISTRY 2013. Available from: http://www.in.gov/legislative/iac/20131120-IR-410120617FRA.xml.pdf.

10. Indiana Patient Registry [Internet]. Available from: https://www.in.gov/isdh/25407.htm (Accessed November 1, 2019).

11. Calland JF, Nathens AB, Young JS, Neal ML, Goble S, Abelson J, Fildes JJ, Hemmila MR. The effect of dead-on-arrival and emergency department death classification on risk-adjusted performance in the American College of Surgeons Trauma Quality Improvement Program. J Trauma Acute Care Surg. 2012 Nov;73(5):1086-91; discussion 91-2. PubMed PMID: 23117375. Epub 2012/11/03.

12. Association AH. AHA Annual Survey of Hospitals. 2013-2016.

13. Health ISDo. State of Indiana Trauma Registry Data Dictionary 2015 [January 19, 2019]. Available from: https://www.in.gov/isdh/files/NEW_VERSION_2015_Indiana_Data_Dictionary.pdf

14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83. PubMed PMID: 3558716. Epub 1987/01/01.

15. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care. 1998 Jan;36(1):8-27. PubMed PMID: 9431328. Epub 1998/02/07.

16. Trauma ACoSCo. National Trauma Data Standards Data Dictionary - 2014. https://wwwdshstexasgov/injury/registry/Data-Dictionaries/2014NTDSDataDictionarypdf, Accessed March 2021.
17. Trauma ACoSCo. National Trauma Data Standards Data Dictionary - 2015. https://wwwfacsorg/-/media/files/quality-programs/trauma/ntdb/ntds/data-dictionaries/ntds-data-dictionary-2015ashx Accessed March 2021.
18. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care. 2009 Jun;47(6):626-33. PubMed PMID: 19433995. Epub 2009/05/13.
19. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. Am J Epidemiol. 1989 Jan;129(1):125-37. PubMed PMID: 2910056. Epub 1989/01/01.
20. Zhang Z. Model building strategy for logistic regression: purposeful selection. Ann Transl Med. 2016 Mar;4(6):111. PubMed PMID: 27127764. Pubmed Central PMCID: PMC4828741. Epub 2016/04/30.
21. Afifi RBBaAA. Comparison of Stopping Rules in Forward "Stepwise" Regression. Journal of the American Statistical Association. 1977;72(357):46-53.
22. Pregibon D. Logistic Regression Diagnostics. The Annals of Statistics. 1981;9(4):705–24.
23. Stef van Buuren KG-O. MICE: Multivariate Imputation by Chained Equations in R. Journal of Statistical Software. 2011;45(3):1-67.
24. Xu Y, Goodacre R. On Splitting Training and Validation Set: A Comparative Study of Cross-Validation, Bootstrap and Systematic Sampling for Estimating the Generalization Performance of Supervised Learning. J Anal Test. 2018;2(3):249-62. PubMed PMID: 30842888. Pubmed Central PMCID: PMC6373628. Epub 2018/01/01.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988 Sep;44(3):837-45. PubMed PMID: 3203132. Epub 1988/09/01.
26. Buis ML. Discrete uses for uniform(). The Stata Journal. 2007;7(3):434–5.

27. Bertsimas D, Dunn J, Velmahos GC, Kaafarani HMA. Surgical Risk Is Not Linear: Derivation and Validation of a Novel, User-friendly, and Machine-learning-based Predictive OpTimal Trees in Emergency Surgery Risk (POTTER) Calculator. Ann Surg. 2018 Oct;268(4):574-83. PubMed PMID: 30124479. Epub 2018/08/21.

28. Trap-Jensen J. Effects of smoking on the heart and peripheral circulation. Am Heart J. 1988 Jan;115(1 Pt 2):263-7. PubMed PMID: 3276115. Epub 1988/01/01.

29. Yanbaeva DG, Dentener MA, Creutzberg EC, Wesseling G, Wouters EF. Systemic effects of smoking. Chest. 2007 May;131(5):1557-66. PubMed PMID: 17494805. Epub 2007/05/15.

