

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Use of machine learning to develop a prehospital-stage prediction tool for traumatic brain injury

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055918
Article Type:	Original research
Date Submitted by the Author:	02-Aug-2021
Complete List of Authors:	Choi, Yeong Ho; Seoul National University Hospital, Emergency Department Park, Jeong Ho; Seoul National University Hospital, Emergency Department Hong, Ki Jeong; Seoul National University College of Medicine, Emergency Medicine; Seoul National University Seoul Metropolitan Government Boramae Medical Center, Emergency Medicine Ro, Young Sun; Seoul National University Hospital, Emergency Department Song, Kyoung Jun; Seoul Metropolitan Boramae Hospital, Department of Emergency Medicine Shin, Sang Do; Seoul National University Hospital, Department of Emergency Medicine
Keywords:	ACCIDENT & EMERGENCY MEDICINE, Neurological injury < NEUROLOGY, Trauma management < ORTHOPAEDIC & TRAUMA SURGERY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 1 **Title page**
5
6
7 2
8
9 3 **1. Title**
10
11 4 Use of machine learning to develop a prehospital stage prediction tool for traumatic brain
12
13 5 injury
14
15
16 6
17
18 7 **2. Authors**
19
20 8 Yeong Ho Choi, MD
21
22 9 Department of Emergency Medicine, Seoul National University College of Medicine and
23
24 10 Hospital, Seoul, Republic of Korea
25
26 11 Laboratory of Emergency Medical Services, Seoul National University Hospital
27
28 12 Biomedical Research Institute, Seoul, Korea
29
30 13 E-mail: d2uk87@gmail.com
31
32
33
34 14
35
36 15 Jeong Ho Park, MD
37
38 16 Department of Emergency Medicine, Seoul National University College of Medicine and
39
40 17 Hospital, Seoul, Republic of Korea
41
42 18 Laboratory of Emergency Medical Services, Seoul National University Hospital
43
44 19 Biomedical Research Institute, Seoul, Korea
45
46 20 E-mail: timthe@gmail.com
47
48
49
50 21
51
52 22 Ki Jeong Hong, MD, PhD
53
54 23 Department of Emergency Medicine, Seoul National University College of Medicine and
55
56 24 Hospital, Seoul, Republic of Korea
57
58 25 Laboratory of Emergency Medical Services, Seoul National University Hospital
59
60

1
2
3
4 26 Biomedical Research Institute, Seoul, Korea

5
6 27 E-mail: emkjhong@gmail.com

7
8
9 28

10
11 29 Young Sun Ro, MD, DrPH

12
13 30 Department of Emergency Medicine, Seoul National University College of Medicine and

14
15 31 Hospital, Seoul, Republic of Korea

16
17 32 Laboratory of Emergency Medical Services, Seoul National University Hospital

18
19 33 Biomedical Research Institute, Seoul, Korea

20
21 34 E-mail: ro.youngsun@gmail.com

22
23 35

24
25 36 Kyoung Jun Song, MD, PhD

26
27 37 Department of Emergency Medicine, Seoul Metropolitan Government Seoul National

28
29 38 University Boramae Medical Center, Seoul, Republic of Korea

30
31 39 Laboratory of Emergency Medical Services, Seoul National University Hospital

32
33 40 Biomedical Research Institute, Seoul, Korea

34
35 41 E-mail: skciva@gmail.com

36
37 42

38
39 43 Sang Do Shin, MD, PhD

40
41 44 Department of Emergency Medicine, Seoul National University College of Medicine and

42
43 45 Hospital, Seoul, Republic of Korea

44
45 46 Laboratory of Emergency Medical Services, Seoul National University Hospital

46
47 47 Biomedical Research Institute, Seoul, Korea

48
49 48 E-mail: shinsangdo@gmail.com

50
51 49

52
53 50 **3. Address correspondence and requests for reprints: Jeong Ho Park, MD**

1
2
3
4 51 Address: Seoul National University Hospital, 101 Daehak-Ro, Jongno-Gu, Seoul 03080,

5
6 52 Korea

7
8
9 53 Phone: +82-2-2072-1800

10
11 54 FAX: +82-2-741-7855

12
13 55 E-mail: timthe@gmail.com

14
15 56

16
17 57

18
19 58

20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3
4 59 **Abstract**

6 60 **Objectives:** Predicting diagnosis and prognosis of traumatic brain injury (TBI) at the
7
8
9 61 prehospital stage is challenging; however, using comprehensive prehospital information and
10
11 62 machine learning may improve the performance of the predictive model. We developed and
12
13 63 tested predictive models for TBI that use machine learning algorithms using information that
14
15
16 64 can be obtained in the prehospital stage.

17
18 65 **Design:** This was a multi-center retrospective study.

19
20 66 **Setting and participants:** This study was conducted at three tertiary academic emergency
21
22 67 departments (EDs) located in an urban area of South Korea. The data from adult patients with
23
24 68 severe trauma who were assessed by emergency medical service (EMS) providers and
25
26 69 transported to three participating hospitals between 2014 to 2018 were analyzed.

27
28 70 **Results:** We developed and tested five machine learning algorithms—logistic regression
29
30 71 analyses, extreme gradient boosting, support vector machine, random forest, and elastic net
31
32 72 (EN)—to predict TBI, TBI with intracranial hemorrhage or injury (TBI-I), TBI with
33
34 73 emergency department or admission result of admission or transferred (TBI-ND), and TBI
35
36 74 with emergency department or admission result of death (TBI-D). Of the 1,169 patients in the
37
38 75 development cohort, TBI, TBI-I, TBI-ND, and TBI-D was 24.0%, 21.5%, 21.3%, and 3.7%,
39
40 76 respectively. The EN model yielded an AUROC of 0.799 for TBI, 0.844 for TBI-I, 0.811 for
41
42 77 TBI-ND, and 0.871 for TBI-D. The EN model also yielded the highest specificity, and
43
44 78 significant reclassification improvement. Variables related to loss of consciousness, Glasgow
45
46 79 Coma Scale, and light reflex were the three most important variables to predict all outcomes.

47
48 80 **Conclusion:** Our results inform the diagnosis and prognosis of TBI. Machine learning
49
50 81 models resulted in significant performance improvement over that with logistic regression
51
52 82 analyses, and the best performing model was EN.

53
54
55
56
57
58
59
60 83

1
2
3
4 84 **Keywords:** brain injuries; traumatic; outcome; prognosis; machine learning.
5
6
7
8 85
9
10 86
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3
4 87 **Strengths and limitations of this study**
5

- 6 88 ● By using high dimensional prehospital data, we developed and validated prediction
7 89 models for the diagnosis and prognosis of traumatic brain injury using machine
8 90 learning algorithms among patients with severe trauma, identified by emergency
9 91 medical service providers.
- 12 92 ● Machine learning models showed acceptable-to-excellent discrimination performance
13 93 (AUROCs were 0.799–0.871 according to outcomes in the best-performing model).
14 94 When identifying 80% of target patients with traumatic brain injury, the false positive
15 95 rate was almost 19.7–39.0%.
- 17 96 ● We used retrospective analysis of electronically collected prehospital data. We treated
18 97 missing status as a separate category for our analysis, however, there could be different
19 98 reasons for missing data.
- 22 99 ● External validation for other areas should be conducted to generalize the developed
23 100 prediction model.
24
25 101

102 **Introduction**

103 Traumatic brain injury (TBI) is a significant health burden worldwide.^{1 2} It is the leading
104 cause of mortality and disability among young individuals.³ Patients with TBI are vulnerable
105 to hypoxia and hypotension in the early period of their course and these insults are associated
106 with poor outcomes.⁴⁻⁶ Prehospital assessment and management of patients with TBI is
107 important,^{7 8} as early prediction of TBI and correcting hypoxia and hypotension during the
108 prehospital stage could be beneficial.^{9 10} However, the identification of TBI can often be
109 challenging in the prehospital area.⁷ Vulnerable patients, including the elderly or patients who
110 take medications like anti-platelet or anticoagulant drugs, often have TBI owing to low
111 energy insults.¹¹ Prehospital clinical signs are also reported to have poor sensitivity for raised
112 intracranial pressure following TBI.¹²

113 Several prediction models to target patients with TBI have been reported.¹³⁻¹⁵
114 However, most incorporated information that is available only in the hospital, such as
115 laboratory results or image findings.^{13 14 16} In addition, most previous prediction models
116 focused on the outcomes of patients with TBI, not the identification of TBI. Previously,
117 predictors of older adult patients with TBI who required transport to a trauma center were
118 identified. However, this was consensus-based; therefore, there is a lack of clinical data.¹⁷
119 Accurate prehospital prediction of TBI and its severity could prevent delays to definite care
120 for patients with TBI. Most emergency medical service (EMS) providers collect various
121 information including demographics, past medical history, circumstances of the trauma, and
122 clinical signs including vital signs; but those variables have not been evaluated together as
123 predictors of TBI and its severity. Using a variety of prehospital information, and adapting
124 newly emerging machine learning algorithms for predicting diagnosis, disposition, and
125 outcome of TBI, might improve the accuracy of identification of TBI and its severity.¹⁸

1
2
3
4 126 The aim of this study was to develop and test prediction models for the diagnosis and
5
6 127 prognosis of TBI using prehospital information and machine learning algorithms among
7
8 128 patients with severe trauma. We hypothesized that incorporating prehospital information
9
10 129 could achieve acceptable performance in predicting TBI, and machine learning algorithms
11
12 130 could contribute to performance improvement.

17 131 **Materials and Methods**

20 132 *Study design and settings*

23 133 This was a multi-center retrospective study conducted at three tertiary academic emergency
24
25 134 departments (EDs) located in an urban area (Seoul and Bundang) of South Korea. These EDs
26
27 135 received 50,000–90,000 visits annually. We adhered to the Transparent Reporting of a
28
29 136 Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) statement
30
31 137 on reporting predictive models.¹⁹

34 138 The EMS system in South Korea is operated by the National Fire Agency. The EMS
35
36 139 level is considered intermediate, as EMS providers can perform bleeding control, spinal
37
38 140 motion restriction, immobilization and splintage, advanced airway management, and
39
40 141 administer fluid intravenously. As only physicians can declare death in South Korea, EMS
41
42 142 providers cannot stop resuscitation and must transport all patients including those in cardiac
43
44 143 arrest to the ED. For all EMS transport, EMS providers record an ambulance run-sheet by
45
46 144 law. Since 2012, the National Fire Agency adapted the United States Centers for Disease
47
48 145 Control and Prevention of the United States field triage decision scheme to evaluate patients
49
50 146 with trauma,²⁰ and they developed an EMS severe trauma in-depth registry. For said patients,
51
52 147 EMS providers evaluate whether patients met trauma center transport criteria in the field
53
54 148 triage decision scheme. If they did, the in-depth registry should be recorded, and EMS
55
56
57
58
59
60

1
2
3
4 149 transport protocol recommends that patients are transferred to a near regional trauma center;
5
6 150 but it is not mandatory.
7
8

9 151 The Ministry of Health and Welfare designated three ED levels according to the
10
11 152 resources and functional requirements; level 1 (n = 36) and level 2 (n = 118) EDs have more
12
13 153 resources and better facilities for emergency care and must be staffed by emergency
14
15 154 physicians 24 hours a day/365 days a year; whereas level 3 EDs (n = 248) can be staffed by
16
17 155 general physicians. In accordance with the EMS Act, all EDs participated annually in a
18
19 156 nationwide functional performance evaluation program, which was administered by the
20
21 157 Ministry of Health and Welfare. The three participating hospitals in this study were all level 1
22
23 158 EDs that can perform acute trauma care for patients with TBI 24 hours a day/365 days a
24
25 159 year—including emergency neurosurgical operation and angiographic interventions.
26
27
28
29

30 31 160 ***Data source***

32
33
34 161 We used an EMS ambulance run-sheet, EMS trauma in-depth registry, and ED administrative
35
36 162 database. The EMS database information, including ambulance run-sheet and trauma in-depth
37
38 163 registry, was collected electronically by EMS providers using tablets. The EMS record
39
40 164 review for each severe trauma has been performed by EMS medical directors of each fire
41
42 165 department since 2012. The ED administrative database contains patients' demographic
43
44 166 characteristics, route of visit, time of visit, and diagnosis and disposition. We merged the
45
46 167 EMS database with the ED administrative database based on patients' arrival time, age, and
47
48 168 sex.
49
50
51

52 53 169 ***Study population***

54
55
56 170 We included adult (age ≥ 15) EMS users who were transported to participating hospitals with
57
58 171 severe trauma from January 1, 2014 to December 31, 2018. Severe trauma was assessed by
59
60

1
2
3
4 172 EMS providers and defined as patients who fulfilled trauma center transport criteria
5
6 173 (physiologic criteria, anatomic criteria, mechanism of injury criteria, or special patients or
7
8 174 system consideration criteria) in the field triage decision scheme.²¹ Patients were excluded if
9
10 175 they had out-of-hospital cardiac arrest or their main cause of EMS call was medical or
11
12 176 nontraumatic injury including choking, drowning, fire, flame, heat, cold, poisoning, chemical,
13
14 177 sexual assault, weather, or natural disaster. Patients with an unknown outcome were also
15
16 178 excluded.
17
18
19
20
21

22 179 ***Outcome measure***

23
24 180 The primary outcome measure was the diagnosis of TBI. TBI diagnosis was defined as
25
26 181 patients whose diagnostic code, according to the International Statistical Classification of
27
28 182 Diseases and Related Health Problems (ICD-10), was between S06.0 and S06.9.^{22 23} The ED
29
30 183 administrative database has two types of primary diagnostic codes: the final diagnostic codes
31
32 184 at ED discharge and at hospital discharge. We extracted up to 20 codes for each. We defined
33
34 185 the diagnostic code as positive for TBI if a confirmative diagnostic code was found in any
35
36 186 level of the discharge record. A secondary outcome measure was the diagnosis of TBI with
37
38 187 intracranial hemorrhage or injury (TBI-I), defined as ED discharge or hospital discharge
39
40 188 diagnosis ICD-10 code S06.1–S06.9. Concussion (ICD-10 code with S06.0) was excluded in
41
42 189 TBI-I. A tertiary outcome was TBI with non-discharge (TBI-ND). Non-discharge was
43
44 190 defined as patients whose ED discharge disposition included admission, transfer, or death.
45
46 191 Quaternary outcome measure was TBI with death (TBI-D). Death was defined as patients
47
48 192 whose ED discharge disposition or hospital discharge disposition was death.
49
50
51
52
53
54
55

56 193 ***Variables and preprocessing***

57
58 194 We collected patients' demographic data, circumstances of trauma, chief complaints, EMS
59
60

1
2
3
4 195 vital sign assessment, EMS management and hospital outcomes. The detailed descriptions of
5
6 196 each variable are described in Supplementary Table 1. Categorical variables were
7
8
9 197 preprocessed with the one-hot encoding (dummy variable encoding) method. Continuous
10
11 198 variables were divided into four quantiles and unknown or missing values were categorized
12
13 199 as a fifth category. One-hot encoding was also applied to discretized continuous variables.
14
15 200 Preprocessing measures including discretization results of continuous variables are presented
16
17
18 201 in Supplementary Table 1.

22 202 ***Model development***

23
24 203 We developed prediction models for outcomes by using five machine learning algorithms:
25
26 204 logistic regression analyses (LR), extreme gradient boost (XGB), random forest (RF), support
27
28 205 vector machine (SVM), and elastic net (EN). The LR algorithm was chosen as baseline
29
30 206 comparison algorithm because it is widely used in the medical field and has been used for
31
32 207 previous prediction model development in TBI studies.^{14 24} Backward stepwise LR was
33
34 208 selected for feature selection. The other four algorithms were selected based on their ability
35
36 209 to model nonlinear associations, their relative ease of implementation, and their general
37
38 210 acceptance in the machine learning community.²⁵⁻²⁹ All algorithms have a method to
39
40 211 calculate the probability of the outcome occurring and algorithms other than LR need
41
42 212 hyperparameter tuning for proper training and prediction.

43
44 213 The study population was split into training cohorts that included development,
45
46 214 validation, and test cohorts. The development cohort included a training cohort from which
47
48 215 each of the machine learning prediction models were derived and a validation cohort in which
49
50 216 the prediction models were applied to adjust the hyperparameters of the algorithm. The test
51
52 217 cohort was used for the final evaluation of the performance of the prediction models.
53
54 218 Chronological split was used for data split. Patients enrolled from January 1, 2014 to
55
56
57
58
59
60

1
2
3
4 219 December 31, 2016 were used as the training cohort; patients from January 1, 2017 to
5
6 220 December 31, 2017 were used as the validation cohort; and patients from January 1, 2018 to
7
8 221 December 31, 2018 were used as the test cohort. Hyperparameter tuning using validation data
9
10 222 was conducted by, first, a random search within 10,000 randomly generated hyperparameters;
11
12 223 then, grid search hyperparameters chosen around from random search with five candidates
13
14 224 per each hyperparameter. Finally, hyperparameter with best area under receiver-operation
15
16 225 curve (AUROC) in validation cohorts were selected. Test data were separated during training
17
18 226 and tuning processes and used to measure algorithm performance.
19
20
21
22
23

24 227 ***Statistical analysis***

26 228 The demographic findings and outcomes of the study population were described in this study.
27
28 229 Additionally, the baseline characteristics of the training cohort and the validation cohort were
29
30 230 compared. The continuous variables were compared by using Student's T-test or the
31
32 231 Wilcoxon rank sum test, and the categorical variables were compared by using the chi-
33
34 232 squared test or the Fisher exact test, as appropriate.
35
36

37 233 We assessed discrimination performance by comparing the AUROC for each model
38
39 234 in the test cohort. We considered an AUROC of 0.5 as no discrimination, 0.7 to 0.8 as
40
41 235 acceptable, 0.8 to 0.9 as excellent, and more than 0.9 is considered outstanding.³⁰ Area under
42
43 236 the precision-recall curve (AUPRC) was assessed for each model in the test cohort. We
44
45 237 assessed the calibration power by using the Hosmer–Lemeshow test, the scaled Brier score,
46
47 238 and a calibration plot in the test cohort.³¹ For the delineation of test characteristics, the
48
49 239 sensitivity, specificity, and positive and negative predictive values with 95% CIs were
50
51 240 determined using a cutoff probability at a sensitivity of 80%. Given that poor sensitivity of
52
53 241 clinical predictors for TBI in previous studies,^{12 32} and almost 75% sensitivity level for other
54
55 242 severe disease prediction in prehospital settings,^{33 34} we thought that 80% sensitivity was an
56
57
58
59
60

1
2
3
4 243 appropriate target for our prediction model. We calculated false positive rate as 1 –
5
6 244 specificity. The added prognostic power of each prediction model compared to the LR model
7
8
9 245 was also evaluated by continuous net reclassification index (NRI). NRI is a statistical method
10
11 246 to quantify how well a new model correctly reclassifies the study population with the other
12
13 247 models. Details of NRI are described elsewhere.³⁵

14
15 248 By using a model-specific metric, the variable importance of each model was
16
17
18 249 assessed, except for the SVM algorithm. The variable importance was determined by the
19
20 250 coefficient effect sizes for the LR model. The XGB and RF models were ranked by variable
21
22 251 importance on the selection frequency of the variable as a decision node. The absolute value
23
24 252 of the coefficients corresponding to the tuned model were used for the measurement of
25
26 253 variable importance in the EN algorithm.³⁶ To compare the variable importance of each
27
28
29 254 prediction models efficiently, top 5 variables of each model was presented.

30
31 255 All statistical analyses were performed with R Statistical Software (version 4.0.1; R
32
33 256 Foundation for Statistical Computing, Vienna, Austria). Packages included caret, e1071,
34
35 257 xgboost, randomForest, and glmnet for the analysis of the machine learning algorithms.
36
37
38
39

40 258 ***No patient and public involvement***

41
42 259 This research was done without patient involvement. Patients were not invited to comment on
43
44 260 the study design and were not consulted to develop patient relevant outcomes or interpret the
45
46 261 results. Patients were not invited to contribute to the writing or editing of this document for
47
48
49 262 readability or accuracy.
50

51 263
52
53
54
55
56
57
58
59
60

264 **Result**

265 *Demographic findings*

266 Among the 157,134 EMS users transported to three hospitals from 2014 to 2018, 1,169
267 patients were included in the final analysis (Figure 1). Patients were split into 2 datasets: data
268 from 2014 to 2017, consisting of 867 patients (74.2%) in the development cohort; and the
269 remaining data from 2018 consisting of 302 patients (25.8%) in the test cohort (Figure 1).
270 Among the development cohort, data from 2014 to 2016—consisting of 661 patients—were
271 used as the training cohort, and 2017 data—consisting of 206 patients—were used as the
272 validation cohort in the model.

273 Table 1 shows key demographic findings of the development and test cohorts. Median
274 (IQR) age was 52 years (35–66) in the development cohort and 56 years (40–69) in the test
275 cohort. Traffic accident was most common mechanism of trauma (43.3% for the development
276 cohort and 41.4% for the test cohort). The proportion of patients with alert mental status was
277 58.1% for the development cohort and 69.5% in the test cohort. Overall, TBI, TBI-I, TBI-
278 ND, TBI-D occurred in 215 (24.8%), 195 (22.5%), 192 (22.1%), and 32 (3.7%) in the
279 development cohort; and 66 (21.9%), 56 (18.5%), 57 (18.9%), and 11 (3.6%) in the test
280 cohort. All demographic characteristics of the development and test cohorts are described in
281 Supplementary Table 2.

282 *Main analysis*

283 The discrimination and NRI of the prediction models on the test cohort are presented in Table
284 2. The AUROC for outcomes were 0.770–0.806 for TBI, 0.820–0.844 for TBI-I, 0.767–0.811
285 for TBI-ND, and 0.664–0.889 for TBI-D (Table 2 and Supplementary Figure 1). Compared to
286 LR, XGB performed significantly well in predicting TBI, and RF and EN performed well in

1
2
3
4 287 predicting TBI-ND and TBI-D. EN model generally performed well on all outcomes. The
5
6 288 AUROC of the EN model for outcomes were 0.799 (95% CI: 0.732–0.867), 0.844 (95% CI:
7
8 289 0.779–0.910), 0.811 (95% CI: 0.741–0.882), and 0.871 (95% CI: 0.764–0.978) for TBI, TBI-
9
10 290 I, TBI-ND, and TBI-D, respectively. Machine learning models generally resulted in
11
12 291 significant reclassification improvement compared to LR for TBI, TBI-I, and TBI-ND. For
13
14 292 prediction TBI-D, AUROC difference, and reclassification improvement compared to LR
15
16 293 was non-significant in all machine learning models. The precision-recall curve is shown in
17
18 294 Supplementary Figure 2. AUPRC were 0.479–0.564 for TBI, 0.469–0.606 for TBI-I, 0.477–
19
20 295 0.551 for TBI-ND and 0.094–0.140 for TBI-D. EN model showed highest AUPRC among all
21
22 296 prediction models. Supplementary Figure 3 shows the calibration plot of prediction models
23
24 297 according to outcomes. All prediction models generally showed poor calibration. Given the
25
26 298 high AUROC and AUPRC among prediction models, and reclassification improvement
27
28 299 compared to LR, we determined EN as a best-performing prediction model in our analysis.

30
31
32 300 Using cutoff of 80% sensitivity, specificity was 47.5–68.2% for TBI, 71.1–81.3% for
33
34 301 TBI-I, 46.1–74.3% for TBI-ND, and 42.6–0 for TBI-D. EN showed the highest specificity
35
36 302 and PPV among all outcomes. False positive rate (1 – specificity) was almost 19.7–39.0%
37
38 303 according to outcomes in the EN model. The 95% CI of specificity of the EN model was not
39
40 304 overlapped with LR in TBI, TBI-ND, and TBI-D predictions. NPV was almost 89–99% for
41
42 305 all outcomes in the prediction models (Table 3).

43
44 306 Table 4 shows the top 5 variable importance of prediction models according to
45
46 307 outcomes. Variables related to patients' symptom of loss of consciousness, Glasgow Coma
47
48 308 Scale component, and light reflex were the three most important variables to predict all
49
50 309 outcomes. Compared to other outcomes, the difference between variable importance for TBI-
51
52 310 D was prominent, and the mechanism of injury, heart rate, and age showed the highest
53
54 311 importance for predicting TBI-D.

312 Discussion

313 By using prehospital data from EMS users visiting three teaching hospitals, we developed
314 and validated prediction models for the diagnosis and prognosis of TBI using machine
315 learning algorithms among patients with severe trauma, identified by EMS providers in South
316 Korea. We found that 24% of patients were diagnosed with TBI, 22% showed intracranial
317 injury, 21% could not be discharged from the ED with a TBI diagnosis, and 4% showed TBI-
318 related death. Machine learning models showed acceptable-to-excellent discrimination
319 performance (AUROCs were 0.799–0.871 according to outcomes in the best-performing EN
320 model). When identifying 80% of target patients with TBI, the false positive rate was almost
321 19.7–39.0%. Consciousness status related variables ranging from patients' symptom to EMS
322 providers' assessment showed the highest importance for predicting all outcomes. This study
323 adds considerably to the understanding of prehospital prediction performance of TBI among
324 patients with severe trauma. Use of comprehensive prehospital information and certain
325 machine learning approaches led to increased performance with a diminished false positive
326 rate compared to those of the traditional statistical model.

327 Several studies reported that EMS providers' assessment using prehospital
328 information is effective for the identification of patients with severe trauma who require
329 direct transport to a trauma center.³⁷⁻³⁹ Because TBI accounts for a significant portion of
330 patients with severe trauma,³⁸ and the majority of patients have poor access to trauma
331 centers,⁴⁰ identification of TBI among patients with severe trauma by EMS providers could
332 contribute to proper prehospital management and destination hospital decisions.⁶ However,
333 prehospital identification of TBI is challenging.⁴¹ Prehospital clinical signs showed poor
334 predictive performance for differentiating patients with TBI.¹² and previous prediction
335 models related to TBI mostly focused on TBI outcomes.^{13 14 16} One study reported the
336 predictors for mild TBI with persistent symptoms; but a single-center case-control study

1
2
3
4 337 design and ED-based model development lacks applicability to prehospital settings.³² In this
5
6 338 study, we developed and tested TBI prediction models that used prehospital information, and
7
8
9 339 we found acceptable discrimination power for the prediction of diagnosis and prognosis of
10
11 340 TBI. Uniquely, we incorporated various demographic variables, trauma circumstances,
12
13 341 patients' complaints, and EMS assessment information in the prediction models, and we
14
15
16 342 adapted the machine learning algorithms.

17
18 343 When using a cutoff for 80% sensitivity for TBI detection, the false positive rate was
19
20 344 19.7–39.0% (Table 2). Those false positive rate levels are plausible for detecting severe
21
22
23 345 diseases in EMS settings. A previous study reported a 26% of false positive rate of EMS
24
25 346 triage for myocardial infarction with a sensitivity of 74% and 50% of false positive rate of
26
27 347 EMS recognition of stroke in sensitivity of 74%.^{33 34} Considering the prevalence of outcomes
28
29 348 (24% in TBI, 22% in TBI-I, 21% in TBI-ND, and 4% in TBI-D; Table 1), there would be 16,
30
31 349 9, 12, and 67 false-positive patients for every 10 patients that are accurately identified as TBI,
32
33
34 350 TBI-I, TBI-ND, and TBI-D, respectively. Because of the low prevalence of TBI-D, a similar
35
36
37 351 specificity of the prediction model for outcomes resulted in a very low positive predictive
38
39 352 value and a high proportion of false positive cases, which suggested the limited applicability
40
41 353 of prediction models for TBI-D in prehospital settings.

42
43 354 Consciousness-status-related variables ranging from patients' complaints to EMS
44
45 355 assessment showed the highest importance regardless of models and outcomes in our study.
46
47
48 356 Consciousness status is closely associated with head trauma. Head trauma can result in
49
50 357 structural brain injury or physiological disruption of brain function, which could result in
51
52
53 358 altered mental status.⁴² Mental status is also associated with TBI severity,⁴³ and its
54
55 359 association with TBI outcomes have been reported.^{13 14 16} History taking and physical
56
57 360 examination for altered mental status is key to early diagnosis and proper management of TBI
58
59
361 in prehospital settings.⁴⁴

1
2
3
4 362 We adapted machine learning algorithms for the prediction of TBI-related outcomes
5
6 363 and found an improvement in discrimination and an increase in specificity with the same
7
8
9 364 sensitivity thresholds. However, the LR model also showed acceptable or similar
10
11 365 performance compared to machine learning models, according to the outcomes. In clinical
12
13 366 prediction models, a previous systematic review reported no performance benefit of the
14
15 367 machine learning model over LR.⁴⁵ The previous study stated that machine learning models
16
17 368 tend to show high performance with a strong signal-to-noise ratio problem like gaming,
18
19 369 image recognition. However, clinical prediction problems often result in a poor signal-to-
20
21 370 noise ratio.^{45 46} If we could use unstructured data, which has strong signal-to-noise ratio like
22
23 371 continuous vital sign monitoring data or audiovisual data for patients' appearance, machine
24
25 372 learning models might perform better than LR models. In addition, if we analyzed more
26
27 373 patient data, the performance improvement of machine models might be elucidated.

31
32 374 Precise assessment in prehospital field could contribute to improved patient-related
33
34 375 outcomes. High demand of EMS call and response,⁴⁷ disparity in accessibility to definitive
35
36 376 care capable hospitals according to regions,⁴⁰ and the importance of timely management in
37
38 377 acute disease care are the chief reasons behind the necessity for the accurate assessment of
39
40 378 EMS providers. Although information acquisition and processing is quite difficult in
41
42 379 prehospital areas, various instruments and information systems could attribute to diminish
43
44 380 those problems. Complex data acquisition like mobile CT or other unstructured data^{48 49},
45
46 381 information sharing through telemedicine,⁵⁰ and decision support tools in prehospital
47
48 382 environments⁵¹ could contribute to the accurate assessment of EMS providers. More
49
50 383 information acquisition and real-time processing of those data could improve the clinical
51
52 384 prediction models in prehospital areas, which could lead to the improvement of patients'
53
54 385 safety and outcomes.

1
2
3
4 386 Our study had several limitations. First, our data were collected at three teaching
5
6 387 hospitals in urban areas of South Korea. Therefore, external validation for other areas should
7
8
9 388 be conducted to generalize the developed prediction model. Second, we used retrospective
10
11 389 analysis of electronically collected prehospital and hospital data. There might be various
12
13 390 information loss and missing data. We treated missing status as a separate category for our
14
15 391 analysis;⁵² however, there could be different reasons for missing data. Third, there is a
16
17 392 possibility that the prediction model was overfitted or underfitted. To minimize this issue, we
18
19 393 rigorously searched hyperparameters and carefully chose hyperparameters according to the
20
21 394 performance in independent validation cohorts. Lastly, this study was performed in an
22
23 395 intermediate-service-level EMS system. The generalization of our study findings to different
24
25 396 EMS settings should be made with caution.

26
27
28
29 397 In conclusion, we presented data on TBI among patients with severe trauma assessed
30
31 398 by EMS providers, and our results inform the development of prediction models for the
32
33 399 diagnosis and prognosis of TBI in our population. We used various information that can be
34
35 400 obtained in prehospital settings and showed acceptable outcome performance. The consistent
36
37 401 importance of consciousness-status-related variables emphasizes the importance of
38
39 402 assessment and monitoring of consciousness status in prehospital areas. Although
40
41 403 prospective, and implementation studies are needed for TBI prediction in prehospital areas,
42
43 404 our study outlined a novel method for the precise assessment of EMS providers using a
44
45 405 machine-learning-based prediction model. Further collection of various types of patient-
46
47 406 related data would contribute to the enhanced performance of the clinical prediction model in
48
49 407 prehospital settings.

50
51
52
53
54 408

1
2
3
4 **409 Author Contribution Statement**

5
6
7 410 YHC and JH Park designed and developed the study, analysed and interpreted the data, and
8
9 411 drafted the initial manuscript. KJH, YSR, KJS and SDS were involved in the acquisition of
10
11 412 data, the development of the research question and assisted with analysis and interpretation of
12
13
14 413 data. All authors revised the drafts for intellectual content and edited the manuscript. All
15
16 414 authors reviewed and approved the final draft.

17
18
19
20 415

21
22
23 **416 Funding**

24
25
26 417 This study was supported by grant No. '04-2019-0680' from the Seoul National University
27
28 418 Hospital Research Fund.

29
30
31 419

32
33
34 **420 Competing Interests**

35
36 421 There are no conflicts of interest for all authors in this study.

37
38
39 422

40
41 **423 Patients consent**

42
43 424 Not required

44
45
46 425

47
48
49 **426 Data availability statement**

50
51 427 No data are available. We do not have ethics approval to share data.

52
53
54 428

1
2
3
4 429 **Ethical statements**
5

6 430 This study complied with the Declaration of Helsinki, and its protocol was approved by the
7
8 431 Institutional Review Board of the Seoul National University Hospital with a waiver of
9
10 432 informed consent (IRB No: E-2006-004-1128).
11
12
13 433

14
15
16
17 434 **References**
18

- 19 435 1. Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *The*
20
21 436 *Lancet Neurology* 2008;7(8):728-41.
22
23
24 437 2. Hsia RY, Markowitz AJ, Lin F, et al. Ten-year trends in traumatic brain injury: a
25
26 438 retrospective cohort study of California emergency department and hospital revisits and
27
28 439 readmissions. *BMJ Open* 2018;8(12):e022297. doi: 10.1136/bmjopen-2018-022297
29
30 440 [published Online First: 2018/12/16]
31
32
33 441 3. Finfer SR, Cohen J. Severe traumatic brain injury. *Resuscitation* 2001;48(1):77-90. doi:
34
35 442 10.1016/s0300-9572(00)00321-x [published Online First: 2001/02/13]
36
37
38 443 4. DeWitt DS, Jenkins LW, Prough DS. Enhanced vulnerability to secondary ischemic insults
39
40 444 after experimental traumatic brain injury. *New Horiz* 1995;3(3):376-83. [published
41
42 445 Online First: 1995/08/01]
43
44
45 446 5. McHugh GS, Engel DC, Butcher I, et al. Prognostic value of secondary insults in traumatic
46
47 447 brain injury: results from the IMPACT study. *J Neurotrauma* 2007;24(2):287-93. doi:
48
49 448 10.1089/neu.2006.0031 [published Online First: 2007/03/23]
50
51
52 449 6. Spaite DW, Bobrow BJ, Keim SM, et al. Association of Statewide Implementation of the
53
54 450 Prehospital Traumatic Brain Injury Treatment Guidelines With Patient Survival
55
56 451 Following Traumatic Brain Injury: The Excellence in Prehospital Injury Care (EPIC)
57
58 452 Study. *JAMA Surg* 2019;154(7):e191152. doi: 10.1001/jamasurg.2019.1152 [published
59
60

- 1
2
3
4 453 Online First: 2019/05/09]
5
6
7 454 7. Pelieu I, Kull C, Walder B. Prehospital and Emergency Care in Adult Patients with Acute
8
9 455 Traumatic Brain Injury. *Med Sci (Basel)* 2019;7(1) doi: 10.3390/medsci7010012
10
11 456 [published Online First: 2019/01/24]
12
13 457 8. Goldberg SA, Rojanasartikul D, Jagoda A. The prehospital management of traumatic brain
14
15 458 injury. *Handb Clin Neurol* 2015;127:367-78. doi: 10.1016/B978-0-444-52892-
16
17 459 6.00023-4 [published Online First: 2015/02/24]
18
19
20 460 9. Chi JH, Knudson MM, Vassar MJ, et al. Prehospital hypoxia affects outcome in patients
21
22 461 with traumatic brain injury: a prospective multicenter study. *J Trauma*
23
24 462 2006;61(5):1134-41. doi: 10.1097/01.ta.0000196644.64653.d8 [published Online First:
25
26 463 2006/11/14]
27
28
29 464 10. Barton CW, Hemphill JC, Morabito D, et al. A novel method of evaluating the impact of
30
31 465 secondary brain insults on functional outcomes in traumatic brain-injured patients.
32
33 466 *Acad Emerg Med* 2005;12(1):1-6. doi: 10.1197/j.aem.2004.08.043 [published Online
34
35 467 First: 2005/01/07]
36
37
38 468 11. Sasser SM, Hunt RC, Faul M, et al. Guidelines for field triage of injured patients:
39
40 469 recommendations of the National Expert Panel on Field Triage, 2011. *Morbidity and*
41
42 470 *Mortality Weekly Report: Recommendations and Reports* 2012;61(1):1-20.
43
44
45 471 12. Ter Avest E, Taylor S, Wilson M, et al. Prehospital clinical signs are a poor predictor of
46
47 472 raised intracranial pressure following traumatic brain injury. *Emerg Med J*
48
49 473 2021;38(1):21-26. doi: 10.1136/emermed-2020-209635 [published Online First:
50
51 474 2020/09/20]
52
53
54 475 13. Collaborators MCT, Perel P, Arango M, et al. Predicting outcome after traumatic brain
55
56 476 injury: practical prognostic models based on large cohort of international patients. *BMJ*
57
58 477 2008;336(7641):425-9. doi: 10.1136/bmj.39461.643438.25 [published Online First:

- 1
2
3
4 478 2008/02/14]
5
6
7 479 14. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain
8
9 480 injury: development and international validation of prognostic scores based on
10
11 481 admission characteristics. *PLoS Med* 2008;5(8):e165; discussion e65. doi:
12
13 482 10.1371/journal.pmed.0050165 [published Online First: 2008/08/08]
14
15
16 483 15. Gozt AK, Hellewell SC, Thorne J, et al. Predicting outcome following mild traumatic brain
17
18 484 injury: protocol for the longitudinal, prospective, observational Concussion Recovery
19
20 485 (CREST) cohort study. *BMJ Open* 2021;11(5):e046460. doi: 10.1136/bmjopen-2020-
21
22 486 046460 [published Online First: 2021/05/15]
23
24
25 487 16. Miller PR, Chang MC, Hoth JJ, et al. Predicting Mortality and Independence at Discharge
26
27 488 in the Aging Traumatic Brain Injury Population Using Data Available at Admission. *J*
28
29 489 *Am Coll Surg* 2017;224(4):680-85. doi: 10.1016/j.jamcollsurg.2016.12.053 [published
30
31 490 Online First: 2017/03/07]
32
33
34 491 17. Wasserman EB, Shah MN, Jones CM, et al. Identification of a neurologic scale that
35
36 492 optimizes EMS detection of older adult traumatic brain injury patients who require
37
38 493 transport to a trauma center. *Prehosp Emerg Care* 2015;19(2):202-12. doi:
39
40 494 10.3109/10903127.2014.959225 [published Online First: 2014/10/08]
41
42
43 495 18. Hale AT, Stonko DP, Brown A, et al. Machine-learning analysis outperforms conventional
44
45 496 statistical models and CT classification systems in predicting 6-month outcomes in
46
47 497 pediatric patients sustaining traumatic brain injury. *Neurosurgical Focus FOC*
48
49 498 2018;45(5):E2. doi: 10.3171/2018.8.Focus17773
50
51
52 499 19. Collins GS, Reitsma JB, Altman DG, et al. Transparent Reporting of a multivariable
53
54 500 prediction model for Individual Prognosis Or Diagnosis (TRIPOD). *Ann Intern Med*
55
56 501 2015;162(10):735-6. doi: 10.7326/L15-5093-2 [published Online First: 2015/05/20]
57
58
59 502 20. Sasser SM, Hunt RC, Sullivent EE, et al. Guidelines for field triage of injured patients:

- 1
2
3
4 503 recommendations of the National Expert Panel on Field Triage. 2009
5
6 504 21. Sasser SM, Hunt RC, Faul M, et al. Guidelines for field triage of injured patients:
7
8 505 recommendations of the National Expert Panel on Field Triage, 2011. *MMWR Recomm*
9
10 506 *Rep* 2012;61(RR-1):1-20. [published Online First: 2012/01/13]
11
12
13 507 22. Andelic N, Anke A, Skandsen T, et al. Incidence of hospital-admitted severe traumatic
14
15 508 brain injury and in-hospital fatality in Norway: a national cohort study.
16
17 509 *Neuroepidemiology* 2012;38(4):259-67. doi: 10.1159/000338032 [published Online
18
19 510 First: 2012/06/09]
20
21
22 511 23. Ro YS, Shin SD, Holmes JF, et al. Comparison of clinical performance of cranial computed
23
24 512 tomography rules in patients with minor head injury: a multicenter prospective study.
25
26 513 *Acad Emerg Med* 2011;18(6):597-604. doi: 10.1111/j.1553-2712.2011.01094.x
27
28 514 [published Online First: 2011/06/17]
29
30
31 515 24. Gang MC, Hong KJ, Shin SD, et al. New prehospital scoring system for traumatic brain
32
33 516 injury to predict mortality and severe disability using motor Glasgow Coma Scale,
34
35 517 hypotension, and hypoxia: a nationwide observational study. *Clin Exp Emerg Med*
36
37 518 2019;6(2):152-59. doi: 10.15441/ceem.18.027 [published Online First: 2019/07/03]
38
39
40 519 25. Chen T, Guestrin C. XGBoost: A Scalable Tree Boosting System. Proceedings of the 22nd
41
42 520 ACM SIGKDD International Conference on Knowledge Discovery and Data Mining.
43
44 521 San Francisco, California, USA: Association for Computing Machinery, 2016:785–94.
45
46
47 522 26. Zou H, Hastie T. Regularization and variable selection via the elastic net. *Journal of the*
48
49 523 *Royal Statistical Society: Series B (Statistical Methodology)* 2005;67(2):301-20. doi:
50
51 524 10.1111/j.1467-9868.2005.00503.x
52
53
54 525 27. Dong Q, Taylor RA, Moore CL, et al. Predicting urinary tract infections in the emergency
55
56 526 department with machine learning. *Plos One* 2018;13(3) doi:
57
58 527 10.1371/journal.pone.0194085
59
60

- 1
2
3
4 528 28. Breiman RF. Vaccines as tools for advancing more than public health: perspectives of a
5
6 529 former director of the National Vaccine Program office. *Clin Infect Dis*
7
8 530 2001;32(2):283-8. doi: 10.1086/318461 [published Online First: 2001/02/15]
9
10
11 531 29. Hearst MA, Dumais ST, Osuna E, et al. Support vector machines. *IEEE Intelligent Systems*
12
13 532 *and their Applications* 1998;13(4):18-28. doi: 10.1109/5254.708428
14
15
16 533 30. Hosmer Jr DW, Lemeshow S, Sturdivant RX. Applied logistic regression: John Wiley &
17
18 534 Sons 2013.
19
20 535 31. Fenlon C, O'Grady L, Doherty ML, et al. A discussion of calibration techniques for
21
22 536 evaluating binary and categorical predictive models. *Prev Vet Med* 2018;149:107-14.
23
24 537 doi: 10.1016/j.prevetmed.2017.11.018 [published Online First: 2018/01/02]
25
26
27 538 32. Wojcik SM. Predicting mild traumatic brain injury patients at risk of persistent symptoms
28
29 539 in the Emergency Department. *Brain Inj* 2014;28(4):422-30. doi:
30
31 540 10.3109/02699052.2014.884241 [published Online First: 2014/02/26]
32
33
34 541 33. Oostema JA, Konen J, Chassee T, et al. Clinical predictors of accurate prehospital stroke
35
36 542 recognition. *Stroke* 2015;46(6):1513-7. doi: 10.1161/STROKEAHA.115.008650
37
38 543 [published Online First: 2015/04/30]
39
40
41 544 34. Swan PY, Nighswonger B, Boswell GL, et al. Factors associated with false-positive
42
43 545 emergency medical services triage for percutaneous coronary intervention. *West J*
44
45 546 *Emerg Med* 2009;10(4):208-12. [published Online First: 2010/01/05]
46
47
48 547 35. Park JH, Shin SD, Song KJ, et al. Prediction of good neurological recovery after out-of-
49
50 548 hospital cardiac arrest: A machine learning analysis. *Resuscitation* 2019;142:127-35.
51
52 549 doi: 10.1016/j.resuscitation.2019.07.020 [published Online First: 2019/07/31]
53
54
55 550 36. Weng SF, Reys J, Kai J, et al. Can machine-learning improve cardiovascular risk prediction
56
57 551 using routine clinical data? *PLoS One* 2017;12(4):e0174944. doi:
58
59 552 10.1371/journal.pone.0174944 [published Online First: 2017/04/05]
60

- 1
2
3
4 553 37. Esposito TJ, Offner PJ, Jurkovich GJ, et al. Do prehospital trauma center triage criteria
5
6 554 identify major trauma victims? *Arch Surg* 1995;130(2):171-6. doi:
7
8 555 10.1001/archsurg.1995.01430020061010 [published Online First: 1995/02/01]
9
10
11 556 38. Ocak G, Sturms LM, Hoogeveen JM, et al. Prehospital identification of major trauma
12
13 557 patients. *Langenbecks Arch Surg* 2009;394(2):285-92. doi: 10.1007/s00423-008-0340-
14
15 558 4 [published Online First: 2008/06/27]
16
17
18 559 39. Fries GR, McCalla G, Levitt MA, et al. A prospective comparison of paramedic judgment
19
20 560 and the trauma triage rule in the prehospital setting. *Ann Emerg Med* 1994;24(5):885-
21
22 561 9. doi: 10.1016/s0196-0644(94)70207-1 [published Online First: 1994/11/01]
23
24
25 562 40. Branas CC, MacKenzie EJ, Williams JC, et al. Access to trauma centers in the United States.
26
27 563 *JAMA* 2005;293(21):2626-33. doi: 10.1001/jama.293.21.2626 [published Online First:
28
29 564 2005/06/02]
30
31
32 565 41. Whiting MD, Dengler BA, Rodriguez CL, et al. Prehospital Detection of Life-Threatening
33
34 566 Intracranial Pathology: An Unmet Need for Severe TBI in Austere, Rural, and Remote
35
36 567 Areas. *Front Neurol* 2020;11:599268. doi: 10.3389/fneur.2020.599268 [published
37
38 568 Online First: 2020/11/17]
39
40
41 569 42. Management of Concussion/m TBIWG. VA/DoD Clinical Practice Guideline for
42
43 570 Management of Concussion/Mild Traumatic Brain Injury. *J Rehabil Res Dev*
44
45 571 2009;46(6):CP1-68. [published Online First: 2010/01/30]
46
47
48 572 43. Grote S, Bocker W, Mutschler W, et al. Diagnostic value of the Glasgow Coma Scale for
49
50 573 traumatic brain injury in 18,002 patients with severe multiple injuries. *J Neurotrauma*
51
52 574 2011;28(4):527-34. doi: 10.1089/neu.2010.1433 [published Online First: 2011/01/27]
53
54
55 575 44. Badjatia N, Carney N, Crocco TJ, et al. Guidelines for prehospital management of traumatic
56
57 576 brain injury 2nd edition. *Prehosp Emerg Care* 2008;12 Suppl 1:S1-52. doi:
58
59 577 10.1080/10903120701732052 [published Online First: 2008/09/06]
60

- 1
2
3
4 578 45. Christodoulou E, Ma J, Collins GS, et al. A systematic review shows no performance
5
6 579 benefit of machine learning over logistic regression for clinical prediction models. *J*
7
8 580 *Clin Epidemiol* 2019;110:12-22. doi: 10.1016/j.jclinepi.2019.02.004 [published Online
9
10 581 First: 2019/02/15]
- 11
12
13 582 46. Ennis M, Hinton G, Naylor D, et al. A comparison of statistical learning methods on the
14
15 583 Gusto database. *Stat Med* 1998;17(21):2501-8. doi: 10.1002/(sici)1097-
16
17 584 0258(19981115)17:21<2501::aid-sim938>3.0.co;2-m [published Online First:
18
19 585 1998/11/20]
- 20
21
22 586 47. Crowe RP, Bower JK, Cash RE, et al. Association of Burnout with Workforce-Reducing
23
24 587 Factors among EMS Professionals. *Prehosp Emerg Care* 2018;22(2):229-36. doi:
25
26 588 10.1080/10903127.2017.1356411 [published Online First: 2017/08/26]
- 27
28
29 589 48. Hov MR, Zakariassen E, Lindner T, et al. Interpretation of Brain CT Scans in the Field by
30
31 590 Critical Care Physicians in a Mobile Stroke Unit. *J Neuroimaging* 2018;28(1):106-11.
32
33 591 doi: 10.1111/jon.12458 [published Online First: 2017/08/03]
- 34
35
36 592 49. Nakada TA, Masunaga N, Nakao S, et al. Development of a prehospital vital signs chart
37
38 593 sharing system. *Am J Emerg Med* 2016;34(1):88-92. doi: 10.1016/j.ajem.2015.09.048
39
40 594 [published Online First: 2015/10/29]
- 41
42
43 595 50. Kim Y, Groombridge C, Romero L, et al. Decision Support Capabilities of Telemedicine
44
45 596 in Emergency Prehospital Care: Systematic Review. *J Med Internet Res*
46
47 597 2020;22(12):e18959. doi: 10.2196/18959 [published Online First: 2020/12/09]
- 48
49
50 598 51. Reisner AT, Khitrov MY, Chen L, et al. Development and validation of a portable platform
51
52 599 for deploying decision-support algorithms in prehospital settings. *Appl Clin Inform*
53
54 600 2013;4(3):392-402. doi: 10.4338/ACI-2013-04-RA-0023 [published Online First:
55
56 601 2013/10/25]
- 57
58
59 602 52. Maslove DM, Podchiyska T, Lowe HJ. Discretization of continuous features in clinical

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

603 datasets. *J Am Med Inform Assoc* 2013;20(3):544-53. doi: 10.1136/amiajnl-2012-
604 000929 [published Online First: 2012/10/13]

605

For peer review only

1
2
3
4 606 **Figure legends**
5

6
7 607 Figure 1. Population flow. EMS, emergency medical service; OHCA, out-of-hospital cardiac
8
9 608 arrest; TBI, traumatic brain injury.