30. Townsend LL, Esquivel MM, Uribe-Leitz T, Weiser TG, Maggio PM, Spain DA, Tennakoon L, Staudenmayer K. The prevalence of psychiatric diagnoses and associated mortality in hospitalized US trauma patients. J Surg Res. 2017 Jun 1;213:171-6. PubMed PMID: 28601311. Epub 2017/06/12.

Table 1. Patient characteristics

	All patients (N=84,903)	Training Cohort (n=42,451)	Testing Cohort (n=42,452)	p-value*
Age, years (%)				0.37
16-24	10.77	10.69	10.85	
25-34	10.30	10.30	10.30	
35-44	9.17	9.07	9.26	
45-54	11.34	11.41	11.27	
55-64	13.19	13.15	13.23	
65-74	13.03	13.14	12.92	
>=75	32.18	32.21	32.16	
Race (%)				0.20
White	84.88	84.77	84.98	
Black	8.98	8.92	9.03	
Other	1.97	1.98	1.96	
NA/not known	3.55	3.66	3.45	
Female (%)	47.05	46.97	47.12	0.06
Payer type (%)				0.22
Private/commercial	25.29	25.53	25.06	
Medicaid	6.70	6.55	6.86	
Medicare	39.61	39.70	39.51	
Other	20.13	19.98	20.28	
NA/not known	8.17	8.16	8.18	
Mechanism (%)				0.40
Adverse reaction/overdose/poisoning	0.54	0.55	0.53	
Assault	6.30	6.29	6.30	
Burn/electrocution	1.90	1.88	1.92	
Cut/pierce	1.56	1.53	1.59	
Fall	53.74	53.71	53.77	

Firearm	1.11	1.08	1.14	
Hanging/asphyxiation/drowning	0.14	0.13	0.15	
Machinery	0.96	0.95	0.96	
Motor vehicle accident	22.11	22.01	22.20	
Natural	0.04	0.05	0.02	
Other/not known	2.68	2.65	2.70	
Overexertion	0.26	0.29	0.24	
Pedestrian/pedestrian cyclist/ pedestrian struck	2.83	2.92	2.74	
Struck by/against	2.70	2.81	2.60	
Transport	0.68	0.69	0.68	
Injury Severity Score, mean (SD)	8 (7)	8 (7)	8 (7)	0.33
Initial Systolic Blood Pressure, mean (SD)	142 (27)	142 (27)	142 (27)	0.17
Initial Heart Rate, mean (SD)	86 (19)	86 (19)	86 (19)	0.70
Glasgow coma scale, mean (SD)	14 (3)	14 (3)	14 (3)	0.44
Inter-hospital transfer (%)	18.99	19.05	19.94	0.19
American College of Surgeons trauma verification level (%)				0.93
I	16.60	16.61	16.60	
II	30.32	30.27	30.36	
III	7.24	7.19	7.28	
Non-trauma center	45.84	45.93	45.76	
Hospital beds				0.28
<200	56.35	56.02	56.64	
201-400	25.77	25.87	25.66	
401-600	6.41	6.49	6.33	
>600	11.49	11.62	11.36	
Teaching	69.42	69.60	69.25	0.28
Non-profit	91.92	91.95	91.88	0.64

*Chi-square used to calculate p-values for categorical variables, and t-test used to calculate p-values for continuous variables

Table 2. Prevalence of comorbidities used to develop trauma comorbidity index and comparison between training and testing cohorts (%)