10 609
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

610 Table 1. Key characteristics of the development and test cohorts.

	n (%) or Median (IQR)			P
	Total	Development cohort	Test cohort	
Total	N = 1169	n = 867	n = 302	
Demographics				
Age, years	53 (36–66)	52 (35–66)	56 (40–69)	< 0.01
Male	809 (69.2)	592 (68.3)	217 (71.9)	0.25
Job, unemployed	299 (25.6)	197 (22.7)	102 (33.8)	< 0.01
Diabetes	62 (5.3)	35 (4.0)	27 (8.9)	< 0.01
Hypertension	105 (9.0)	61 (7.0)	44 (14.6)	< 0.01
Circumstances of trauma				
Location, road/highway	444 (38.0)	326 (37.6)	118 (39.1)	0.65
Season, summer	336 (28.7)	253 (29.2)	83 (27.5)	0.57
Weekday, weekend	811 (69.4)	599 (69.1)	212 (70.2)	0.72
Time, 6 p.m. to midnight	361 (30.9)	265 (30.6)	96 (31.8)	0.69
Mechanism of injury, TA	500 (42.8)	375 (43.3)	125 (41.4)	0.57
Chief complaint				
Fracture/abrasion/laceration	302 (25.8)	204 (23.5)	98 (32.5)	< 0.01
EMS vital sign assessment				
SBP, mmHg*	130 (109–150)	130 (104–146)	131 (115–150)	< 0.01
DBP, mmHg*	80 (70–91)	80 (69–90)	80 (70–92)	0.21
RR, mmHg*	18 (16–20)	18 (16–20)	18 (16–20)	0.33
HR, /min*	86 (75–99)	86 (74–99)	86 (76–100)	0.40
SpO ₂ , %*	98 (95–99)	98 (95–99)	98 (96–99)	0.67
AVPU scale, Alert	714 (61.1)	504 (58.1)	210 (69.5)	< 0.01
EMS management				
Intravenous route	176 (15.1)	129 (14.9)	47 (15.6)	0.77
Hemorrhage control	586 (50.1)	426 (49.1)	160 (53.0)	0.25
Spinal motion restriction	811 (69.4)	606 (69.9)	205 (67.9)	0.51
Oxygen supply	233 (19.9)	176 (20.3)	57 (18.9)	0.59
In-hospital mortality	90 (7.7)	74 (8.5)	16 (5.3)	0.07
Outcomes				
TBI	281 (24.0)	215 (24.8)	66 (21.9)	0.30
TBI with intracranial injury	251 (21.5)	195 (22.5)	56 (18.5)	0.15
TBI-related non-discharge	249 (21.3)	192 (22.1)	57 (18.9)	0.23
TBI-related death	43 (3.7)	32 (3.7)	11 (3.6)	0.95

611 IQR, interquartile range; TA, traffic accident; SBP, systolic blood pressure; DBP, diastolic
612 blood pressure; RR, respiratory rate; ED, emergency department; TBI, traumatic brain injury.

613 Table 2. Discrimination and reclassification of prediction models for outcomes on test
614 cohort.

Outcome	Model	AUROC (95% CI)	p ^a	NRI (95% CI)	p ^b	AUPRC
TBI						
	LR	0.770 (0.698, 0.841)	NA	NA	NA	0.492
	XGB	0.809 (0.743, 0.876)	0.04	0.689 (0.427, 0.951)	< 0.01	0.552
	SVM	0.776 (0.708, 0.844)	0.77	0.339 (0.072, 0.607)	0.01	0.479
	RF	0.800 (0.735, 0.865)	0.13	0.308 (0.047, 0.569)	0.02	0.532
	EN	0.799 (0.732, 0.867)	0.06	0.698 (0.441, 0.954)	< 0.01	0.564
TBI-I						
	LR	0.820 (0.751, 0.890)	NA	NA	NA	0.551
	XGB	0.838 (0.775, 0.901)	0.28	0.539 (0.258, 0.821)	< 0.01	0.554
	SVM	0.812 (0.748, 0.875)	0.66	0.729 (0.464, 0.994)	< 0.01	0.469
	RF	0.836 (0.772, 0.899)	0.38	0.333 (0.058, 0.607)	0.02	0.552
	EN	0.844 (0.779, 0.910)	0.15	1.093 (0.845, 1.342)	< 0.01	0.606
TBI-ND						
	LR	0.767 (0.690, 0.844)	NA	NA	NA	0.482
	XGB	0.800 (0.727, 0.873)	0.07	0.605 (0.326, 0.884)	< 0.01	0.496
	SVM	0.778 (0.704, 0.852)	0.56	0.285 (-0.001, 0.572)	0.05	0.477
	RF	0.809 (0.739, 0.880)	0.03	0.194 (-0.059, 0.448)	0.13	0.535
	EN	0.811 (0.741, 0.882)	0.02	0.768 (0.496, 1.039)	< 0.01	0.551
TBI-D						
	LR	0.664 (0.490, 0.838)	NA	NA	NA	0.138
	XGB	0.714 (0.512, 0.917)	0.64	-0.026 (-0.605, 0.553)	0.93	0.094
	SVM	0.814 (0.718, 0.910)	0.09	0.209 (-0.325, 0.742)	0.44	0.140
	RF	0.889 (0.801, 0.976)	< 0.01	-0.204 (-0.742, 0.334)	0.46	0.196
	EN	0.871 (0.764, 0.978)	0.01	0.119 (-0.415, 0.654)	0.66	0.293

615 ^aComparing the AUROC and the logistic regression model.

616 ^bComparing the NRI and the logistic regression model.

617 AUROC, area under the receiver operating characteristic curve; CI, confidence interval;
618 NRI, net reclassification index; AUPRC, area under precision-recall curve; TBI,
619 traumatic brain injury, TBI-I, traumatic brain injury with intracranial injury; TBI-ND;
620 traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with death;
621 LR, logistic regression analysis; XGB, extreme gradient boosting; SVM, support vector
622 machine; RF, random forest; EN, elastic net

623

624

625

626 Table 3. Test characteristics of prediction models for outcomes on test cohort.

Outcome	Model	Specificity (95% CI)	Sensitivity (95% CI)	PPV (95% CI)	NPV (95% CI)	Cutoff
TBI						
	LR	47.5 (40.9, 54.0)	80.3 (68.7, 89.1)	29.9 (23.3, 37.3)	89.6 (82.9, 94.3)	0.136
	XGB	72.5 (66.3, 78.1)	80.3 (68.7, 89.1)	44.9 (35.7, 54.3)	92.9 (88.2, 96.2)	0.268
	SVM	64.8 (58.4, 70.9)	80.3 (68.7, 89.1)	39.0 (30.7, 47.7)	92.2 (87.0, 95.8)	0.191
	RF	68.2 (61.9, 74.1)	80.3 (68.7, 89.1)	41.4 (32.8, 50.4)	92.5 (87.6, 96.0)	0.185
	EN	61.0 (54.5, 67.3)	80.3 (68.7, 89.1)	36.6 (28.7, 44.9)	91.7 (86.3, 95.5)	0.205
TBI-I						
	LR	71.1 (65.0, 76.7)	80.4 (67.6, 89.8)	38.8 (29.9, 48.3)	94.1 (89.7, 97.0)	0.164
	XGB	74.0 (68.0, 79.4)	80.4 (67.6, 89.8)	41.3 (31.9, 51.1)	94.3 (90.0, 97.1)	0.143
	SVM	71.1 (65.0, 76.7)	80.4 (67.6, 89.8)	38.8 (29.9, 48.3)	94.1 (89.7, 97.0)	0.172
	RF	76.0 (70.2, 81.2)	80.4 (67.6, 89.8)	43.3 (33.6, 53.3)	94.4 (90.3, 97.2)	0.205
	EN	81.3 (75.9, 86.0)	80.4 (67.6, 89.8)	49.5 (38.8, 60.1)	94.8 (90.9, 97.4)	0.204
TBI-ND						
	LR	46.1 (39.8, 52.6)	80.7 (68.1, 90.0)	25.8 (19.6, 32.9)	91.1 (84.7, 95.5)	0.090
	XGB	66.5 (60.2, 72.4)	80.7 (68.1, 90.0)	35.9 (27.7, 44.9)	93.7 (89.0, 96.8)	0.242
	SVM	59.2 (52.7, 65.4)	80.7 (68.1, 90.0)	31.5 (24.1, 39.7)	92.9 (87.7, 96.4)	0.147
	RF	60.4 (54.0, 66.6)	80.7 (68.1, 90.0)	32.2 (24.6, 40.5)	93.1 (88.0, 96.5)	0.138
	EN	74.3 (68.3, 79.6)	80.7 (68.1, 90.0)	42.2 (32.8, 52.0)	94.3 (90.0, 97.1)	0.201
TBI-D						
	LR	42.6 (36.9, 48.5)	81.8 (48.2, 97.7)	5.1 (2.4, 9.5)	98.4 (94.4, 99.8)	0.005
	XGB	57.7 (51.8, 63.5)	81.8 (48.2, 97.7)	6.8 (3.2, 12.5)	98.8 (95.8, 99.9)	0.002
	SVM	74.2 (68.8, 79.2)	81.8 (48.2, 97.7)	10.7 (5.0, 19.4)	99.1 (96.7, 99.9)	0.039
	RF	74.9 (69.5, 79.8)	81.8 (48.2, 97.7)	11.0 (5.1, 19.8)	99.1 (96.8, 99.9)	0.005
	EN	79.0 (73.9, 83.6)	81.8 (48.2, 97.7)	12.9 (6.1, 23.0)	99.1 (96.9, 99.9)	0.033

627 TBI, traumatic brain injury; TBI-I, traumatic brain injury with intracranial injury; TBI-
628 ND; traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with
629 death; LR, logistic regression analysis; XGB, extreme gradient boosting; SVM, support
630 vector machine; RF, random forest; EN, elastic net.
631

632 Table 4. Top 5 important variables for outcomes in descending order using model
 633 specific metrics

Outcome	Rank	LR	XGB	RF	EN
TBI					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	Loss of consciousness
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	GCS, Motor, 1
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 2
	4	Light reflex	Other mechanism	Light reflex	GCS, Eye, 1
	5	GCS, Motor, 1	GCS, Verbal, 2	GCS, Motor, 1	GCS, Verbal, 1
TBI-I					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	GCS, Eye, 1
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	Loss of consciousness
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 1
	4	Light reflex	GCS, Verbal, 2	Light reflex	GCS, Verbal, 1
	5	GCS, Motor, 1	Other mechanism	GCS, Motor, 1	Light reflex
TBI-ND					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	Loss of consciousness
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 1
	4	Light reflex	GCS, Verbal, 2	GCS, Verbal, 2	GCS, Verbal, 1
	5	GCS, Motor, 1	GCS, Motor, 1	GCS, Motor, 4	Light reflex
TBI-D					
	1	Loss of consciousness	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 2
	2	GCS, Verbal, 1	Oxygen saturation<96%	Light reflex	GCS, Verbal, 1
	3	GCS, Eye, 1	Fall mechanism	Loss of consciousness	Loss of consciousness
	4	Light reflex	Afternoon	GCS, Eye, 1	Age over 80
	5	GCS, Motor, 1	Light reflex	GCS, Motor, 1	HR 87-99

634 TBI, traumatic brain injury, TBI-I, traumatic brain injury with intracranial injury; TBI-
 635 ND; traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with
 636 death; LR, logistic regression; XGB, extreme gradient boosting; RF, random forest; EN,
 637 elastic net; GCS, Glasgow coma scale; HR, heart rate.

638

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

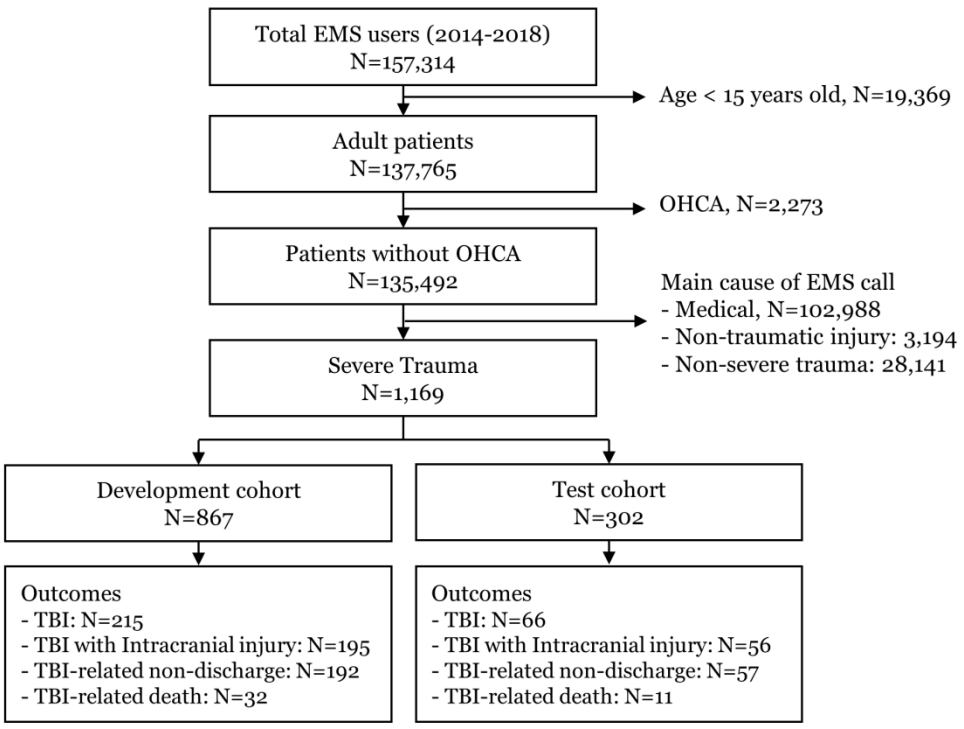


Figure 1

165x119mm (300 x 300 DPI)

Supplementary Table 1. List of analyzed variables.

Variables	Descriptions	Type of raw data	Category	Preprocessing
Gender	Sex of the patients	Binary	Male, Female	
Age	Age of patients	Continuous	15-39 years, 40-59 years, 60-79 years, and 80- years	Discretization and one hot encoding
Job	Job of patients	Categorical	Unemployed, Student/Housewife; Office/Commercial/Service workers; Industrial/Agricultural/Fishery/Miner worker; Others	One hot encoding Missing data were classified into others
Diabetes	History of diabetes mellitus	Binary	Yes, No	Missing data were classified into no
Hypertension	History of hypertension	Binary	Yes, No	Missing data were classified into no
Location of injury	Location of injury	Categorical	home/residential area/medical facility/school/gym; Road/highway; Off-road traffic area; Others	One hot encoding Missing data were classified into others
Season	Season when injury occurred	Categorical	Spring, Summer, Fall, Winter	One hot encoding
Weekend	Whether Injury occurred on weekday or weekend	Binary	Weekday, Weekend	
Daytime	When injury was occurred	Categorical	Night (Midnight to 5AM), Morning (6AM to 11AM), Afternoon (Midday to 5PM), Evening (6PM to 11PM)	One hot encoding Missing time were imputed using EMS call time
Mechanism of injury	Mechanism of injury	Categorical	Slip down, Fall down, Traffic accident, Other	One hot encoding Missing data were classified into others
Glasgow coma scale eye	Eye element of Glasgow coma scale	Categorical	1;2;3;4;Unknown	One hot encoding
Glasgow coma scale Verbal	Verbal element of Glasgow coma scale	Categorical	1;2;3;4;5;Unknown	One hot encoding
Glasgow coma scale Motor	Motor element of Glasgow coma scale	Categorical	1;2;3;4;5;6;Unknown	One hot encoding
Light Reflex any Abnormal	Any abnormality of light reflex on any side	Categorical	No, Yes, Unknown	One hot encoding Missing data were classified into unknown

Systolic blood pressure	blood	Systolic blood pressure	Continuous	-107 mmHg, 108-130 mmHg, 131-145 mmHg, 146- mmHg, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Diastolic pressure	blood	Diastolic blood pressure	Continuous	-69 mmHg, 70-80 mmHg, 81-91 mmHg, 92- mmHg, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Heart rate		Heart rate	Continuous	-74/min, 75-86/min, 87-99/min, 100-/min, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Respiratory rate		Respiratory rate	Continuous	-16/min, 17-18/min, 19-20/min, 21-/min, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Oxygen saturation		Oxygen saturation	Continuous	-95%, 96-98%, 99%, 100%, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Body temperature		Body temperature	Continuous	-36°C, 36.1-36.3°C, 36.4-36.8°C, 36.9-°C, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Chest pain or abdominal pain		Symptom of chest pain or abdominal pain	Binary	Yes, No	

Fracture, abrasion, or laceration	Symptom of fracture, abrasion, or laceration	Binary	Yes, No	
Loss of consciousness	Symptom of loss of consciousness	Binary	Yes, No	
Dyspnea	Symptom of dyspnea	Binary	Yes, No	
Nose bleeding	Symptom of nose bleeding	Binary	Yes, No	
Nausea or vomiting	Symptom of nausea or vomiting	Binary	Yes, No	
Headache, paralysis or dizziness	Symptom of headache, paralysis or dizziness	Binary	Yes, No	

Supplementary Table 2. Demographic characteristics of development and test cohorts

Characteristics	N (%) or Median (IQR)			P-value
	Total	Development	Test	
Total	1169	867	302	
Demographics				
Male	809 (69.2)	592 (68.3)	217 (71.9)	0.25
Age, years	53 (36-66)	52 (35-66)	56 (40-69)	<0.01
Job of patients				<0.01
Unemployed	299 (25.6)	197 (22.7)	102 (33.8)	
Student/Housewife	161 (13.8)	129 (14.9)	32 (10.6)	
Office/Commercial/Service worker	283 (24.2)	176 (20.3)	107 (35.4)	
Industrial/Agricultural/Fishery/Minery worker	36 (3.1)	25 (2.9)	11 (3.6)	
Others	390 (33.4)	340 (39.2)	50 (16.6)	
Past medical history				
Diabetes	62 (5.3)	35 (4.0)	27 (8.9)	<0.01
Hypertension	105 (9.0)	61 (7.0)	44 (14.6)	<0.01
Circumstances of Trauma				
Location of trauma				0.52
Residential/Nursing/Education/Exercise facility	303 (25.9)	218 (25.1)	85 (28.1)	
Road/Highway	444 (38.0)	326 (37.6)	118 (39.1)	
Off-road traffic area	181 (15.5)	140 (16.1)	41 (13.6)	
Others	241 (20.6)	183 (21.1)	58 (19.2)	
Season of trauma				<0.01
Spring	249 (21.3)	167 (19.3)	82 (27.2)	
Summer	336 (28.7)	253 (29.2)	83 (27.5)	
Fall	304 (26.0)	242 (27.9)	62 (20.5)	
Winter	280 (24.0)	205 (23.6)	75 (24.8)	
Weekday	811 (69.4)	599 (69.1)	212 (70.2)	0.72
Time of trauma				0.83
6A-MD	281 (24.0)	206 (23.8)	75 (24.8)	
MD-6P	266 (22.8)	203 (23.4)	63 (20.9)	
6P-MN	361 (30.9)	265 (30.6)	96 (31.8)	
MN-6A	261 (22.3)	193 (22.3)	68 (22.5)	
Mechanism of Trauma				0.60
Traffic accident	500 (42.8)	375 (43.3)	125 (41.4)	
Slip down	325 (27.8)	232 (26.8)	93 (30.8)	
Fall down	171 (14.6)	129 (14.9)	42 (13.9)	
Others	173 (14.8)	131 (15.1)	42 (13.9)	
Chief complaint				
Altered mentality	279 (23.9)	223 (25.7)	56 (18.5)	0.01
Fracture/Abrasion/Laceration	302 (25.8)	204 (23.5)	98 (32.5)	<0.01
Chest/Abdominal pain	47 (4.0)	31 (3.6)	16 (5.3)	0.19
Dyspnea	25 (2.1)	20 (2.3)	5 (1.7)	0.50

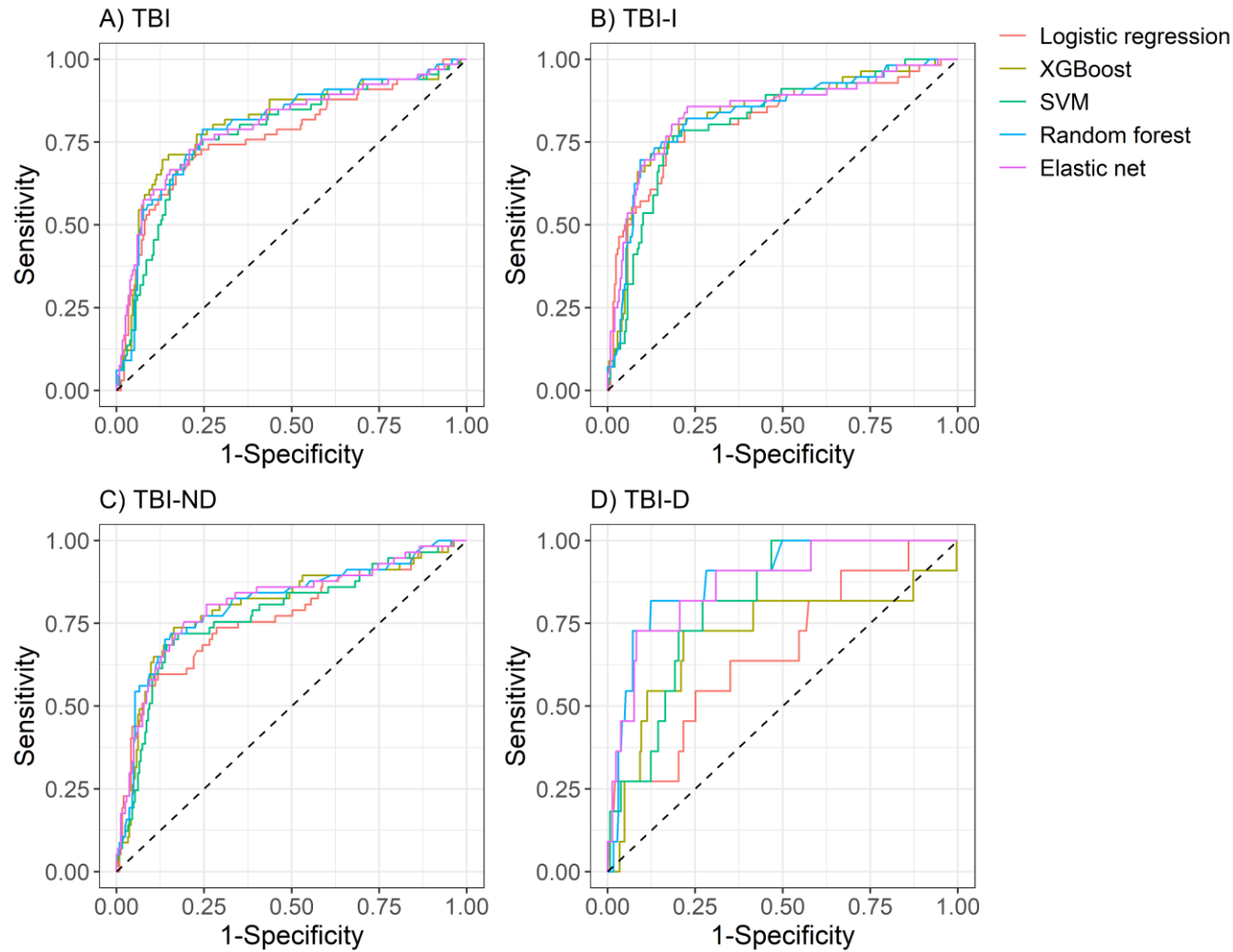
1					
2					
3					
4					
5	Epistaxis	44 (3.8)	30 (3.5)	14 (4.6)	0.36
6	Headache/Paralysis/Dizziness/Vertigo	95 (8.1)	64 (7.4)	31 (10.3)	0.11
7	Nausea/Vomiting	32 (2.7)	20 (2.3)	12 (4.0)	0.13
8	EMS Vital sign assessment				
9		130 (109-		131 (115-	
10	SBP, mmHg	150)	130 (104-146)	150)	<0.01
11	Missing	65 (5.6)	56 (6.5)	9 (3.0)	0.02
12	DBP, mmHg	80 (70-91)	80 (69-90)	80 (70-92)	<0.01
13	Missing	75 (6.4)	65 (7.5)	10 (3.3)	0.01
14	HR, /min	86 (75-99)	86 (74-99)	86 (76-100)	<0.01
15	Missing	31 (2.7)	28 (3.2)	3 (1.0)	0.04
16	RR, /min	18 (16-20)	18 (16-20)	18 (16-20)	<0.01
17	Missing	36 (3.1)	33 (3.8)	3 (1.0)	0.01
18	SpO2, %	98 (95-99)	98 (95-99)	98 (96-99)	<0.01
19	Missing	38 (3.3)	33 (3.8)	5 (1.7)	0.07
20	Temperature, °C	36.5 (36-		36.5 (36-	
21		36.8)	36.5 (36-36.8)	36.7)	<0.01
22	Missing	94 (8.0)	65 (7.5)	29 (9.6)	0.25
23	AVPU scale				<0.01
24	Alert	714 (61.1)	504 (58.1)	210 (69.5)	
25	Verbal	168 (14.4)	136 (15.7)	32 (10.6)	
26	Pain	199 (17.0)	158 (18.2)	41 (13.6)	
27	Unresponsive	88 (7.5)	69 (8.0)	19 (6.3)	
28	Abnormal light reflex	165 (14.1)	132 (15.2)	33 (10.9)	<0.01
29	Missing	66 (5.6)	57 (6.6)	9 (3.0)	
30	GCS scale component				
31	Glasgow coma scale eye				<0.01
32	4	558 (47.7)	380 (43.8)	178 (58.9)	
33	3	128 (10.9)	109 (12.6)	19 (6.3)	
34	2	110 (9.4)	82 (9.5)	28 (9.3)	
35	1	174 (14.9)	141 (16.3)	33 (10.9)	
36	Unknown	199 (17.0)	155 (17.9)	44 (14.6)	
37	Glasgow coma scale Verbal				0.01
38	5	520 (44.5)	359 (41.4)	161 (53.3)	
39	4	118 (10.1)	88 (10.1)	30 (9.9)	
40	3	25 (2.1)	19 (2.2)	6 (2.0)	
41	2	132 (11.3)	105 (12.1)	27 (8.9)	
42	1	174 (14.9)	141 (16.3)	33 (10.9)	
43	Unknown	200 (17.1)	155 (17.9)	45 (14.9)	
44	Glasgow coma scale Motor				<0.01
45	6	499 (42.7)	333 (38.4)	166 (55.0)	
46	5	124 (10.6)	103 (11.9)	21 (7.0)	
47	4	158 (13.5)	123 (14.2)	35 (11.6)	
48	3	47 (4.0)	39 (4.5)	8 (2.6)	
49	2	17 (1.5)	15 (1.7)	2 (0.7)	
50	1	125 (10.7)	99 (11.4)	26 (8.6)	
51	Unknown	199 (17.0)	155 (17.9)	44 (14.6)	
52					
53					
54					
55					
56					
57					
58					
59					
60					

1					
2					
3					
4					
5	EMS management				
6	Intravenous route	176 (15.1)	129 (14.9)	47 (15.6)	0.77
7	Hemorrhage control	586 (50.1)	426 (49.1)	160 (53.0)	0.25
8	Spinal motion restriction	811 (69.4)	606 (69.9)	205 (67.9)	0.51
9	Advanced airway management	4 (0.3)	2 (0.2)	2 (0.7)	0.28
10	Oxygen supply	233 (19.9)	176 (20.3)	57 (18.9)	0.59
11					
12	Field triage decision scheme criteria				
13	Physiological criteria				
14	SBP<90 mmHg	58 (5.0)	42 (4.8)	16 (5.3)	0.75
15	RR<10 or >29 /min	11 (0.9)	11 (1.3)	0 (0.0)	0.08
16	Non-Alert	429 (36.7)	343 (39.6)	86 (28.5)	<0.01
17					
18	Anatomic criteria				
19	All penetrating injuries to head, neck,				
20	torso and extremities proximal to elbow				
21	or knee	34 (2.9)	23 (2.7)	11 (3.6)	0.38
22	Chest wall instability or deformity	4 (0.3)	4 (0.5)	0 (0.0)	0.58
23	Two or more proximal long bone				
24	fractures	19 (1.6)	13 (1.5)	6 (2.0)	0.60
25	Crush, degloved, mangled or				
26	pulseless extremity	15 (1.3)	13 (1.5)	2 (0.7)	0.38
27	Amputation proximal to wrist or ankle	9 (0.8)	9 (1.0)	0 (0.0)	0.12
28	Pelvic fractures	8 (0.7)	6 (0.7)	2 (0.7)	>0.95
29	Open or depressed skull fracture	17 (1.5)	9 (1.0)	8 (2.6)	0.05
30	Paralysis	21 (1.8)	11 (1.3)	10 (3.3)	0.02
31					
32	Mechanism of injury criteria				
33	Fall > 6 meter	113 (9.7)	84 (9.7)	29 (9.6)	>0.95
34					
35	High-risk auto crash	96 (8.2)	73 (8.4)	23 (7.6)	0.66
36	Auto vs pedestrian/bicyclist thrown,				
37	run over, or with significant (>30km/h)				
38	impact	119 (10.2)	83 (9.6)	36 (11.9)	0.25
39	Motorcycle crash > 30 km/hour	105 (9.0)	70 (8.1)	35 (11.6)	0.07
40					
41	ED disposition				0.11
42	Discharge	320 (27.4)	241 (27.8)	79 (26.2)	
43	Transfer	444 (38.0)	316 (36.4)	128 (42.4)	
44	Admitted	366 (31.3)	276 (31.8)	90 (29.8)	
45					
46	In-hospital mortality	90 (7.7)	74 (8.5)	16 (5.3)	0.07
47					
48	Outcomes				
49	TBI	281 (24.0)	215 (24.8)	66 (21.9)	0.30
50	TBI with intracranial injury	251 (21.5)	195 (22.5)	56 (18.5)	0.15
51	TBI-related non-discharge	249 (21.3)	192 (22.1)	57 (18.9)	0.23
52					
53	TBI-related death	43 (3.7)	32 (3.7)	11 (3.6)	>0.95

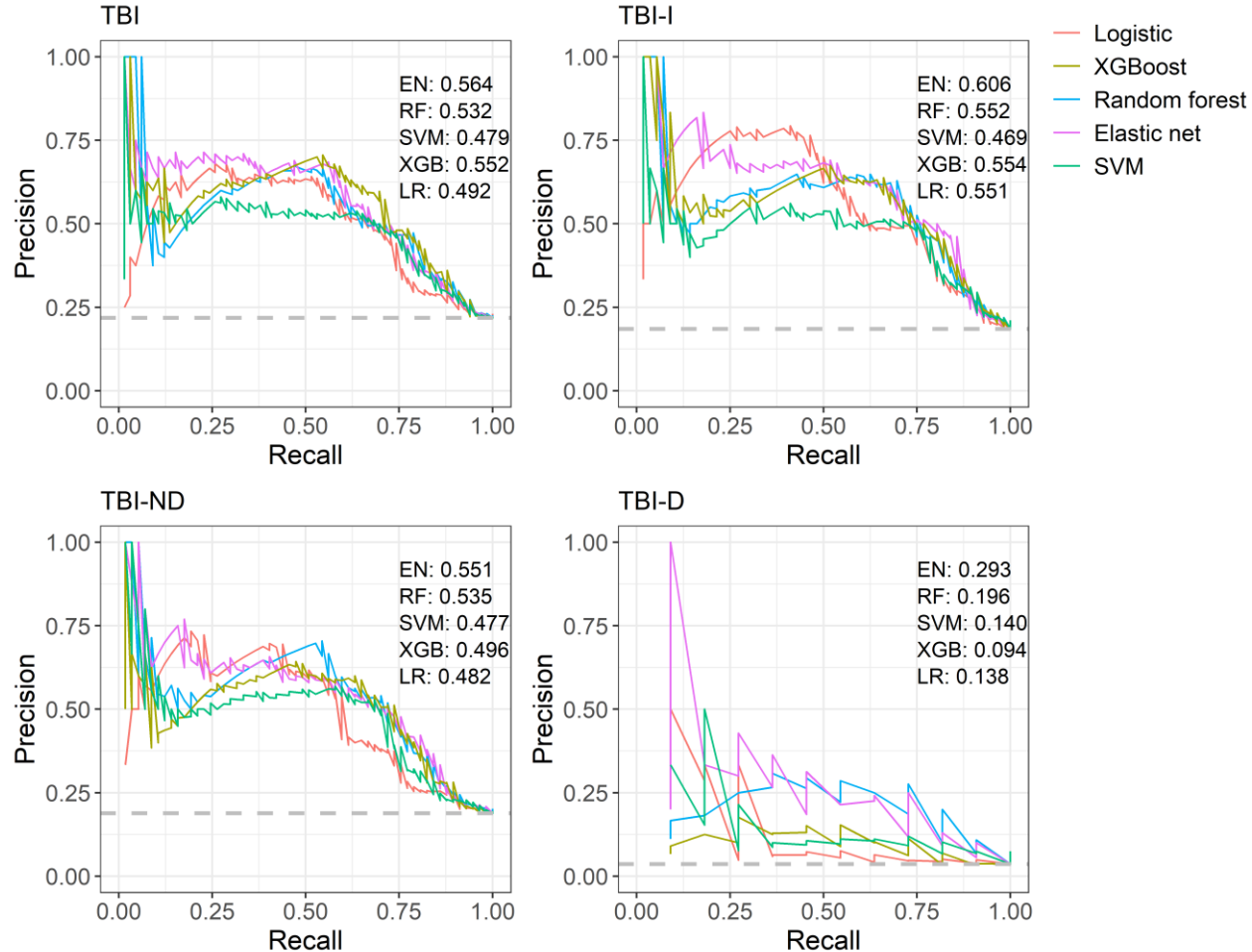
IQR, interquartile range; SBP, systolic blood pressure; RR, respiratory rate; ED, emergency department; TBI,

traumatic brain injury.

Supplementary Figure 1. Receiver operating characteristics of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death.

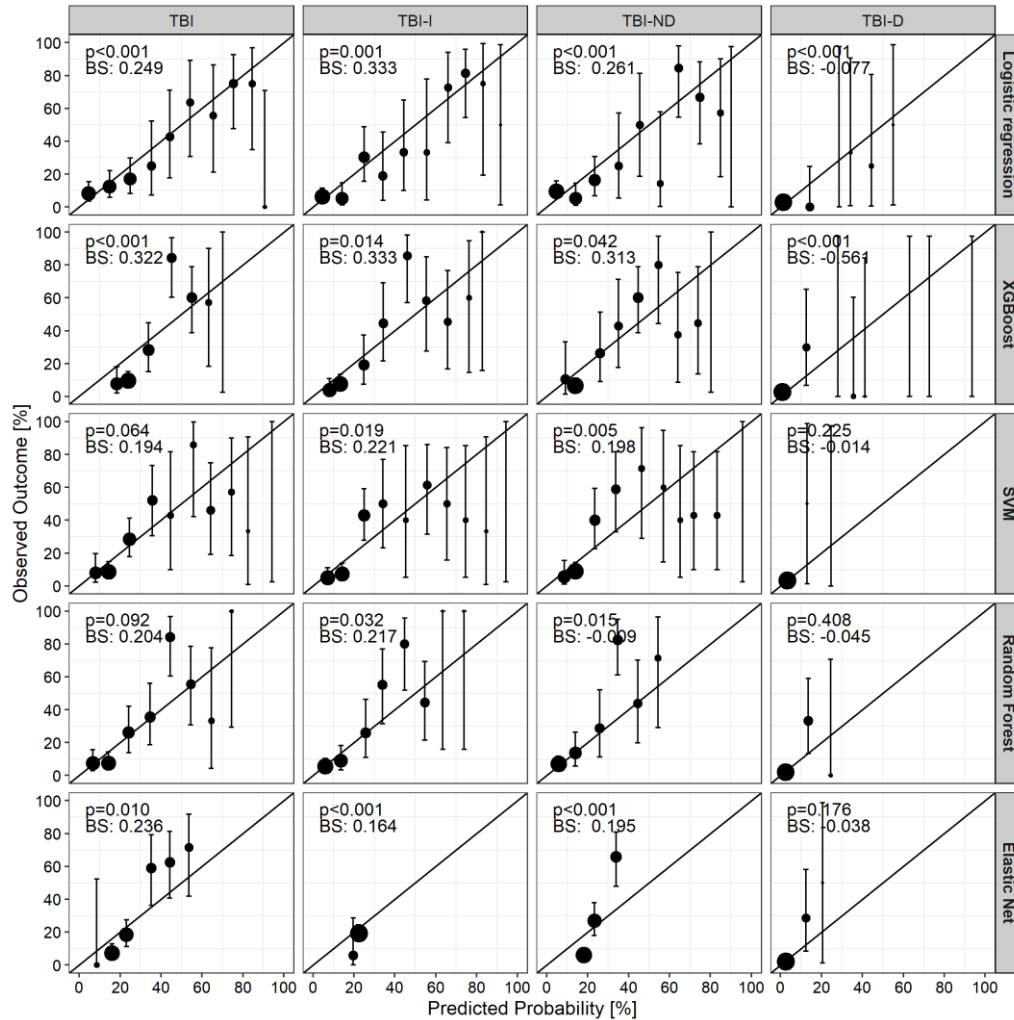


Supplementary Figure 2. Precision-recall curve of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death; LR, logistic regression analysis; XGB, extreme gradient boosting; RF, random forest, EN, elastic net.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

Supplementary Figure 3. Calibration plot of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death; p, p-value of Hosmer-Lemeshow test; BS, scaled Brier score.



TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item	Checklist Item	Page	
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	4
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	7
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	8
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	8-9
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	9
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	8-9
	5b	D;V	Describe eligibility criteria for participants.	10
	5c	D;V	Give details of treatments received, if relevant.	N/A
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	10-11
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	N/A
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	11
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	N/A
Sample size	8	D;V	Explain how the study size was arrived at.	14
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	11
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	11
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	11-12
	10c	V	For validation, describe how the predictions were calculated.	12-13
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12-13
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	N/A
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	N/A
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	12
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	14
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	14
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	14
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	14
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	N/A
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	N/A
	15b	D	Explain how to use the prediction model.	14-15
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	14-15
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	N/A
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	19
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	16-17
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Suppl
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	20

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development and validation of a prehospital-stage prediction tool for traumatic brain injury: a multicentre retrospective cohort study in Korea

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055918.R1
Article Type:	Original research
Date Submitted by the Author:	25-Oct-2021
Complete List of Authors:	Choi, Yeong Ho; Seoul National University Hospital, Emergency Department; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Park, Jeong Ho; Seoul National University Hospital, Emergency Department; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Hong, Ki Jeong; Seoul National University Hospital, Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Ro, Young Sun; Seoul National University Hospital, Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Song, Kyoung Jun; Seoul Metropolitan Boramae Hospital, Department of Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Shin, Sang Do; Seoul National University Hospital, Department of Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services
Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Emergency medicine, Health informatics
Keywords:	ACCIDENT & EMERGENCY MEDICINE, Neurological injury < NEUROLOGY, Trauma management < ORTHOPAEDIC & TRAUMA SURGERY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 1 **Title page**
5
6
7 2
8

9 3 **1. Title**

10
11 4 Development and validation of a prehospital-stage prediction tool for traumatic brain
12
13 5 injury: a multicentre retrospective cohort study in Korea
14
15
16 6

17
18 7 **2. Authors**

19
20 8 Yeong Ho Choi, MD

21
22 9 Department of Emergency Medicine, Seoul National University College of Medicine and
23
24 10 Hospital, Seoul, Republic of Korea

25
26 11 Laboratory of Emergency Medical Services, Seoul National University Hospital

27
28 12 Biomedical Research Institute, Seoul, Korea

29
30 13 E-mail: d2uk87@gmail.com
31
32
33
34 14

35
36 15 Jeong Ho Park, MD

37
38 16 Department of Emergency Medicine, Seoul National University College of Medicine and
39
40 17 Hospital, Seoul, Republic of Korea

41
42 18 Laboratory of Emergency Medical Services, Seoul National University Hospital

43
44 19 Biomedical Research Institute, Seoul, Korea

45
46 20 E-mail: timthe@gmail.com
47
48
49
50 21

51
52 22 Ki Jeong Hong, MD, PhD

53
54 23 Department of Emergency Medicine, Seoul National University College of Medicine and
55
56 24 Hospital, Seoul, Republic of Korea
57
58
59
60

1
2
3
4 25 Laboratory of Emergency Medical Services, Seoul National University Hospital
5
6 26 Biomedical Research Institute, Seoul, Korea
7
8
9 27 E-mail: emkjhong@gmail.com
10
11 28
12
13 29 Young Sun Ro, MD, DrPH
14
15 30 Department of Emergency Medicine, Seoul National University College of Medicine and
16
17 31 Hospital, Seoul, Republic of Korea
18
19 32 Laboratory of Emergency Medical Services, Seoul National University Hospital
20
21 33 Biomedical Research Institute, Seoul, Korea
22
23 34 E-mail: ro.youngsun@gmail.com
24
25 35
26
27 36 Kyoung Jun Song, MD, PhD
28
29 37 Department of Emergency Medicine, Seoul Metropolitan Government Seoul National
30
31 38 University Boramae Medical Center, Seoul, Republic of Korea
32
33 39 Laboratory of Emergency Medical Services, Seoul National University Hospital
34
35 40 Biomedical Research Institute, Seoul, Korea
36
37 41 E-mail: skciva@gmail.com
38
39 42
40
41 43 Sang Do Shin, MD, PhD
42
43 44 Department of Emergency Medicine, Seoul National University College of Medicine and
44
45 45 Hospital, Seoul, Republic of Korea
46
47 46 Laboratory of Emergency Medical Services, Seoul National University Hospital
48
49 47 Biomedical Research Institute, Seoul, Korea
50
51 48 E-mail: shinsangdo@gmail.com
52
53
54
55
56
57
58
59
60

1
2
3
4 495
6 50 **3. Address correspondence and requests for reprints: Jeong Ho Park, MD**7
8
9 51 Address: Seoul National University Hospital, 101 Daehak-Ro, Jongno-Gu, Seoul 03080,10
11 52 Korea12
13 53 Phone: +82-2-2072-180014
15 54 FAX: +82-2-741-785516
17 55 E-mail: timthe@gmail.com18
19
20 5621
22
23 5724
25 58
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 59 **Abstract**

6 60 **Objectives:** Predicting diagnosis and prognosis of traumatic brain injury (TBI) at the
7
8
9 61 prehospital stage is challenging; however, using comprehensive prehospital information and
10
11 62 machine learning may improve the performance of the predictive model. We developed and
12
13 63 tested predictive models for TBI that use machine learning algorithms using information that
14
15
16 64 can be obtained in the prehospital stage.

17
18 65 **Design:** This was a multi-center retrospective study.

19
20 66 **Setting and participants:** This study was conducted at three tertiary academic emergency
21
22 67 departments (EDs) located in an urban area of South Korea. The data from adult patients with
23
24 68 severe trauma who were assessed by emergency medical service (EMS) providers and
25
26
27 69 transported to three participating hospitals between 2014 to 2018 were analyzed.

28
29 70 **Results:** We developed and tested five machine learning algorithms—logistic regression
30
31 71 analyses, extreme gradient boosting, support vector machine, random forest, and elastic net
32
33 72 (EN)—to predict TBI, TBI with intracranial hemorrhage or injury (TBI-I), TBI with
34
35 73 emergency department or admission result of admission or transferred (TBI-ND), and TBI
36
37 74 with emergency department or admission result of death (TBI-D). Of the 1,169 patients in the
38
39 75 development cohort, TBI, TBI-I, TBI-ND, and TBI-D was 24.0%, 21.5%, 21.3%, and 3.7%,
40
41 76 respectively. The EN model yielded an AUROC of 0.799 for TBI, 0.844 for TBI-I, 0.811 for
42
43 77 TBI-ND, and 0.871 for TBI-D. The EN model also yielded the highest specificity, and
44
45
46 78 significant reclassification improvement. Variables related to loss of consciousness, Glasgow
47
48 79 Coma Scale, and light reflex were the three most important variables to predict all outcomes.

49
50 80 **Conclusion:** Our results inform the diagnosis and prognosis of TBI. Machine learning
51
52 81 models resulted in significant performance improvement over that with logistic regression
53
54
55 82 analyses, and the best performing model was EN.
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

83

84 **Keywords:** brain injuries; traumatic; outcome; prognosis; machine learning.

85

86

For peer review only

1
2
3
4 87 **Strengths and limitations of this study**

5
6 88 • This is an original research to develop and internally validate prehospital-stage prediction
7
8 89 models for traumatic brain injury using high dimensional prehospital information.

9
10 90 • Machine learning models showed acceptable-to-excellent discrimination performance.

11
12
13 91 • The retrospective observational study design could lead to certain types of bias (eg,
14
15 92 selection bias, confounding bias).

16
17 93 • External validation for other areas should be conducted to generalize the developed
18
19 94 prediction model.

20
21
22 95
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

96 **Introduction**

97 Traumatic brain injury (TBI) is a significant health burden worldwide.¹ It is the leading cause
98 of mortality and disability among young individuals.² Patients with TBI are vulnerable to
99 hypoxia and hypotension in the early period of their course and these insults are associated
100 with poor outcomes.^{3 4} Prehospital assessment and management of patients with TBI is
101 important,⁵ as early prediction of TBI and correcting hypoxia and hypotension during the
102 prehospital stage could be beneficial.³ However, the identification of TBI can often be
103 challenging in the prehospital area.⁵ Vulnerable patients, including the elderly or patients who
104 take medications like anti-platelet or anticoagulant drugs, often have TBI owing to low
105 energy insults.⁶ Prehospital clinical signs are also reported to have poor sensitivity for raised
106 intracranial pressure following TBI.⁷

107 Several prediction models to target patients with TBI have been reported.⁸⁻¹²
108 However, most incorporated information that is available only in the hospital, such as
109 laboratory results or image findings.^{8 9 13} In addition, most previous prediction models
110 focused on the outcomes of patients with TBI,¹⁴⁻¹⁶ not the identification of TBI. Previously,
111 predictors of older adult patients with TBI who required transport to a trauma center were
112 identified. However, this was consensus-based; therefore, there is a lack of clinical data.¹⁷
113 Accurate prehospital prediction of TBI and its severity could prevent delays to definite care
114 for patients with TBI. Most emergency medical service (EMS) providers collect various
115 information including demographics, past medical history, circumstances of the trauma, and
116 clinical signs including vital signs; but those variables have not been evaluated together as
117 predictors of TBI and its severity. Using a variety of prehospital information, and adapting
118 newly emerging machine learning algorithms for predicting diagnosis, disposition, and
119 outcome of TBI, might improve the accuracy of identification of TBI and its severity.