	All patients (N=84,903)	Training Cohort (n=42,451)	Testing Cohort (n=42,452)	p-value*
Advanced directive	1.23	1.16	1.30	0.06
Bleeding disorder	6.96	7.03	6.89	0.42
Chemotherapy	0.36	0.35	0.36	0.86
Chronic obstructive pulmonary disease	8.08	8.01	8.15	0.48
Chronic renal failure	2.08	2.00	2.15	0.14
Cirrhosis	0.62	0.62	0.62	1.00
Congestive heart failure	5.70	5.66	5.74	0.65
Current smoker	20.21	19.97	20.46	0.08
Dementia	5.75	5.86	5.63	0.17
Diabetes Mellitus	15.84	15.89	15.79	0.69
Disseminated cancer	0.89	0.86	0.93	0.29
Drug use disorder	2.55	2.60	2.49	0.31
Functionally dependent	3.74	3.72	3.75	0.82
History of myocardial infarction	14.01	13.86	14.15	0.21
History of myocardial infarct within last six months	0.85	0.90	0.81	0.18
History of peripheral vascular disease	0.63	0.62	0.63	0.83
Hypertension	24.80	24.96	24.63	0.28
Major psychiatric illness	4.69	4.60	4.78	0.21
Steroid use	0.61	0.62	0.60	0.79

*Chi-square used to calculate p-value

Table 3. p-values from bivariate regression and risk-adjusted coefficients used to develop the trauma comorbidity index (TCI) with mortality as the outcome and coefficients for the Charlson and Elixhauser comorbidity indices (CCI, and ECI) for corresponding comorbidities

	p-value	Coefficient		
		TCI	CCI	ECI
Advanced directive	<0.001	1.24	--	--
Bleeding disorder	<0.001	0.86	--	1
Chemotherapy	0.02	1.02	--	--
Chronic obstructive pulmonary disease	<0.001	0.45	1	1
Chronic renal failure	0.07	0.44	2	1
Cirrhosis	0.05	0.91	3	1
Congestive heart disease	<0.001	0.87	1	1
Current smoker	<0.001	-0.41	--	--
Dementia	0.003	-0.01	1	--
Diabetes Mellitus	0.05	0.22	1	1
Disseminated cancer	0.003	0.75	6	1
Drug use disorder	0.17	-1.04	--	1
Functionally dependent	<0.001	0.32	--	--
History of myocardial infarction	0.05	0.15	1	--
History of myocardial infarct within last six months	0.20	0.53	1	--
History of peripheral vascular disease	0.20	0.75	1	1
Hypertension	0.11	0.09	--	1
Major psychiatric illness	0.22	-0.31	--	--
Steroid use	0.002	0.78	--	--

"--" not included in index

* Coefficients with positive values denote an association with increased mortality and negative values indicate an association with decreased mortality.

Table 4. Comparison of mortality models with different comorbidity measures between training and testing cohorts

Method of measurement	Training cohort, c-statistic	Testing cohort, c-statistic	p-value
NCI	0.909	0.915	0.32
CCI	0.913	0.921	0.16
ECI	0.914	0.920	0.29
TCC	0.914	0.920	0.25
CIS	0.918	0.925	0.23
TCI	0.918	0.924	0.33