1
2
3
4 120 The aim of this study was to develop and test prediction models for the diagnosis and
5
6 121 prognosis of TBI using prehospital information and machine learning algorithms among
7
8 122 patients with severe trauma. We hypothesized that incorporating prehospital information
9
10 123 could achieve acceptable performance in predicting TBI, and machine learning algorithms
11
12 124 could contribute to performance improvement.
13
14
15
16

17 125 **Materials and Methods**

18 19 20 126 *Study design and settings*

21
22
23 127 This was a multi-center retrospective study conducted at three tertiary academic emergency
24
25 128 departments (EDs) located in an urban area (Seoul and Bundang) of South Korea. These EDs
26
27 129 received 50,000–90,000 visits annually and are not designated trauma centers. We adhered to
28
29 130 the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or
30
31 131 Diagnosis (TRIPOD) statement on reporting predictive models.¹⁸
32
33

34 132 The EMS system in South Korea is operated by the National Fire Agency. The EMS
35
36 133 level is considered intermediate, as EMS providers can perform bleeding control, spinal
37
38 134 motion restriction, immobilization and splintage, advanced airway management, and
39
40 135 administer fluid intravenously. As only physicians can declare death in South Korea, EMS
41
42 136 providers cannot stop resuscitation and must transport all patients including those in cardiac
43
44 137 arrest to the ED. For all EMS transport, EMS providers record an ambulance run-sheet by
45
46 138 law. Since 2012, the National Fire Agency adapted the United States Centers for Disease
47
48 139 Control and Prevention of the United States field triage decision scheme to evaluate patients
49
50 140 with trauma,¹⁹ and they developed an EMS severe trauma in-depth registry. For said patients,
51
52 141 EMS providers evaluate whether patients met trauma center transport criteria in the field
53
54 142 triage decision scheme. If they did, the in-depth registry should be recorded, and EMS
55
56
57
58
59
60

1
2
3
4 143 transport protocol recommends that patients are transferred to a near regional trauma center;
5
6 144 but it is not mandatory.
7

8
9 145 The Ministry of Health and Welfare designated three ED levels according to the
10
11 146 resources and functional requirements; level 1 (n = 36) and level 2 (n = 118) EDs have more
12
13 147 resources and better facilities for emergency care and must be staffed by emergency
14
15 148 physicians 24 hours a day/365 days a year; whereas level 3 EDs (n = 248) can be staffed by
16
17 149 general physicians. In accordance with the EMS Act, all EDs participated annually in a
18
19 150 nationwide functional performance evaluation program, which was administered by the
20
21 151 Ministry of Health and Welfare. The three participating hospitals in this study were all level 1
22
23 152 EDs that can perform acute trauma care for patients with TBI 24 hours a day/365 days a
24
25 153 year—including emergency neurosurgical operation and angiographic interventions. The
26
27 154 Ministry of Health and Welfare also designated trauma centers in Korea. Total 16 trauma
28
29 155 centers were designated as trauma centers in 2018. Among them, 15 were Level I EDs.
30
31
32
33
34

35 156 ***Data source***

36
37
38 157 We used an EMS ambulance run-sheet, EMS trauma in-depth registry, and ED administrative
39
40 158 database. The EMS database information, including ambulance run-sheet and trauma in-depth
41
42 159 registry, was collected electronically by EMS providers using tablets. The EMS record
43
44 160 review for each severe trauma has been performed by EMS medical directors of each fire
45
46 161 department since 2012. The ED administrative database contains patients' demographic
47
48 162 characteristics, route of visit, time of visit, and diagnosis and disposition. We merged the
49
50 163 EMS database with the ED administrative database based on patients' arrival time, age, and
51
52 164 sex.
53
54
55
56
57
58
59
60

1
2
3
4 165 ***Study population***
5

6
7 166 We included adult (age ≥ 15) EMS users who were transported to participating hospitals with
8
9 167 severe trauma from January 1, 2014 to December 31, 2018. Severe trauma was assessed by
10
11 168 EMS providers and defined as patients who fulfilled trauma center transport criteria
12
13
14 169 (physiologic criteria, anatomic criteria, mechanism of injury criteria, or special patients or
15
16 170 system consideration criteria) in the field triage decision scheme.²⁰ Patients were excluded if
17
18 171 they had out-of-hospital cardiac arrest or their main cause of EMS call was medical or
19
20 172 nontraumatic injury including choking, drowning, fire, flame, heat, cold, poisoning, chemical,
21
22 173 sexual assault, weather, or natural disaster. Patients with an unknown outcome were also
23
24
25 174 excluded.
26
27

28
29 175 ***Outcome measure***
30

31
32 176 The primary outcome measure was the diagnosis of TBI. TBI diagnosis was defined as
33
34 177 patients whose diagnostic code, according to the International Statistical Classification of
35
36 178 Diseases and Related Health Problems (ICD-10), was between S06.0 and S06.9.^{21 22}
37
38
39 179 Although S06.7 is codes for the duration of unconscious, we included S06.7 in our study
40
41 180 outcome according to the previous studies.²¹⁻²³ However, no patients only have S06.7 code
42
43 181 for TBI diagnosis in our study. The ED administrative database has two types of primary
44
45 182 diagnostic codes: the final diagnostic codes at ED discharge and at hospital discharge. We
46
47 183 extracted up to 20 codes for each. We defined the diagnostic code as positive for TBI if a
48
49 184 confirmative diagnostic code was found in any level of the discharge record. Because ICD 10
50
51 185 code is not directly linked to the severity of TBI, we further included a variety of additional
52
53 186 outcome measures to perform analysis that take into account severity. A secondary outcome
54
55 187 measure was TBI diagnosis with intracranial hemorrhage or injury (TBI-I), defined as TBI
56
57
58
59
60

1
2
3
4 188 patients excluding concussion (ICD 10 code with S06.0). A tertiary outcome was TBI with
5
6 189 non-discharge (TBI-ND), defined as TBI patients excluding ED discharged patients. Because
7
8
9 190 TBI-ND patients needed further management by hospitalization or transfer, we thought that
10
11 191 this group of patients had clinically significant severity. A quaternary outcome measure was
12
13 192 TBI with death (TBI-D), defined as TBI patients who died in ED or hospital. Because TBI-D
14
15
16 193 patients are most severe group, TBI-D patients were also included in TBI-ND.

194 ***Variables and preprocessing***

195 We collected patients' demographic data, circumstances of trauma, chief complaints, EMS
196 vital sign assessment, EMS management and hospital outcomes. The detailed descriptions of
197 each variable are described in Supplementary Table 1. Categorical variables were
198 preprocessed with the one-hot encoding (dummy variable encoding) method. Continuous
199 variables were divided into four quantiles and unknown or missing values were categorized
200 as a fifth category. One-hot encoding was also applied to discretized continuous variables.
201 Preprocessing measures including discretization results of continuous variables are presented
202 in Supplementary Table 1.

203 ***Model development***

204 We developed prediction models for outcomes by using five machine learning algorithms:
205 traditional logistic regression analyses (LR), extreme gradient boost (XGB), random forest
206 (RF), support vector machine (SVM), and elastic net (EN). The LR algorithm was chosen as
207 baseline comparison algorithm because it is widely used in the medical field and has been
208 used for previous prediction model development in TBI studies.¹² Backward stepwise LR was
209 selected for feature selection, and we used the default parameter of stepAIC function from
210 MASS package (version 7.3-53.1) in R for the selection. The other four algorithms were

1
2
3
4 211 selected based on their ability to model nonlinear associations, their relative ease of
5
6 212 implementation, and their general acceptance in the machine learning community.²⁴⁻²⁶ All
7
8
9 213 algorithms have a method to calculate the probability of the outcome occurring and
10
11 214 algorithms other than LR need hyperparameter tuning for proper training and prediction.

12
13 215 The study population was split into training cohorts that included development,
14
15 216 validation, and test cohorts. The development cohort included a training cohort from which
16
17 217 each of the machine learning prediction models were derived and a validation cohort in which
18
19 218 the prediction models were applied to adjust the hyperparameters of the algorithm. The test
20
21 219 cohort was used for the final evaluation of the performance of the prediction models.
22
23 220 Chronological split was used for data split. Patients enrolled from January 1, 2014 to
24
25 221 December 31, 2016 were used as the training cohort; patients from January 1, 2017 to
26
27 222 December 31, 2017 were used as the validation cohort; and patients from January 1, 2018 to
28
29 223 December 31, 2018 were used as the test cohort. Hyperparameter tuning using validation data
30
31 224 was conducted by, first, a random search within 10,000 randomly generated hyperparameters;
32
33 225 then, grid search hyperparameters chosen around from random search with five candidates
34
35 226 per each hyperparameter. Finally, hyperparameter with best area under receiver-operation
36
37 227 curve (AUROC) in validation cohorts were selected. Test data were separated during training
38
39 228 and tuning processes and used to measure algorithm performance.
40
41
42
43
44
45
46

47 229 ***Statistical analysis***

48
49 230 The demographic findings and outcomes of the study population were described in this study.
50
51 231 Additionally, the baseline characteristics of the training cohort and the validation cohort were
52
53 232 compared. The continuous variables were compared by using Student's T-test or the
54
55 233 Wilcoxon rank sum test, and the categorical variables were compared by using the chi-
56
57 234 squared test or the Fisher exact test, as appropriate.
58
59
60

1
2
3
4 235 We assessed discrimination performance by comparing the AUROC for each model
5
6 236 in the test cohort. We considered an AUROC of 0.5 as no discrimination, 0.7 to 0.8 as
7
8
9 237 acceptable, 0.8 to 0.9 as excellent, and more than 0.9 is considered outstanding.²⁷ Area under
10
11 238 the precision-recall curve (AUPRC) was assessed for each model in the test cohort. We
12
13 239 assessed the calibration power by using the Hosmer–Lemeshow test, the scaled Brier score,
14
15 240 and a calibration plot in the test cohort. For the delineation of test characteristics, the
16
17 241 sensitivity, specificity, and positive and negative predictive values with 95% CIs were
18
19
20 242 determined using a cutoff probability at a sensitivity of 80%. Given that poor sensitivity of
21
22 243 clinical predictors for TBI in previous studies,⁷ and almost 75% sensitivity level for other
23
24 244 severe disease prediction in prehospital settings,^{28 29} we thought that 80% sensitivity was an
25
26 245 appropriate target for our prediction model. We calculated false positive rate as 1 –
27
28
29 246 specificity. The added prognostic power of each prediction model compared to the LR model
30
31 247 was also evaluated by continuous net reclassification index (NRI). NRI is a statistical method
32
33 248 to quantify how well a new model correctly reclassifies the study population with the other
34
35 249 models. Details of NRI are described elsewhere.³⁰

36
37
38
39 250 By using a model-specific metric, the variable importance of each model was
40
41 251 assessed, except for the SVM algorithm. The variable importance was determined by the
42
43 252 coefficient effect sizes for the LR model. The XGB and RF models were ranked by variable
44
45 253 importance on the selection frequency of the variable as a decision node. The absolute value
46
47 254 of the coefficients corresponding to the tuned model were used for the measurement of
48
49 255 variable importance in the EN algorithm. To compare the variable importance of each
50
51 256 prediction models efficiently, top 5 variables of each model was presented.
52
53
54
55
56
57
58
59
60

1
2
3
4 257 All statistical analyses were performed with R Statistical Software (version 4.0.1; R
5
6 258 Foundation for Statistical Computing, Vienna, Austria). Packages included caret, e1071,
7
8
9 259 xgboost, randomForest, and glmnet for the analysis of the machine learning algorithms.
10
11

12 260 *Patient and public involvement*

13
14 261 This research was done without patient involvement. Patients were not invited to comment on
15
16
17 262 the study design and were not consulted to develop patient relevant outcomes or interpret the
18
19 263 results. Patients were not invited to contribute to the writing or editing of this document for
20
21 264 readability or accuracy.
22
23

24 265

25 26 27 266 **Result**

28 29 30 267 *Demographic findings*

31
32
33 268 Among the 157,134 EMS users transported to three hospitals from 2014 to 2018, 1,169
34
35 269 patients were included in the final analysis (Figure 1). Patients were split into 2 datasets: data
36
37
38 270 from 2014 to 2017, consisting of 867 patients (74.2%) in the development cohort; and the
39
40 271 remaining data from 2018 consisting of 302 patients (25.8%) in the test cohort (Figure 1).
41
42 272 Among the development cohort, data from 2014 to 2016—consisting of 661 patients—were
43
44 273 used as the training cohort, and 2017 data—consisting of 206 patients—were used as the
45
46 274 validation cohort in the model.
47
48

49 275 Table 1 shows key demographic findings of the development and test cohorts. Median
50
51 276 (IQR) age was 52 years (35–66) in the development cohort and 56 years (40–69) in the test
52
53 277 cohort. Traffic accident was most common mechanism of trauma (43.3% for the development
54
55 278 cohort and 41.4% for the test cohort). The proportion of patients with alert mental status was
56
57
58
59
60

1
2
3
4 279 58.1% for the development cohort and 69.5% in the test cohort. Overall, TBI, TBI-I, TBI-
5
6 280 ND, TBI-D occurred in 215 (24.8%), 195 (22.5%), 192 (22.1%), and 32 (3.7%) in the
7
8 281 development cohort; and 66 (21.9%), 56 (18.5%), 57 (18.9%), and 11 (3.6%) in the test
9
10 282 cohort. All demographic characteristics of the development and test cohorts are described in
11
12 283 Supplementary Table 2.

17 284 *Main analysis*

18
19
20 285 The final hyperparameters of prediction models are described in Supplementary Table 3. The
21
22 286 discrimination and NRI of the prediction models on the test cohort are presented in Table 2.
23
24 287 The AUROC for outcomes were 0.770–0.806 for TBI, 0.820–0.844 for TBI-I, 0.767–0.811
25
26 288 for TBI-ND, and 0.664–0.889 for TBI-D (Table 2 and Supplementary Figure 1). Compared to
27
28 289 LR, XGB performed significantly well in predicting TBI, and RF and EN performed well in
29
30 290 predicting TBI-ND and TBI-D. EN model generally performed well on all outcomes. The
31
32 291 AUROC of the EN model for outcomes were 0.799 (95% CI: 0.732–0.867), 0.844 (95% CI:
33
34 292 0.779–0.910), 0.811 (95% CI: 0.741–0.882), and 0.871 (95% CI: 0.764–0.978) for TBI, TBI-
35
36 293 I, TBI-ND, and TBI-D, respectively. Machine learning models generally resulted in
37
38 294 significant reclassification improvement compared to LR for TBI, TBI-I, and TBI-ND. For
39
40 295 prediction TBI-D, AUROC difference, and reclassification improvement compared to LR
41
42 296 was non-significant in all machine learning models. The precision-recall curve is shown in
43
44 297 Supplementary Figure 2. AUPRC were 0.479–0.564 for TBI, 0.469–0.606 for TBI-I, 0.477–
45
46 298 0.551 for TBI-ND and 0.094–0.140 for TBI-D. EN model showed highest AUPRC among all
47
48 299 prediction models. Supplementary Figure 3 shows the calibration plot of prediction models
49
50 300 according to outcomes. All prediction models generally showed poor calibration. Given the
51
52 301 high AUROC and AUPRC among prediction models, and reclassification improvement
53
54
55
56
57
58
59
60

1
2
3
4 302 compared to LR, we determined EN as a best-performing prediction model in our analysis.

5
6 303 Using cutoff of 80% sensitivity, specificity was 47.5–68.2% for TBI, 71.1–81.3% for
7
8 304 TBI-I, 46.1–74.3% for TBI-ND, and 42.6–.0 for TBI-D. EN showed the highest specificity
9
10 305 and PPV among all outcomes. False positive rate (1 – specificity) was almost 19.7–39.0%
11
12 306 according to outcomes in the EN model. The 95% CI of specificity of the EN model was not
13
14 307 overlapped with LR in TBI, TBI-ND, and TBI-D predictions. NPV was almost 89–99% for
15
16 308 all outcomes in the prediction models (Table 3).

17
18 309 Table 4 shows the top 5 variable importance of prediction models according to
19
20 310 outcomes. Variables related to patients' symptom of loss of consciousness, Glasgow Coma
21
22 311 Scale component, and light reflex were the three most important variables to predict all
23
24 312 outcomes. Compared to other outcomes, the difference between variable importance for TBI-
25
26 313 D was prominent, and the mechanism of injury, heart rate, and age showed the highest
27
28 314 importance for predicting TBI-D.

35 315 **Discussion**

36
37 316 By using prehospital data from EMS users visiting three teaching hospitals, we developed
38
39 317 and validated prediction models for the diagnosis and prognosis of TBI using machine
40
41 318 learning algorithms among patients with severe trauma, identified by EMS providers in South
42
43 319 Korea. We found that 24% of patients were diagnosed with TBI, 22% showed intracranial
44
45 320 injury, 21% could not be discharged from the ED with a TBI diagnosis, and 4% showed TBI-
46
47 321 related death. Machine learning models showed acceptable-to-excellent discrimination
48
49 322 performance (AUROCs were 0.799–0.871 according to outcomes in the best-performing EN
50
51 323 model). When identifying 80% of target patients with TBI, the false positive rate was almost
52
53 324 19.7–39.0%. Consciousness status related variables ranging from patients' symptom to EMS
54
55
56
57
58
59
60

1
2
3
4 325 providers' assessment showed the highest importance for predicting all outcomes. This study
5
6 326 adds considerably to the understanding of prehospital prediction performance of TBI among
7
8
9 327 patients with severe trauma. Use of comprehensive prehospital information and certain
10
11 328 machine learning approaches led to increased performance with a diminished false positive
12
13 329 rate compared to those of the traditional statistical model.

15
16 330 Several studies reported that EMS providers' assessment using prehospital
17
18 331 information is effective for the identification of patients with severe trauma who require
19
20 332 direct transport to a trauma center.³¹⁻³³ Because TBI accounts for a significant portion of
21
22 333 patients with severe trauma,³² and the majority of patients have poor access to trauma
23
24 334 centers,³⁴ identification of TBI among patients with severe trauma by EMS providers could
25
26 335 contribute to proper prehospital management and destination hospital decisions.³ However,
27
28 336 prehospital identification of TBI is challenging.³⁵ Prehospital clinical signs showed poor
29
30 337 predictive performance for differentiating patients with TBI.⁷, and previous prediction
31
32 338 models related to TBI mostly focused on TBI outcomes.^{8 9 13} One study reported the
33
34 339 predictors for mild TBI with persistent symptoms; but a single-center case-control study
35
36 340 design and ED-based model development lacks applicability to prehospital settings.³⁶ In this
37
38 341 study, we developed and tested TBI prediction models that used prehospital information, and
39
40 342 we found acceptable discrimination power for the prediction of diagnosis and prognosis of
41
42 343 TBI. Uniquely, we incorporated various demographic variables, trauma circumstances,
43
44 344 patients' complaints, and EMS assessment information in the prediction models, and we
45
46 345 adapted the machine learning algorithms.

47
48 346 When using a cutoff for 80% sensitivity for TBI detection, the false positive rate was
49
50 347 19.7–39.0% (Table 2). Those false positive rate levels are plausible for detecting severe
51
52 348 diseases in EMS settings. A previous study reported a 26% of false positive rate of EMS
53
54
55
56
57
58
59
60

1
2
3
4 349 triage for myocardial infarction with a sensitivity of 74% and 50% of false positive rate of
5
6 350 EMS recognition of stroke in sensitivity of 74%.^{28 29} Considering the prevalence of outcomes
7
8 351 (24% in TBI, 22% in TBI-I, 21% in TBI-ND, and 4% in TBI-D; Table 1), there would be 16,
9
10 352 9, 12, and 67 false-positive patients for every 10 patients that are accurately identified as TBI,
11
12 353 TBI-I, TBI-ND, and TBI-D, respectively (Supplementary Table 4). Because of the low
13
14 354 prevalence of TBI-D, a similar specificity of the prediction model for outcomes resulted in a
15
16 355 very low positive predictive value and a high proportion of false positive cases, which
17
18 356 suggested the limited applicability of prediction models for TBI-D in prehospital settings.

19
20 357 Consciousness-status-related variables ranging from patients' complaints to EMS
21
22 358 assessment showed the highest importance regardless of models and outcomes in our study.
23
24 359 Consciousness status is closely associated with head trauma. Head trauma can result in
25
26 360 structural brain injury or physiological disruption of brain function, which could result in
27
28 361 altered mental status.³⁷ Mental status is also associated with TBI severity,³⁸ and its
29
30 362 association with TBI outcomes have been reported.^{8 9 13} History taking and physical
31
32 363 examination for altered mental status is key to early diagnosis and proper management of TBI
33
34 364 in prehospital settings.³⁹

35
36 365 We adapted machine learning algorithms for the prediction of TBI-related outcomes
37
38 366 and found an improvement in discrimination and an increase in specificity with the same
39
40 367 sensitivity thresholds. However, the LR model also showed acceptable or similar
41
42 368 performance compared to machine learning models, according to the outcomes. In clinical
43
44 369 prediction models, a previous systematic review reported no performance benefit of the
45
46 370 machine learning model over LR.⁴⁰ The previous study stated that machine learning models
47
48 371 tend to show high performance with a strong signal-to-noise ratio problem like gaming,
49
50 372 image recognition. However, clinical prediction problems often result in a poor signal-to-

1
2
3
4 373 noise ratio.⁴⁰ If we could use unstructured data, which has strong signal-to-noise ratio like
5
6 374 continuous vital sign monitoring data or audiovisual data for patients' appearance, machine
7
8
9 375 learning models might perform better than LR models. In addition, if we analyzed more
10
11 376 patient data, the performance improvement of machine models might be elucidated.

12
13 377 Precise assessment in prehospital field could contribute to improved patient-related
14
15 378 outcomes. High demand of EMS call and response, disparity in accessibility to definitive care
16
17 379 capable hospitals according to regions,³⁴ and the importance of timely management in acute
18
19 380 disease care are the chief reasons behind the necessity for the accurate assessment of EMS
20
21 381 providers. Although information acquisition and processing is quite difficult in prehospital
22
23 382 areas, various instruments and information systems could attribute to diminish those
24
25 383 problems. Complex data acquisition like mobile CT or other unstructured data⁴¹, information
26
27 384 sharing through telemedicine,⁴² and decision support tools in prehospital environments⁴³
28
29 385 could contribute to the accurate assessment of EMS providers. More information acquisition
30
31 386 and real-time processing of those data could improve the clinical prediction models in
32
33 387 prehospital areas, which could lead to the improvement of patients' safety and outcomes.

34
35 388 Our study had several limitations. First, our data were collected at three teaching
36
37 389 hospitals in urban areas of South Korea. Therefore, external validation for other areas should
38
39 390 be conducted to generalize the developed prediction model. Second, we used retrospective
40
41 391 analysis of electronically collected prehospital and hospital data. There might be various
42
43 392 information loss and missing data. We treated missing status as a separate category for our
44
45 393 analysis;⁴⁴ however, there could be different reasons for missing data. Third, there is a
46
47 394 possibility that the prediction model was overfitted or underfitted. The use of large number of
48
49 395 predictors also can contribute to overfitting. To minimize this issue, we rigorously searched
50
51 396 hyperparameters and carefully chose hyperparameters according to the performance in
52
53
54
55
56
57
58
59
60

1
2
3
4 397 independent validation cohorts. Fourth, we selected our study population using trauma center
5
6 398 transport criteria for EMS providers in Korea. Although those criteria are based on the field
7
8 399 triage decision scheme which is the most widely used prehospital trauma triage protocol,⁶
9
10 400 extrapolation to another EMS setting or general trauma patients would be limited. Fifth,
11
12 401 Abbreviated Injury Scale (AIS) codes were not used to identify our study outcome because of
13
14 402 a lack of information. To compensate for this limitation, we further identified TBI-I, TBI-
15
16 403 ND, and TBI-D patients to consider severity. However, different definitions of clinical
17
18 404 severity, including ICU admission or emergency operation, might be possible. Lastly, this
19
20 405 study was performed in an intermediate-service-level EMS system. The generalization of our
21
22 406 study findings to different EMS settings should be made with caution.

27 407 In conclusion, we presented data on TBI among patients with severe trauma assessed
28
29 408 by EMS providers, and our results inform the development of prediction models for the
30
31 409 diagnosis and prognosis of TBI in our population. We used various information that can be
32
33 410 obtained in prehospital settings and showed acceptable outcome performance. The consistent
34
35 411 importance of consciousness-status-related variables emphasizes the importance of
36
37 412 assessment and monitoring of consciousness status in prehospital areas. Although
38
39 413 prospective, and implementation studies are needed for TBI prediction in prehospital areas,
40
41 414 our study outlined a novel method for the precise assessment of EMS providers using a
42
43 415 machine-learning-based prediction model. Further collection of various types of patient-
44
45 416 related data would contribute to the enhanced performance of the clinical prediction model in
46
47 417 prehospital settings.

52 418

1
2
3
4 419 **Author Contribution Statement**
5

6
7 420 YHC and JH Park designed and developed the study, analysed and interpreted the data, and
8
9 421 drafted the initial manuscript. KJH, YSR, KJS and SDS were involved in the acquisition of
10
11 422 data, the development of the research question and assisted with analysis and interpretation of
12
13
14 423 data. All authors revised the drafts for intellectual content and edited the manuscript. All
15
16 424 authors reviewed and approved the final draft.
17
18
19
20 425
21
22

23 426 **Funding**
24

25
26 427 This study was supported by grant No. '04-2019-0680' from the Seoul National University
27
28 428 Hospital Research Fund.
29
30
31 429
32
33

34 430 **Competing Interests**
35

36 431 There are no conflicts of interest for all authors in this study.
37
38
39 432
40

41 433 **Patients consent**
42

43 434 Not required
44
45
46 435
47
48

49 436 **Data availability statement**
50

51 437 No data are available. We do not have ethics approval to share data.
52
53
54 438
55
56
57
58
59
60

1
2
3
4 439 **Ethical statements**

5
6 440 This study complied with the Declaration of Helsinki, and its protocol was approved by the
7
8 441 Institutional Review Board of the Seoul National University Hospital with a waiver of
9
10 442 informed consent (IRB No: E-2006-004-1128).
11
12

13 443

14
15
16
17 444 **References**

- 18
19 445 1. Hsia RY, Markowitz AJ, Lin F, et al. Ten-year trends in traumatic brain injury: a
20
21 446 retrospective cohort study of California emergency department and hospital revisits and
22
23 447 readmissions. *BMJ Open* 2018;8(12):e022297. doi: 10.1136/bmjopen-2018-022297
24
25 448 [published Online First: 2018/12/16]
26
27
28 449 2. Finfer SR, Cohen J. Severe traumatic brain injury. *Resuscitation* 2001;48(1):77-90. doi:
29
30 450 10.1016/s0300-9572(00)00321-x [published Online First: 2001/02/13]
31
32
33 451 3. Spaite DW, Bobrow BJ, Keim SM, et al. Association of Statewide Implementation of the
34
35 452 Prehospital Traumatic Brain Injury Treatment Guidelines With Patient Survival
36
37 453 Following Traumatic Brain Injury: The Excellence in Prehospital Injury Care (EPIC)
38
39 454 Study. *JAMA Surg* 2019;154(7):e191152. doi: 10.1001/jamasurg.2019.1152 [published
40
41 455 Online First: 2019/05/09]
42
43
44 456 4. McHugh GS, Engel DC, Butcher I, et al. Prognostic value of secondary insults in traumatic
45
46 457 brain injury: results from the IMPACT study. *J Neurotrauma* 2007;24(2):287-93. doi:
47
48 458 10.1089/neu.2006.0031 [published Online First: 2007/03/23]
49
50
51 459 5. Pelieu I, Kull C, Walder B. Prehospital and Emergency Care in Adult Patients with Acute
52
53 460 Traumatic Brain Injury. *Med Sci (Basel)* 2019;7(1) doi: 10.3390/medsci7010012
54
55 461 [published Online First: 2019/01/24]
56
57
58 462 6. Sasser SM, Hunt RC, Faul M, et al. Guidelines for field triage of injured patients:
59
60

- 1
2
3
4 463 recommendations of the National Expert Panel on Field Triage, 2011. *Morbidity and*
5
6 464 *Mortality Weekly Report: Recommendations and Reports* 2012;61(1):1-20.
7
8
9 465 7. Ter Avest E, Taylor S, Wilson M, et al. Prehospital clinical signs are a poor predictor of
10
11 466 raised intracranial pressure following traumatic brain injury. *Emerg Med J*
12
13 467 2021;38(1):21-26. doi: 10.1136/emmermed-2020-209635 [published Online First:
14
15 468 2020/09/20]
16
17
18 469 8. Collaborators MCT, Perel P, Arango M, et al. Predicting outcome after traumatic brain injury:
19
20 470 practical prognostic models based on large cohort of international patients. *BMJ*
21
22 471 2008;336(7641):425-9. doi: 10.1136/bmj.39461.643438.25 [published Online First:
23
24 472 2008/02/14]
25
26
27 473 9. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain
28
29 474 injury: development and international validation of prognostic scores based on
30
31 475 admission characteristics. *PLoS Med* 2008;5(8):e165; discussion e65. doi:
32
33 476 10.1371/journal.pmed.0050165 [published Online First: 2008/08/08]
34
35
36 477 10. Gozt AK, Hellewell SC, Thorne J, et al. Predicting outcome following mild traumatic brain
37
38 478 injury: protocol for the longitudinal, prospective, observational Concussion Recovery
39
40 479 (CREST) cohort study. *BMJ Open* 2021;11(5):e046460. doi: 10.1136/bmjopen-2020-
41
42 480 046460 [published Online First: 2021/05/15]
43
44
45 481 11. Huth SF, Slater A, Waak M, et al. Predicting Neurological Recovery after Traumatic Brain
46
47 482 Injury in Children: A Systematic Review of Prognostic Models. *J Neurotrauma*
48
49 483 2020;37(20):2141-49. doi: 10.1089/neu.2020.7158 [published Online First: 2020/05/29]
50
51
52 484 12. Perel P, Edwards P, Wentz R, et al. Systematic review of prognostic models in traumatic
53
54 485 brain injury. *BMC Med Inform Decis Mak* 2006;6:38. doi: 10.1186/1472-6947-6-38
55
56 486 [published Online First: 2006/11/16]
57
58
59
60

- 1
2
3
4 487 13. Miller PR, Chang MC, Hoth JJ, et al. Predicting Mortality and Independence at Discharge
5
6 488 in the Aging Traumatic Brain Injury Population Using Data Available at Admission. *J*
7
8 489 *Am Coll Surg* 2017;224(4):680-85. doi: 10.1016/j.jamcollsurg.2016.12.053 [published
9
10 Online First: 2017/03/07]
11 490
12
13 491 14. Abujaber A, Fadlalla A, Gammoh D, et al. Prediction of in-hospital mortality in patients
14
15 492 with post traumatic brain injury using National Trauma Registry and Machine Learning
16
17 493 Approach. *Scand J Trauma Resusc Emerg Med* 2020;28(1):44. doi: 10.1186/s13049-
18
19 494 020-00738-5 [published Online First: 2020/05/29]
20
21
22 495 15. Gravesteijn BY, Nieboer D, Ercole A, et al. Machine learning algorithms performed no
23
24 496 better than regression models for prognostication in traumatic brain injury. *J Clin*
25
26 497 *Epidemiol* 2020;122:95-107. doi: 10.1016/j.jclinepi.2020.03.005 [published Online
27
28 498 First: 2020/03/24]
29
30
31 499 16. Roozenbeek B, Lingsma HF, Lecky FE, et al. Prediction of outcome after moderate and
32
33 500 severe traumatic brain injury: external validation of the International Mission on
34
35 501 Prognosis and Analysis of Clinical Trials (IMPACT) and Corticoid Randomisation
36
37 502 After Significant Head injury (CRASH) prognostic models. *Crit Care Med*
38
39 503 2012;40(5):1609-17. doi: 10.1097/CCM.0b013e31824519ce [published Online First:
40
41 504 2012/04/19]
42
43
44 505 17. Wasserman EB, Shah MN, Jones CM, et al. Identification of a neurologic scale that
45
46 506 optimizes EMS detection of older adult traumatic brain injury patients who require
47
48 507 transport to a trauma center. *Prehosp Emerg Care* 2015;19(2):202-12. doi:
49
50 508 10.3109/10903127.2014.959225 [published Online First: 2014/10/08]
51
52
53 509 18. Collins GS, Reitsma JB, Altman DG, et al. Transparent Reporting of a multivariable
54
55 510 prediction model for Individual Prognosis Or Diagnosis (TRIPOD). *Ann Intern Med*
56
57
58
59
60

- 1
2
3
4 511 2015;162(10):735-6. doi: 10.7326/L15-5093-2 [published Online First: 2015/05/20]
5
6 512 19. Sasser SM, Hunt RC, Sullivent EE, et al. Guidelines for field triage of injured patients:
7
8 513 recommendations of the National Expert Panel on Field Triage. 2009
9
10 514 20. Sasser SM, Hunt RC, Faul M, et al. Guidelines for field triage of injured patients:
11
12 515 recommendations of the National Expert Panel on Field Triage, 2011. *MMWR Recomm*
13
14 516 *Rep* 2012;61(RR-1):1-20. [published Online First: 2012/01/13]
15
16 517 21. Andelic N, Anke A, Skandsen T, et al. Incidence of hospital-admitted severe traumatic
17
18 518 brain injury and in-hospital fatality in Norway: a national cohort study.
19
20 519 *Neuroepidemiology* 2012;38(4):259-67. doi: 10.1159/000338032 [published Online
21
22 520 First: 2012/06/09]
23
24 521 22. Ro YS, Shin SD, Holmes JF, et al. Comparison of clinical performance of cranial computed
25
26 522 tomography rules in patients with minor head injury: a multicenter prospective study.
27
28 523 *Acad Emerg Med* 2011;18(6):597-604. doi: 10.1111/j.1553-2712.2011.01094.x
29
30 524 [published Online First: 2011/06/17]
31
32 525 23. Chan V, Thuraiajah P, Colantonio A. Defining pediatric traumatic brain injury using
33
34 526 International Classification of Diseases Version 10 Codes: a systematic review. *BMC*
35
36 527 *Neurol* 2015;15:7. doi: 10.1186/s12883-015-0259-7 [published Online First:
37
38 528 2015/02/05]
39
40 529 24. Zou H, Hastie T. Regularization and variable selection via the elastic net. *Journal of the*
41
42 530 *Royal Statistical Society: Series B (Statistical Methodology)* 2005;67(2):301-20. doi:
43
44 531 10.1111/j.1467-9868.2005.00503.x
45
46 532 25. Hearst MA, Dumais ST, Osuna E, et al. Support vector machines. *IEEE Intelligent Systems*
47
48 533 *and their Applications* 1998;13(4):18-28. doi: 10.1109/5254.708428
49
50 534 26. Chen T, Guestrin C. XGBoost: A Scalable Tree Boosting System. Proceedings of the 22nd
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 535 ACM SIGKDD International Conference on Knowledge Discovery and Data Mining.
5
6 536 San Francisco, California, USA: Association for Computing Machinery, 2016:785–94.
7
8
9 537 27. Menard S. Applied logistic regression analysis: Sage 2002. pp. 162.
10
11 538 28. Oostema JA, Konen J, Chassee T, et al. Clinical predictors of accurate prehospital stroke
12
13 539 recognition. *Stroke* 2015;46(6):1513-7. doi: 10.1161/STROKEAHA.115.008650
14
15 540 [published Online First: 2015/04/30]
16
17
18 541 29. Swan PY, Nighswonger B, Boswell GL, et al. Factors associated with false-positive
19
20 542 emergency medical services triage for percutaneous coronary intervention. *West J*
21
22 543 *Emerg Med* 2009;10(4):208-12. [published Online First: 2010/01/05]
23
24
25 544 30. Park JH, Shin SD, Song KJ, et al. Prediction of good neurological recovery after out-of-
26
27 545 hospital cardiac arrest: A machine learning analysis. *Resuscitation* 2019;142:127-35.
28
29 546 doi: 10.1016/j.resuscitation.2019.07.020 [published Online First: 2019/07/31]
30
31
32 547 31. Esposito TJ, Offner PJ, Jurkovich GJ, et al. Do prehospital trauma center triage criteria
33
34 548 identify major trauma victims? *Arch Surg* 1995;130(2):171-6. doi:
35
36 549 10.1001/archsurg.1995.01430020061010 [published Online First: 1995/02/01]
37
38
39 550 32. Ocak G, Sturms LM, Hoogeveen JM, et al. Prehospital identification of major trauma
40
41 551 patients. *Langenbecks Arch Surg* 2009;394(2):285-92. doi: 10.1007/s00423-008-0340-
42
43 552 4 [published Online First: 2008/06/27]
44
45
46 553 33. Fries GR, McCalla G, Levitt MA, et al. A prospective comparison of paramedic judgment
47
48 554 and the trauma triage rule in the prehospital setting. *Ann Emerg Med* 1994;24(5):885-
49
50 555 9. doi: 10.1016/s0196-0644(94)70207-1 [published Online First: 1994/11/01]
51
52
53 556 34. Branas CC, MacKenzie EJ, Williams JC, et al. Access to trauma centers in the United States.
54
55 557 *JAMA* 2005;293(21):2626-33. doi: 10.1001/jama.293.21.2626 [published Online First:
56
57 558 2005/06/02]
58
59
60

- 1
2
3
4 559 35. Whiting MD, Dengler BA, Rodriguez CL, et al. Prehospital Detection of Life-Threatening
5
6 560 Intracranial Pathology: An Unmet Need for Severe TBI in Austere, Rural, and Remote
7
8 561 Areas. *Front Neurol* 2020;11:599268. doi: 10.3389/fneur.2020.599268 [published
9
10 Online First: 2020/11/17]
11 562
12
13 563 36. Wojcik SM. Predicting mild traumatic brain injury patients at risk of persistent symptoms
14
15 564 in the Emergency Department. *Brain Inj* 2014;28(4):422-30. doi:
16
17 565 10.3109/02699052.2014.884241 [published Online First: 2014/02/26]
18
19
20 566 37. Management of Concussion/m TBIWG. VA/DoD Clinical Practice Guideline for
21
22 567 Management of Concussion/Mild Traumatic Brain Injury. *J Rehabil Res Dev*
23
24 568 2009;46(6):CP1-68. [published Online First: 2010/01/30]
25
26
27 569 38. Grote S, Bocker W, Mutschler W, et al. Diagnostic value of the Glasgow Coma Scale for
28
29 570 traumatic brain injury in 18,002 patients with severe multiple injuries. *J Neurotrauma*
30
31 571 2011;28(4):527-34. doi: 10.1089/neu.2010.1433 [published Online First: 2011/01/27]
32
33
34 572 39. Badjatia N, Carney N, Crocco TJ, et al. Guidelines for prehospital management of traumatic
35
36 573 brain injury 2nd edition. *Prehosp Emerg Care* 2008;12 Suppl 1:S1-52. doi:
37
38 574 10.1080/10903120701732052 [published Online First: 2008/09/06]
39
40
41 575 40. Christodoulou E, Ma J, Collins GS, et al. A systematic review shows no performance
42
43 576 benefit of machine learning over logistic regression for clinical prediction models. *J*
44
45 577 *Clin Epidemiol* 2019;110:12-22. doi: 10.1016/j.jclinepi.2019.02.004 [published Online
46
47 First: 2019/02/15]
48 578
49
50 579 41. Nakada TA, Masunaga N, Nakao S, et al. Development of a prehospital vital signs chart
51
52 580 sharing system. *Am J Emerg Med* 2016;34(1):88-92. doi: 10.1016/j.ajem.2015.09.048
53
54 581 [published Online First: 2015/10/29]
55
56
57 582 42. Kim Y, Groombridge C, Romero L, et al. Decision Support Capabilities of Telemedicine
58
59
60

- 1
2
3
4 583 in Emergency Prehospital Care: Systematic Review. *J Med Internet Res*
5
6 584 2020;22(12):e18959. doi: 10.2196/18959 [published Online First: 2020/12/09]
7
8
9 585 43. Reisner AT, Khitrov MY, Chen L, et al. Development and validation of a portable platform
10
11 586 for deploying decision-support algorithms in prehospital settings. *Appl Clin Inform*
12
13 587 2013;4(3):392-402. doi: 10.4338/ACI-2013-04-RA-0023 [published Online First:
14
15 588 2013/10/25]
16
17
18 589 44. Maslove DM, Podchiyska T, Lowe HJ. Discretization of continuous features in clinical
19
20 590 datasets. *J Am Med Inform Assoc* 2013;20(3):544-53. doi: 10.1136/amiajnl-2012-
21
22 591 000929 [published Online First: 2012/10/13]
23
24
25
26 592
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 593 **Figure legends**
5

6
7 594 Figure 1. Population flow. EMS, emergency medical service; OHCA, out-of-hospital cardiac
8
9 595 arrest; TBI, traumatic brain injury.

10 596
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

597 Table 1. Key characteristics of the development and test cohorts.

	n (%) or Median (IQR)			P
	Total	Development cohort	Test cohort	
Total	N = 1169	n = 867	n = 302	
Demographics				
Age, years	53 (36–66)	52 (35–66)	56 (40–69)	< 0.01
Male	809 (69.2)	592 (68.3)	217 (71.9)	0.25
Job, unemployed	299 (25.6)	197 (22.7)	102 (33.8)	< 0.01
Diabetes	62 (5.3)	35 (4.0)	27 (8.9)	< 0.01
Hypertension	105 (9.0)	61 (7.0)	44 (14.6)	< 0.01
Circumstances of trauma				
Location, road/highway	444 (38.0)	326 (37.6)	118 (39.1)	0.65
Season, summer	336 (28.7)	253 (29.2)	83 (27.5)	0.57
Weekday, weekend	811 (69.4)	599 (69.1)	212 (70.2)	0.72
Time, 6 p.m. to midnight	361 (30.9)	265 (30.6)	96 (31.8)	0.69
Mechanism of injury, TA	500 (42.8)	375 (43.3)	125 (41.4)	0.57
Chief complaint				
Fracture/abrasion/laceration	302 (25.8)	204 (23.5)	98 (32.5)	< 0.01
EMS vital sign assessment				
SBP, mmHg	130 (109–150)	130 (104–146)	131 (115–150)	< 0.01
DBP, mmHg	80 (70–91)	80 (69–90)	80 (70–92)	0.21
RR, /min	18 (16–20)	18 (16–20)	18 (16–20)	0.33
HR, /min	86 (75–99)	86 (74–99)	86 (76–100)	0.40
SpO ₂ , %	98 (95–99)	98 (95–99)	98 (96–99)	0.67
AVPU scale, Alert	714 (61.1)	504 (58.1)	210 (69.5)	< 0.01
EMS management				
Intravenous route	176 (15.1)	129 (14.9)	47 (15.6)	0.77
Hemorrhage control	586 (50.1)	426 (49.1)	160 (53.0)	0.25
Spinal motion restriction	811 (69.4)	606 (69.9)	205 (67.9)	0.51
Oxygen supply	233 (19.9)	176 (20.3)	57 (18.9)	0.59
In-hospital mortality	90 (7.7)	74 (8.5)	16 (5.3)	0.07
Outcomes				
TBI	281 (24.0)	215 (24.8)	66 (21.9)	0.30
TBI with intracranial injury	251 (21.5)	195 (22.5)	56 (18.5)	0.15
TBI-related non-discharge	249 (21.3)	192 (22.1)	57 (18.9)	0.23
TBI-related death	43 (3.7)	32 (3.7)	11 (3.6)	0.95

598 IQR, interquartile range; TA, traffic accident; SBP, systolic blood pressure; DBP, diastolic
599 blood pressure; RR, respiratory rate; AVPU, mental status in alert, verbal, pain, and
600 unresponsive scale; ED, emergency department; TBI, traumatic brain injury.

601 Table 2. Discrimination and reclassification of prediction models for outcomes on test
602 cohort.

Outcome	Model	AUROC (95% CI)	p ^a	NRI (95% CI)	p ^b	AUPRC
TBI						
	LR	0.770 (0.698, 0.841)	NA	NA	NA	0.492
	XGB	0.809 (0.743, 0.876)	0.04	0.689 (0.427, 0.951)	< 0.01	0.552
	SVM	0.776 (0.708, 0.844)	0.77	0.339 (0.072, 0.607)	0.01	0.479
	RF	0.800 (0.735, 0.865)	0.13	0.308 (0.047, 0.569)	0.02	0.532
	EN	0.799 (0.732, 0.867)	0.06	0.698 (0.441, 0.954)	< 0.01	0.564
TBI-I						
	LR	0.820 (0.751, 0.890)	NA	NA	NA	0.551
	XGB	0.838 (0.775, 0.901)	0.28	0.539 (0.258, 0.821)	< 0.01	0.554
	SVM	0.812 (0.748, 0.875)	0.66	0.729 (0.464, 0.994)	< 0.01	0.469
	RF	0.836 (0.772, 0.899)	0.38	0.333 (0.058, 0.607)	0.02	0.552
	EN	0.844 (0.779, 0.910)	0.15	1.093 (0.845, 1.342)	< 0.01	0.606
TBI-ND						
	LR	0.767 (0.690, 0.844)	NA	NA	NA	0.482
	XGB	0.800 (0.727, 0.873)	0.07	0.605 (0.326, 0.884)	< 0.01	0.496
	SVM	0.778 (0.704, 0.852)	0.56	0.285 (-0.001, 0.572)	0.05	0.477
	RF	0.809 (0.739, 0.880)	0.03	0.194 (-0.059, 0.448)	0.13	0.535
	EN	0.811 (0.741, 0.882)	0.02	0.768 (0.496, 1.039)	< 0.01	0.551
TBI-D						
	LR	0.664 (0.490, 0.838)	NA	NA	NA	0.138
	XGB	0.714 (0.512, 0.917)	0.64	-0.026 (-0.605, 0.553)	0.93	0.094
	SVM	0.814 (0.718, 0.910)	0.09	0.209 (-0.325, 0.742)	0.44	0.140
	RF	0.889 (0.801, 0.976)	< 0.01	-0.204 (-0.742, 0.334)	0.46	0.196
	EN	0.871 (0.764, 0.978)	0.01	0.119 (-0.415, 0.654)	0.66	0.293

603 ^aComparing the AUROC and the logistic regression model.

604 ^bComparing the NRI and the logistic regression model.