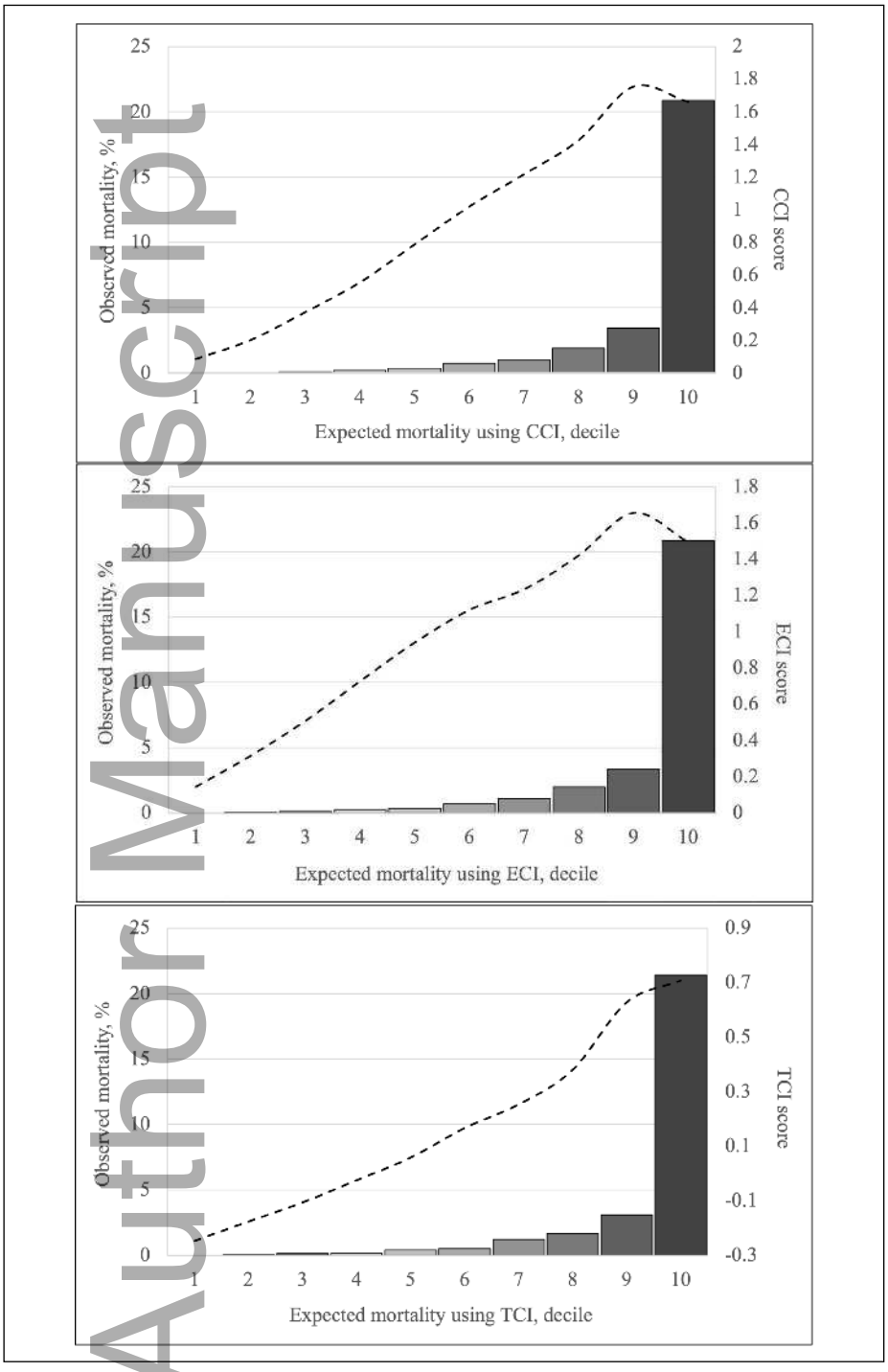
*NCI = no comorbidities included; CCI = Charleson comorbidity index; ECI = Elixhauser comorbidity index; TCC = cumulative count of trauma comorbidities; CIS = comorbidities included separately; TCI = trauma comorbidity index

Table 5. Comparison of c-statistic of mortality models with different comorbidity measures in the testing cohort, p-value

Method of measurement (c-statistic)	NCI (0.915)	CCI (0.921)	ECI (0.920)	TCC (0.921)	CIS (0.925)	TCI (0.924)
NCI (0.915)	--					
CCI (0.921)	<0.001	--				
ECI (0.920)	<0.001	0.27	--			
TCC (0.921)	<0.001	0.42	0.72	--		
CIS (0.925)	<0.001	0.005	0.001	0.001	--	
TCI (0.924)	<0.001	0.03	0.003	0.003	0.11	--

*NCI = no comorbidities included; CCI = Charleson comorbidity index; ECI = Elixhauser comorbidity index; TCC = cumulative count of trauma comorbidities; CIS = comorbidities included separately; TCI = trauma comorbidity index

Comparison of observed and expected mortality using different comorbidity indices with corresponding comorbidity index scores



* CCI = Charlson comorbidity index; ECI = Elixhauser comorbidity index; TCI = trauma comorbidity index

** Expected mortality is stratified by decile of risk-adjusted, predicted mortality

"----" = Comorbidity index score, mean calculated per decile of expected mortality