605 AUROC, area under the receiver operating characteristic curve; CI, confidence interval;

606 NRI, net reclassification index; AUPRC, area under precision-recall curve; TBI,

607 traumatic brain injury, TBI-I, traumatic brain injury with intracranial injury; TBI-ND;

608 traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with death;

609 LR, logistic regression analysis; XGB, extreme gradient boosting; SVM, support vector

610 machine; RF, random forest; EN, elastic net

611

612

613

614 Table 3. Test characteristics of prediction models for outcomes on test cohort.

Outcome	Model	Specificity (95% CI)	Sensitivity (95% CI)	PPV (95% CI)	NPV (95% CI)	Cutoff
TBI						
	LR	47.5 (40.9, 54.0)	80.3 (68.7, 89.1)	29.9 (23.3, 37.3)	89.6 (82.9, 94.3)	0.136
	XGB	72.5 (66.3, 78.1)	80.3 (68.7, 89.1)	44.9 (35.7, 54.3)	92.9 (88.2, 96.2)	0.268
	SVM	64.8 (58.4, 70.9)	80.3 (68.7, 89.1)	39.0 (30.7, 47.7)	92.2 (87.0, 95.8)	0.191
	RF	68.2 (61.9, 74.1)	80.3 (68.7, 89.1)	41.4 (32.8, 50.4)	92.5 (87.6, 96.0)	0.185
	EN	61.0 (54.5, 67.3)	80.3 (68.7, 89.1)	36.6 (28.7, 44.9)	91.7 (86.3, 95.5)	0.205
TBI-I						
	LR	71.1 (65.0, 76.7)	80.4 (67.6, 89.8)	38.8 (29.9, 48.3)	94.1 (89.7, 97.0)	0.164
	XGB	74.0 (68.0, 79.4)	80.4 (67.6, 89.8)	41.3 (31.9, 51.1)	94.3 (90.0, 97.1)	0.143
	SVM	71.1 (65.0, 76.7)	80.4 (67.6, 89.8)	38.8 (29.9, 48.3)	94.1 (89.7, 97.0)	0.172
	RF	76.0 (70.2, 81.2)	80.4 (67.6, 89.8)	43.3 (33.6, 53.3)	94.4 (90.3, 97.2)	0.205
	EN	81.3 (75.9, 86.0)	80.4 (67.6, 89.8)	49.5 (38.8, 60.1)	94.8 (90.9, 97.4)	0.204
TBI-ND						
	LR	46.1 (39.8, 52.6)	80.7 (68.1, 90.0)	25.8 (19.6, 32.9)	91.1 (84.7, 95.5)	0.090
	XGB	66.5 (60.2, 72.4)	80.7 (68.1, 90.0)	35.9 (27.7, 44.9)	93.7 (89.0, 96.8)	0.242
	SVM	59.2 (52.7, 65.4)	80.7 (68.1, 90.0)	31.5 (24.1, 39.7)	92.9 (87.7, 96.4)	0.147
	RF	60.4 (54.0, 66.6)	80.7 (68.1, 90.0)	32.2 (24.6, 40.5)	93.1 (88.0, 96.5)	0.138
	EN	74.3 (68.3, 79.6)	80.7 (68.1, 90.0)	42.2 (32.8, 52.0)	94.3 (90.0, 97.1)	0.201
TBI-D						
	LR	42.6 (36.9, 48.5)	81.8 (48.2, 97.7)	5.1 (2.4, 9.5)	98.4 (94.4, 99.8)	0.005
	XGB	57.7 (51.8, 63.5)	81.8 (48.2, 97.7)	6.8 (3.2, 12.5)	98.8 (95.8, 99.9)	0.002
	SVM	74.2 (68.8, 79.2)	81.8 (48.2, 97.7)	10.7 (5.0, 19.4)	99.1 (96.7, 99.9)	0.039
	RF	74.9 (69.5, 79.8)	81.8 (48.2, 97.7)	11.0 (5.1, 19.8)	99.1 (96.8, 99.9)	0.005
	EN	79.0 (73.9, 83.6)	81.8 (48.2, 97.7)	12.9 (6.1, 23.0)	99.1 (96.9, 99.9)	0.033

615 TBI, traumatic brain injury; TBI-I, traumatic brain injury with intracranial injury; TBI-
616 ND; traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with
617 death; LR, logistic regression analysis; XGB, extreme gradient boosting; SVM, support
618 vector machine; RF, random forest; EN, elastic net.

619

620 Table 4. Top 5 important variables for outcomes in descending order using model
621 specific metrics

Outcome	Rank	LR	XGB	RF	EN
TBI					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	Loss of consciousness
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	GCS, Motor, 1
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 2
	4	Light reflex	Other mechanism	Light reflex	GCS, Eye, 1
	5	GCS, Motor, 1	GCS, Verbal, 2	GCS, Motor, 1	GCS, Verbal, 1
TBI-I					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	GCS, Eye, 1
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	Loss of consciousness
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 1
	4	Light reflex	GCS, Verbal, 2	Light reflex	GCS, Verbal, 1
	5	GCS, Motor, 1	Other mechanism	GCS, Motor, 1	Light reflex
TBI-ND					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	Loss of consciousness
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 1
	4	Light reflex	GCS, Verbal, 2	GCS, Verbal, 2	GCS, Verbal, 1
	5	GCS, Motor, 1	GCS, Motor, 1	GCS, Motor, 4	Light reflex
TBI-D					
	1	Loss of consciousness	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 2
	2	GCS, Verbal, 1	Oxygen saturation<96%	Light reflex	GCS, Verbal, 1
	3	GCS, Eye, 1	Fall mechanism	Loss of consciousness	Loss of consciousness
	4	Light reflex	Afternoon	GCS, Eye, 1	Age over 80
	5	GCS, Motor, 1	Light reflex	GCS, Motor, 1	HR 87-99

622 TBI, traumatic brain injury; TBI-I, traumatic brain injury with intracranial injury; TBI-
623 ND; traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with
624 death; LR, logistic regression; XGB, extreme gradient boosting; RF, random forest; EN,
625 elastic net; GCS, Glasgow coma scale; HR, heart rate.

626

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

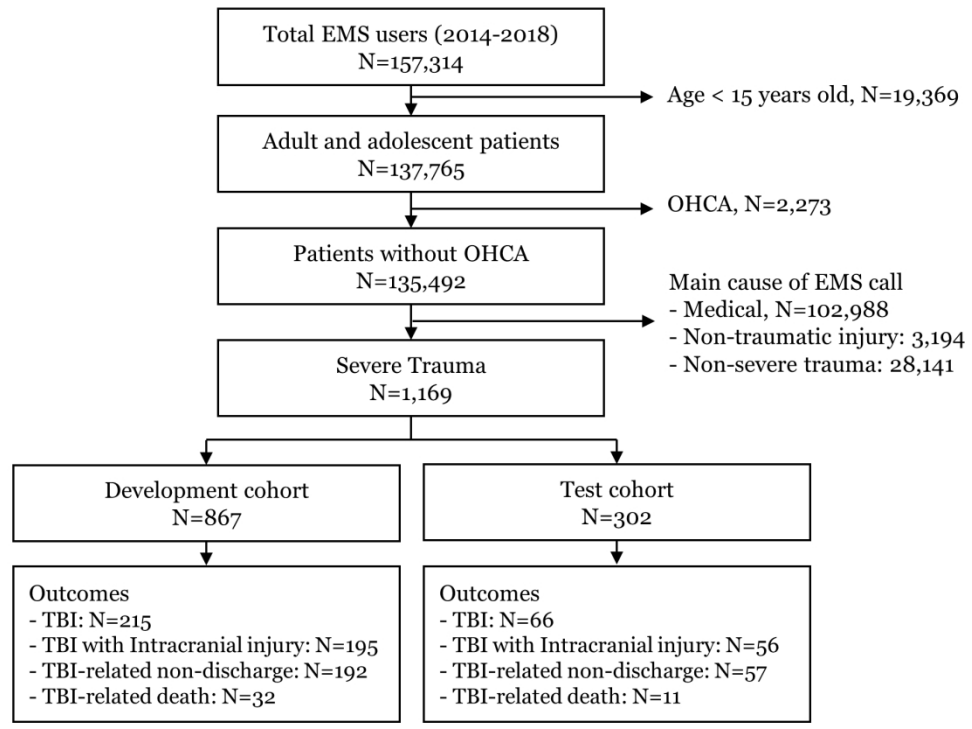


Figure 1

165x119mm (300 x 300 DPI)

Supplementary Table 1. List of analyzed variables.

Variables	Descriptions	Type of raw data	Category	Preprocessing
Gender	Sex of the patients	Binary	Male, Female	
Age	Age of patients	Continuous	15-39 years, 40-59 years, 60-79 years, and 80- years	Discretization and one hot encoding
Job	Job of patients	Categorical	Unemployed, Student/Housewife; Office/Commercial/Service workers; Industrial/Agricultural/Fishery/Miner worker; Others	One hot encoding Missing data were classified into others
Diabetes	History of diabetes mellitus	Binary	Yes, No	Missing data were classified into no
Hypertension	History of hypertension	Binary	Yes, No	Missing data were classified into no
Location of injury	Location of injury	Categorical	home/residential area/medical facility/school/gym; Road/highway; Off-road traffic area; Others	One hot encoding Missing data were classified into others
Season	Season when injury occurred	Categorical	Spring, Summer, Fall, Winter	One hot encoding
Weekend	Whether Injury occurred on weekday or weekend	Binary	Weekday, Weekend	
Daytime	When injury was occurred	Categorical	Night (Midnight to 5AM), Morning (6AM to 11AM), Afternoon (Midday to 5PM), Evening (6PM to 11PM)	One hot encoding Missing time were imputed using EMS call time
Mechanism of injury	Mechanism of injury	Categorical	Slip down, Fall down, Traffic accident, Other	One hot encoding Missing data were classified into others
Glasgow coma scale eye	Eye element of Glasgow coma scale	Categorical	1;2;3;4;Unknown	One hot encoding
Glasgow coma scale Verbal	Verbal element of Glasgow coma scale	Categorical	1;2;3;4;5;Unknown	One hot encoding
Glasgow coma scale Motor	Motor element of Glasgow coma scale	Categorical	1;2;3;4;5;6;Unknown	One hot encoding
Light Reflex any Abnormal	Any abnormality of light reflex on any side	Categorical	No, Yes, Unknown	One hot encoding Missing data were classified into unknown

Systolic blood pressure	blood	Systolic blood pressure	Continuous	-107 mmHg, 108-130 mmHg, 131-145 mmHg, 146- mmHg, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Diastolic pressure	blood	Diastolic blood pressure	Continuous	-69 mmHg, 70-80 mmHg, 81-91 mmHg, 92- mmHg, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Heart rate		Heart rate	Continuous	-74/min, 75-86/min, 87-99/min, 100-/min, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Respiratory rate		Respiratory rate	Continuous	-16/min, 17-18/min, 19-20/min, 21-/min, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Oxygen saturation		Oxygen saturation	Continuous	-95%, 96-98%, 99%, 100%, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Body temperature		Body temperature	Continuous	-36°C, 36.1-36.3°C, 36.4-36.8°C, 36.9-°C, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Chest pain or abdominal pain		Symptom of chest pain or abdominal pain	Binary	Yes, No	

Fracture, abrasion, or laceration	Symptom of fracture, abrasion, or laceration	Binary	Yes, No	
Loss of consciousness	Symptom of loss of consciousness (whether patients had loss of consciousness between injury and EMS provider's assessment)	Binary	Yes, No	
Dyspnea	Symptom of dyspnea	Binary	Yes, No	
Nose bleeding	Symptom of nose bleeding	Binary	Yes, No	
Nausea or vomiting	Symptom of nausea or vomiting	Binary	Yes, No	
Headache, paralysis or dizziness	Symptom of headache, paralysis or dizziness	Binary	Yes, No	

Supplementary Table 2. Demographic characteristics of development and test cohorts

Characteristics	N (%) or Median (IQR)			P-value
	Total	Development	Test	
Total	1169	867	302	
Demographics				
Male	809 (69.2)	592 (68.3)	217 (71.9)	0.25
Age, years	53 (36-66)	52 (35-66)	56 (40-69)	<0.01
Job of patients				<0.01
Unemployed	299 (25.6)	197 (22.7)	102 (33.8)	
Student/Housewife	161 (13.8)	129 (14.9)	32 (10.6)	
Office/Commercial/Service worker	283 (24.2)	176 (20.3)	107 (35.4)	
Industrial/Agricultural/Fishery/Minery worker	36 (3.1)	25 (2.9)	11 (3.6)	
Others	390 (33.4)	340 (39.2)	50 (16.6)	
Past medical history				
Diabetes	62 (5.3)	35 (4.0)	27 (8.9)	<0.01
Hypertension	105 (9.0)	61 (7.0)	44 (14.6)	<0.01
Circumstances of Trauma				
Location of trauma				0.52
Residential/Nursing/Education/Exercise facility	303 (25.9)	218 (25.1)	85 (28.1)	
Road/Highway	444 (38.0)	326 (37.6)	118 (39.1)	
Off-road traffic area	181 (15.5)	140 (16.1)	41 (13.6)	
Others	241 (20.6)	183 (21.1)	58 (19.2)	
Season of trauma				<0.01
Spring	249 (21.3)	167 (19.3)	82 (27.2)	
Summer	336 (28.7)	253 (29.2)	83 (27.5)	
Fall	304 (26.0)	242 (27.9)	62 (20.5)	
Winter	280 (24.0)	205 (23.6)	75 (24.8)	
Weekday	811 (69.4)	599 (69.1)	212 (70.2)	0.72
Time of trauma				0.83
6A-MD	281 (24.0)	206 (23.8)	75 (24.8)	
MD-6P	266 (22.8)	203 (23.4)	63 (20.9)	
6P-MN	361 (30.9)	265 (30.6)	96 (31.8)	
MN-6A	261 (22.3)	193 (22.3)	68 (22.5)	
Mechanism of Trauma				0.60
Traffic accident	500 (42.8)	375 (43.3)	125 (41.4)	
Slip down	325 (27.8)	232 (26.8)	93 (30.8)	
Fall down	171 (14.6)	129 (14.9)	42 (13.9)	
Others	173 (14.8)	131 (15.1)	42 (13.9)	
Chief complaint				
Altered mentality	279 (23.9)	223 (25.7)	56 (18.5)	0.01
Fracture/Abrasion/Laceration	302 (25.8)	204 (23.5)	98 (32.5)	<0.01
Chest/Abdominal pain	47 (4.0)	31 (3.6)	16 (5.3)	0.19
Dyspnea	25 (2.1)	20 (2.3)	5 (1.7)	0.50

1					
2					
3					
4					
5	Epistaxis	44 (3.8)	30 (3.5)	14 (4.6)	0.36
6	Headache/Paralysis/Dizziness/Vertigo	95 (8.1)	64 (7.4)	31 (10.3)	0.11
7	Nausea/Vomiting	32 (2.7)	20 (2.3)	12 (4.0)	0.13
8	EMS Vital sign assessment				
9		130 (109-		131 (115-	
10	SBP, mmHg	150)	130 (104-146)	150)	<0.01
11	Missing	65 (5.6)	56 (6.5)	9 (3.0)	0.02
12	DBP, mmHg	80 (70-91)	80 (69-90)	80 (70-92)	<0.01
13	Missing	75 (6.4)	65 (7.5)	10 (3.3)	0.01
14	HR, /min	86 (75-99)	86 (74-99)	86 (76-100)	<0.01
15	Missing	31 (2.7)	28 (3.2)	3 (1.0)	0.04
16	RR, /min	18 (16-20)	18 (16-20)	18 (16-20)	<0.01
17	Missing	36 (3.1)	33 (3.8)	3 (1.0)	0.01
18	SpO2, %	98 (95-99)	98 (95-99)	98 (96-99)	<0.01
19	Missing	38 (3.3)	33 (3.8)	5 (1.7)	0.07
20	Temperature, °C	36.5 (36-		36.5 (36-	
21		36.8)	36.5 (36-36.8)	36.7)	<0.01
22	Missing	94 (8.0)	65 (7.5)	29 (9.6)	0.25
23	AVPU scale				<0.01
24	Alert	714 (61.1)	504 (58.1)	210 (69.5)	
25	Verbal	168 (14.4)	136 (15.7)	32 (10.6)	
26	Pain	199 (17.0)	158 (18.2)	41 (13.6)	
27	Unresponsive	88 (7.5)	69 (8.0)	19 (6.3)	
28	Abnormal light reflex	165 (14.1)	132 (15.2)	33 (10.9)	<0.01
29	Missing	66 (5.6)	57 (6.6)	9 (3.0)	
30	GCS scale component				
31	Glasgow coma scale eye				<0.01
32	4	558 (47.7)	380 (43.8)	178 (58.9)	
33	3	128 (10.9)	109 (12.6)	19 (6.3)	
34	2	110 (9.4)	82 (9.5)	28 (9.3)	
35	1	174 (14.9)	141 (16.3)	33 (10.9)	
36	Unknown	199 (17.0)	155 (17.9)	44 (14.6)	
37	Glasgow coma scale Verbal				0.01
38	5	520 (44.5)	359 (41.4)	161 (53.3)	
39	4	118 (10.1)	88 (10.1)	30 (9.9)	
40	3	25 (2.1)	19 (2.2)	6 (2.0)	
41	2	132 (11.3)	105 (12.1)	27 (8.9)	
42	1	174 (14.9)	141 (16.3)	33 (10.9)	
43	Unknown	200 (17.1)	155 (17.9)	45 (14.9)	
44	Glasgow coma scale Motor				<0.01
45	6	499 (42.7)	333 (38.4)	166 (55.0)	
46	5	124 (10.6)	103 (11.9)	21 (7.0)	
47	4	158 (13.5)	123 (14.2)	35 (11.6)	
48	3	47 (4.0)	39 (4.5)	8 (2.6)	
49	2	17 (1.5)	15 (1.7)	2 (0.7)	
50	1	125 (10.7)	99 (11.4)	26 (8.6)	
51	Unknown	199 (17.0)	155 (17.9)	44 (14.6)	
52					
53					
54					
55					
56					
57					
58					
59					
60					

1					
2					
3					
4					
5	EMS management				
6	Intravenous route	176 (15.1)	129 (14.9)	47 (15.6)	0.77
7	Hemorrhage control	586 (50.1)	426 (49.1)	160 (53.0)	0.25
8	Spinal motion restriction	811 (69.4)	606 (69.9)	205 (67.9)	0.51
9	Advanced airway management	4 (0.3)	2 (0.2)	2 (0.7)	0.28
10	Oxygen supply	233 (19.9)	176 (20.3)	57 (18.9)	0.59
11					
12	Field triage decision scheme criteria*				
13	Physiological criteria				
14	SBP<90 mmHg	58 (5.0)	42 (4.8)	16 (5.3)	0.75
15	RR<10 or >29 /min	11 (0.9)	11 (1.3)	0 (0.0)	0.08
16	Non-Alert	429 (36.7)	343 (39.6)	86 (28.5)	<0.01
17					
18	Anatomic criteria				
19	All penetrating injuries to head, neck,				
20	torso and extremities proximal to elbow				
21	or knee	34 (2.9)	23 (2.7)	11 (3.6)	0.38
22	Chest wall instability or deformity	4 (0.3)	4 (0.5)	0 (0.0)	0.58
23	Two or more proximal long bone				
24	fractures	19 (1.6)	13 (1.5)	6 (2.0)	0.60
25	Crush, degloved, mangled or				
26	pulseless extremity	15 (1.3)	13 (1.5)	2 (0.7)	0.38
27	Amputation proximal to wrist or ankle	9 (0.8)	9 (1.0)	0 (0.0)	0.12
28	Pelvic fractures	8 (0.7)	6 (0.7)	2 (0.7)	>0.95
29	Open or depressed skull fracture	17 (1.5)	9 (1.0)	8 (2.6)	0.05
30	Paralysis	21 (1.8)	11 (1.3)	10 (3.3)	0.02
31					
32	Mechanism of injury criteria				
33	Fall > 6 meter	113 (9.7)	84 (9.7)	29 (9.6)	>0.95
34					
35	High-risk auto crash	96 (8.2)	73 (8.4)	23 (7.6)	0.66
36	Auto vs pedestrian/bicyclist thrown,				
37	run over, or with significant (>30km/h)				
38	impact	119 (10.2)	83 (9.6)	36 (11.9)	0.25
39	Motorcycle crash > 30 km/hour	105 (9.0)	70 (8.1)	35 (11.6)	0.07
40					
41	ED disposition				0.11
42	Discharge	320 (27.4)	241 (27.8)	79 (26.2)	
43	Transfer	444 (38.0)	316 (36.4)	128 (42.4)	
44	Admitted	366 (31.3)	276 (31.8)	90 (29.8)	
45					
46	In-hospital mortality	90 (7.7)	74 (8.5)	16 (5.3)	0.07
47					
48	Outcomes				
49	TBI	281 (24.0)	215 (24.8)	66 (21.9)	0.30
50	TBI with intracranial injury	251 (21.5)	195 (22.5)	56 (18.5)	0.15
51	TBI-related non-discharge	249 (21.3)	192 (22.1)	57 (18.9)	0.23
52					
53	TBI-related death	43 (3.7)	32 (3.7)	11 (3.6)	>0.95

*EMS providers check specific criteria orderly from physiologic, anatomical, and mechanism of injury. If the preceding criteria are satisfied, the information of the latter criteria is not collected.

1
2
3
4 IQR, interquartile range; SBP, systolic blood pressure; RR, respiratory rate; ED, emergency department; TBI,
5
6 traumatic brain injury.
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

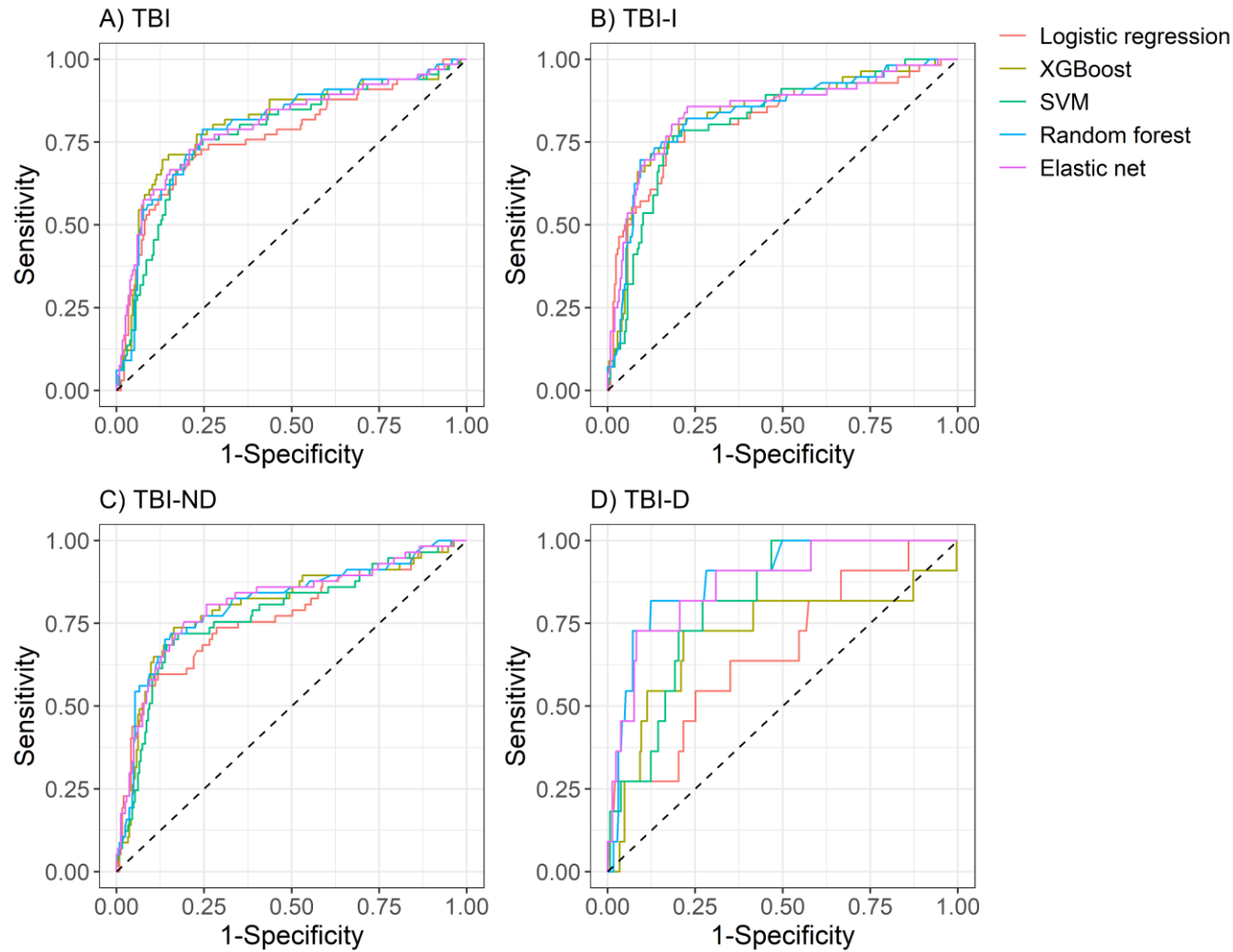
Supplementary Table 3. Hyperparameters of the final prediction models*

Model	Outcome	Hyperparameters
Elastic net	TBI	alpha: 0.325, lambda: 0.07506346
	TBI-I	alpha: 0.325, lambda: 0.07506346
	TBI-ND	alpha: 0.325, lambda: 0.07017153
	TBI-D	alpha: 0.325, lambda: 0.01565599
Random forest	TBI	ntree:500, mtry: 18
	TBI-I	ntree:500, mtry: 18
	TBI-ND	ntree:500, mtry: 18
	TBI-D	ntree:500, mtry: 15
Support vector machine	TBI	sigma: 0.008047; C: 4
	TBI-I	sigma: 0.008047; C: 4
	TBI-ND	sigma: 0.008047; C: 4
	TBI-D	sigma: 0.008047; C: 4
Extreme gradient boosting	TBI	nrounds: 299; max_depth: 1; eta: 0.4807096; gamma: 2.336623; colsample_bytree: 0.3657893; min_child_weight: 8; subsample: 0.8182623
	TBI-I	nrounds: 299; max_depth: 1; eta: 0.4807096; gamma: 2.336623; colsample_bytree: 0.3657893; min_child_weight: 8; subsample: 0.8182623
	TBI-ND	nrounds: 301; max_depth: 1; eta: 0.02154674; gamma: 4.696105; colsample_bytree: 0.590754; min_child_weight: 1; subsample: 0.5070866
	TBI-D	nrounds: 50; max_depth: 0.3; eta: 0.3; gamma: 0; colsample_bytree: 0.8; min_child_weight: 1; subsample: 0.5510204

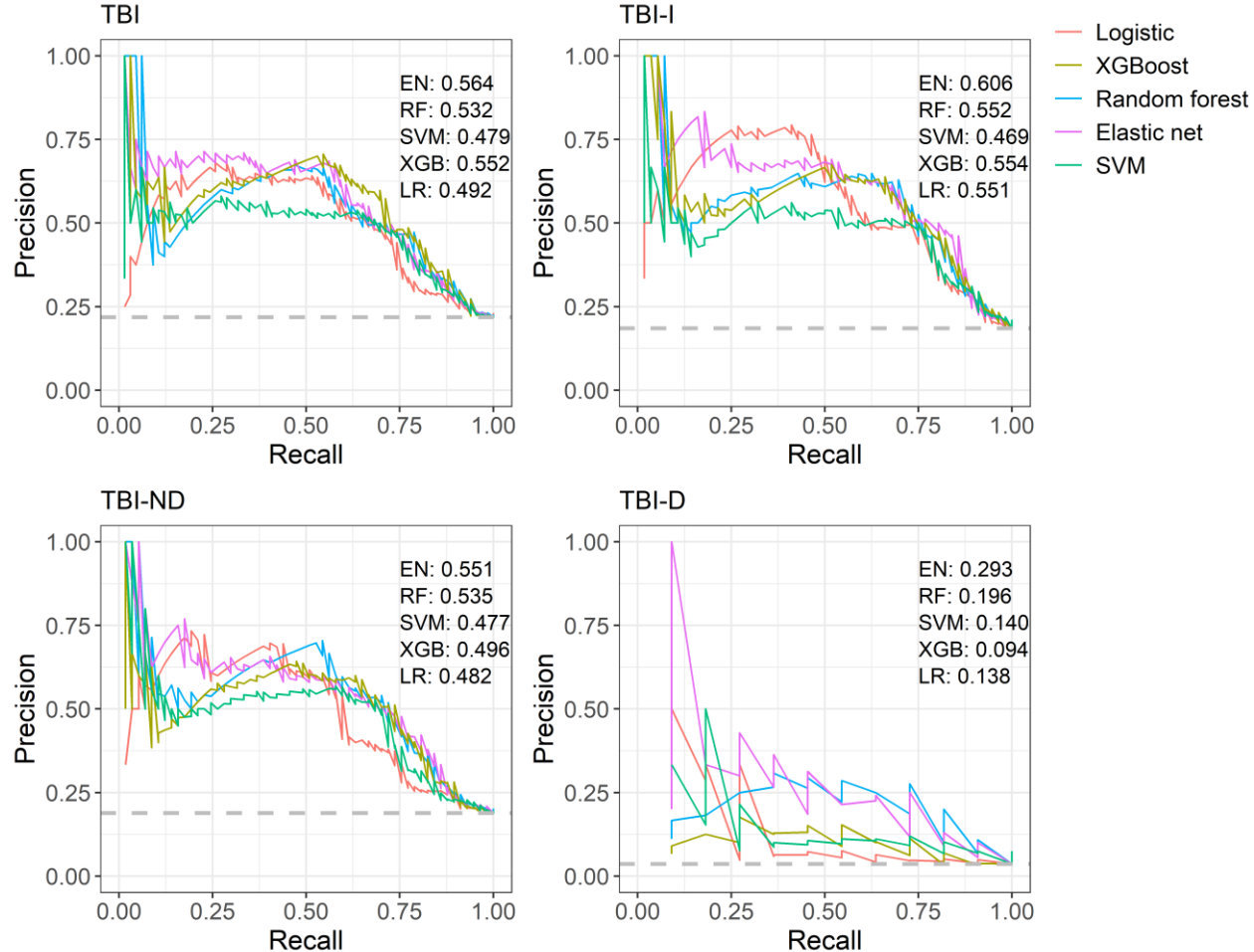
*Aside from the hyperparameters mentioned, all other hyperparameters are used as the default value.

TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death.

Supplementary Figure 1. Receiver operating characteristics of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death.

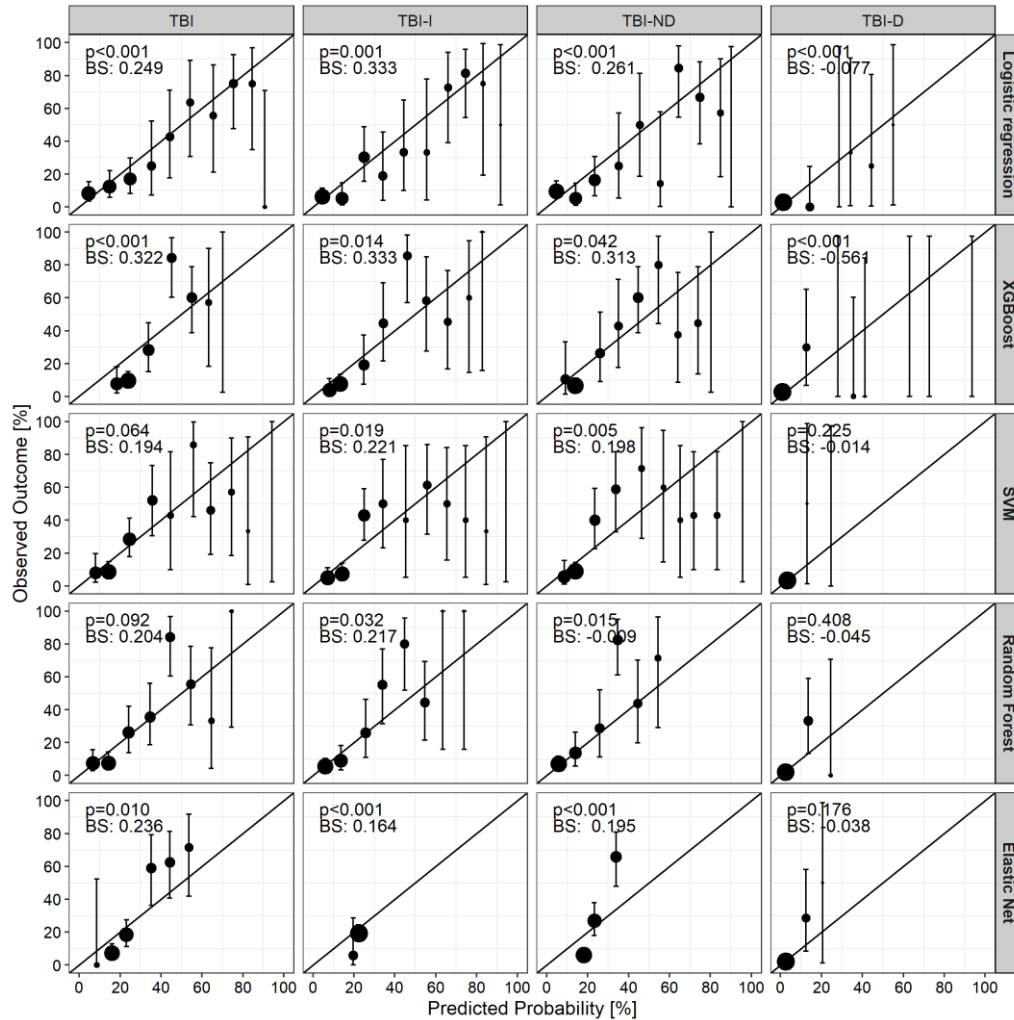


Supplementary Figure 2. Precision-recall curve of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death; LR, logistic regression analysis; XGB, extreme gradient boosting; RF, random forest, EN, elastic net.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

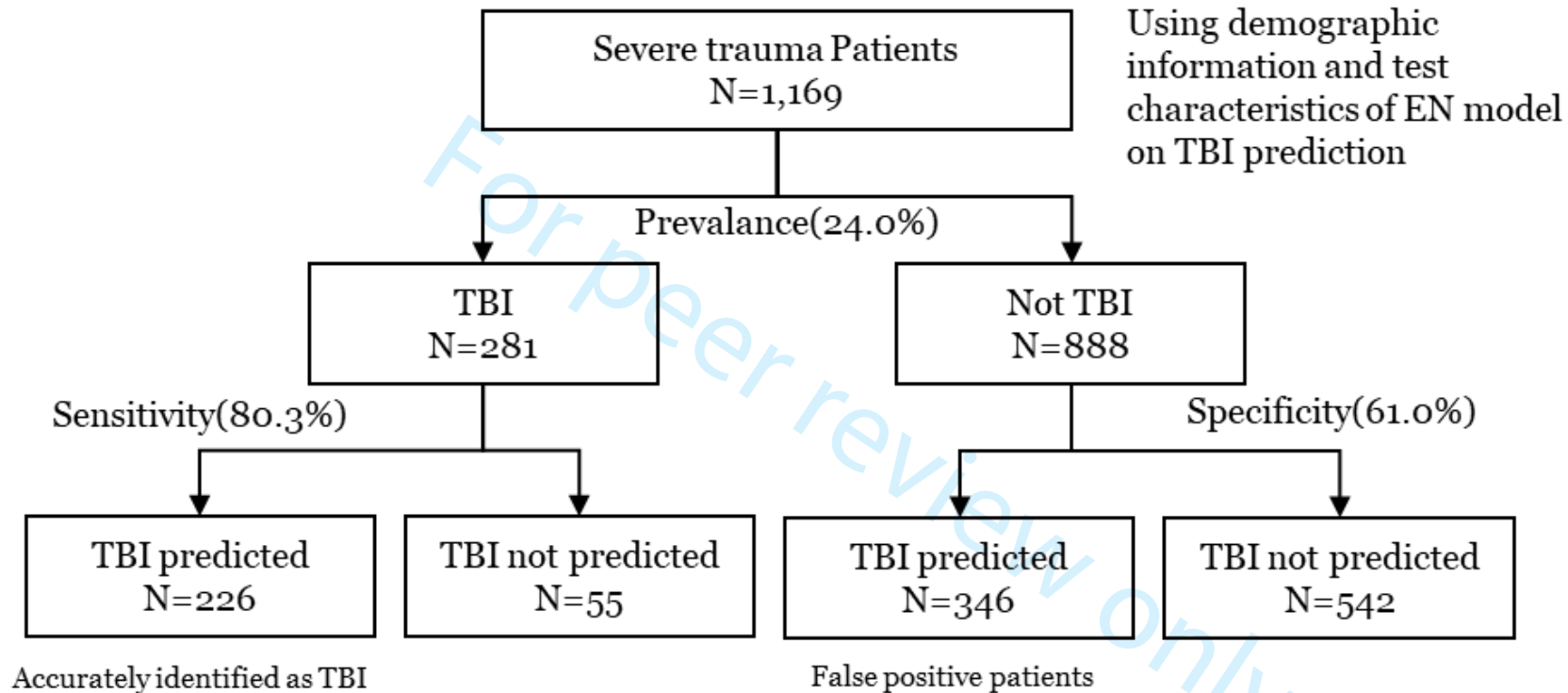
Supplementary Figure 3. Calibration plot of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death; p, p-value of Hosmer-Lemeshow test; BS, scaled Brier score.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

For peer review only

Supplementary Table 4. Example of calculating false-positive patients for accurately identified patients. TBI, traumatic brain injury; EN, elastic net.



False-positive patients for every 10 patients that are accurately identified as TBI :
 $346/226 \times 10 = 15.3$, rounded up to 16 patients

TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item	Checklist Item	Page	
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	4
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	7
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	8
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	8-9
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	9
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	8-9
	5b	D;V	Describe eligibility criteria for participants.	10
	5c	D;V	Give details of treatments received, if relevant.	N/A
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	10-11
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	N/A
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	11
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	N/A
Sample size	8	D;V	Explain how the study size was arrived at.	14
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	11
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	11
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	11-12
	10c	V	For validation, describe how the predictions were calculated.	12-13
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12-13
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	N/A
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	N/A
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	12
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	14
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	14
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	14
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	14
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	N/A
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	N/A
	15b	D	Explain how to use the prediction model.	14-15
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	14-15
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	N/A
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	19-20
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	16-17
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	18-19
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Suppl
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	20

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development and validation of a prehospital-stage prediction tool for traumatic brain injury: a multicentre retrospective cohort study in Korea

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055918.R2
Article Type:	Original research
Date Submitted by the Author:	16-Dec-2021
Complete List of Authors:	Choi, Yeong Ho; Seoul National University Hospital, Emergency Department; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Park, Jeong Ho; Seoul National University Hospital, Emergency Department; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Hong, Ki Jeong; Seoul National University Hospital, Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Ro, Young Sun; Seoul National University Hospital, Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Song, Kyoung Jun; Seoul Metropolitan Boramae Hospital, Department of Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services Shin, Sang Do; Seoul National University Hospital, Department of Emergency Medicine; Seoul National University Hospital Biomedical Research Institute, Laboratory of Emergency Medical Services
Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Emergency medicine, Health informatics
Keywords:	ACCIDENT & EMERGENCY MEDICINE, Neurological injury < NEUROLOGY, Trauma management < ORTHOPAEDIC & TRAUMA SURGERY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 1 **Title page**
5
6
7 2
8

9 3 **1. Title**

10
11 4 Development and validation of a prehospital-stage prediction tool for traumatic brain
12
13 5 injury: a multicentre retrospective cohort study in Korea
14
15
16 6

17
18 7 **2. Authors**

19
20 8 Yeong Ho Choi, MD

21
22 9 Department of Emergency Medicine, Seoul National University College of Medicine and
23
24 10 Hospital, Seoul, Republic of Korea

25
26 11 Laboratory of Emergency Medical Services, Seoul National University Hospital

27
28 12 Biomedical Research Institute, Seoul, Korea

29
30 13 E-mail: d2uk87@gmail.com
31
32
33
34 14

35
36 15 Jeong Ho Park, MD

37
38 16 Department of Emergency Medicine, Seoul National University College of Medicine and
39
40 17 Hospital, Seoul, Republic of Korea

41
42 18 Laboratory of Emergency Medical Services, Seoul National University Hospital

43
44 19 Biomedical Research Institute, Seoul, Korea

45
46 20 E-mail: timthe@gmail.com
47
48
49
50 21

51
52 22 Ki Jeong Hong, MD, PhD

53
54 23 Department of Emergency Medicine, Seoul National University College of Medicine and
55
56 24 Hospital, Seoul, Republic of Korea
57
58
59
60

1
2
3
4 25 Laboratory of Emergency Medical Services, Seoul National University Hospital
5
6 26 Biomedical Research Institute, Seoul, Korea
7
8
9 27 E-mail: emkjhong@gmail.com
10
11 28
12
13 29 Young Sun Ro, MD, DrPH
14
15 30 Department of Emergency Medicine, Seoul National University College of Medicine and
16
17 31 Hospital, Seoul, Republic of Korea
18
19 32 Laboratory of Emergency Medical Services, Seoul National University Hospital
20
21 33 Biomedical Research Institute, Seoul, Korea
22
23 34 E-mail: ro.youngsun@gmail.com
24
25 35
26
27 36 Kyoung Jun Song, MD, PhD
28
29 37 Department of Emergency Medicine, Seoul Metropolitan Government Seoul National
30
31 38 University Boramae Medical Center, Seoul, Republic of Korea
32
33 39 Laboratory of Emergency Medical Services, Seoul National University Hospital
34
35 40 Biomedical Research Institute, Seoul, Korea
36
37 41 E-mail: skciva@gmail.com
38
39 42
40
41 43 Sang Do Shin, MD, PhD
42
43 44 Department of Emergency Medicine, Seoul National University College of Medicine and
44
45 45 Hospital, Seoul, Republic of Korea
46
47 46 Laboratory of Emergency Medical Services, Seoul National University Hospital
48
49 47 Biomedical Research Institute, Seoul, Korea
50
51 48 E-mail: shinsangdo@gmail.com
52
53
54
55
56
57
58
59
60

1
2
3
4 495
6 50 **3. Address correspondence and requests for reprints: Jeong Ho Park, MD**7
8
9 51 Address: Seoul National University Hospital, 101 Daehak-Ro, Jongno-Gu, Seoul 03080,10
11 52 Korea12
13 53 Phone: +82-2-2072-180014
15 54 FAX: +82-2-741-785516
17 55 E-mail: timthe@gmail.com18
19
20 5621
22
23 5724
25 58
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 59 **Abstract**

6 60 **Objectives:** Predicting diagnosis and prognosis of traumatic brain injury (TBI) at the
7
8
9 61 prehospital stage is challenging; however, using comprehensive prehospital information and
10
11 62 machine learning may improve the performance of the predictive model. We developed and
12
13 63 tested predictive models for TBI that use machine learning algorithms using information that
14
15
16 64 can be obtained in the prehospital stage.

17
18 65 **Design:** This was a multi-center retrospective study.

19
20 66 **Setting and participants:** This study was conducted at three tertiary academic emergency
21
22 67 departments (EDs) located in an urban area of South Korea. The data from adult patients with
23
24 68 severe trauma who were assessed by emergency medical service (EMS) providers and
25
26
27 69 transported to three participating hospitals between 2014 to 2018 were analyzed.

28
29 70 **Results:** We developed and tested five machine learning algorithms—logistic regression
30
31 71 analyses, extreme gradient boosting, support vector machine, random forest, and elastic net
32
33 72 (EN)—to predict TBI, TBI with intracranial hemorrhage or injury (TBI-I), TBI with
34
35 73 emergency department or admission result of admission or transferred (TBI-ND), and TBI
36
37 74 with emergency department or admission result of death (TBI-D). A total of 1,169 patients
38
39 75 were included in the final analysis, and the proportions of TBI, TBI-I, TBI-ND, and TBI-D
40
41 76 were 24.0%, 21.5%, 21.3%, and 3.7%, respectively. The EN model yielded an AUROC of
42
43 77 0.799 for TBI, 0.844 for TBI-I, 0.811 for TBI-ND, and 0.871 for TBI-D. The EN model also
44
45 78 yielded the highest specificity, and significant reclassification improvement. Variables related
46
47 79 to loss of consciousness, Glasgow Coma Scale, and light reflex were the three most important
48
49 80 variables to predict all outcomes.

50
51 81 **Conclusion:** Our results inform the diagnosis and prognosis of TBI. Machine learning
52
53 82 models resulted in significant performance improvement over that with logistic regression
54
55
56
57
58
59
60

1
2
3
4 83 analyses, and the best performing model was EN.
5
6

7 84

8
9 85 **Keywords:** brain injuries; traumatic; outcome; prognosis; machine learning.
10
11

12 86
13

14 87
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3
4 88 **Strengths and limitations of this study**

5
6 89 • This study presented prehospital factors that could predict traumatic brain injury in trauma
7
8 90 patients chosen by model-specific metrics.

9
10
11 91 • We treated the missing variables as a different category, reflecting prehospital field
12
13 92 uncertainties and increasing data utilization.

14
15 93 • The retrospective observational study design could lead to certain types of bias (eg,
16
17 94 selection bias, confounding bias).

18
19
20 95 • External validation for other areas should be conducted to generalize the developed
21
22 96 prediction model.

23
24
25 97
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

98 **Introduction**

99 Traumatic brain injury (TBI) is a significant health burden worldwide.¹ It is the leading cause
100 of mortality and disability among young individuals.² Patients with TBI are vulnerable to
101 hypoxia and hypotension in the early period of their course and these insults are associated
102 with poor outcomes.^{3 4} Prehospital assessment and management of patients with TBI is
103 important,⁵ as early prediction of TBI and correcting hypoxia and hypotension during the
104 prehospital stage could be beneficial.³ However, the identification of TBI can often be
105 challenging in the prehospital area.⁵ Vulnerable patients, including the elderly or patients who
106 take medications like anti-platelet or anticoagulant drugs, often have TBI owing to low
107 energy insults.⁶ Prehospital clinical signs are also reported to have poor sensitivity for raised
108 intracranial pressure following TBI.⁷

109 Several prediction models to target patients with TBI have been reported.⁸⁻¹²
110 However, most incorporated information that is available only in the hospital, such as
111 laboratory results or image findings.^{8 9 13} In addition, most previous prediction models
112 focused on the outcomes of patients with TBI,¹⁴⁻¹⁶ not the identification of TBI. Previously,
113 predictors of older adult patients with TBI who required transport to a trauma center were
114 identified. However, this was consensus-based; therefore, there is a lack of clinical data.¹⁷
115 Accurate prehospital prediction of TBI and its severity could prevent delays to definite care
116 for patients with TBI. Most emergency medical service (EMS) providers collect various
117 information including demographics, past medical history, circumstances of the trauma, and
118 clinical signs including vital signs; but those variables have not been evaluated together as
119 predictors of TBI and its severity. Using a variety of prehospital information, and adapting
120 newly emerging machine learning algorithms for predicting diagnosis, disposition, and
121 outcome of TBI, might improve the accuracy of identification of TBI and its severity.

1
2
3
4 122 The aim of this study was to develop and test prediction models for the diagnosis and
5
6 123 prognosis of TBI using prehospital information and machine learning algorithms among
7
8 124 patients with severe trauma. We hypothesized that incorporating prehospital information
9
10 125 could achieve acceptable performance in predicting TBI, and machine learning algorithms
11
12 126 could contribute to performance improvement.
13
14
15
16

17 127 **Materials and Methods**

18 19 20 128 *Study design and settings*

21
22
23 129 This was a multi-center retrospective study conducted at three tertiary academic emergency
24
25 130 departments (EDs) located in an urban area (Seoul and Bundang) of South Korea. These EDs
26
27 131 received 50,000–90,000 visits annually and are not designated trauma centers. We adhered to
28
29 132 the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or
30
31 133 Diagnosis (TRIPOD) statement on reporting predictive models.¹⁸
32
33

34 134 The EMS system in South Korea is operated by the National Fire Agency. The EMS
35
36 135 level is considered intermediate, as EMS providers can perform bleeding control, spinal
37
38 136 motion restriction, immobilization and splintage, advanced airway management, and
39
40 137 administer fluid intravenously. As only physicians can declare death in South Korea, EMS
41
42 138 providers cannot stop resuscitation and must transport all patients including those in cardiac
43
44 139 arrest to the ED. For all EMS transport, EMS providers record an ambulance run-sheet by
45
46 140 law. Since 2012, the National Fire Agency adapted the United States Centers for Disease
47
48 141 Control and Prevention of the United States field triage decision scheme to evaluate patients
49
50 142 with trauma,¹⁹ and they developed an EMS severe trauma in-depth registry. For said patients,
51
52 143 EMS providers evaluate whether patients met trauma center transport criteria in the field
53
54 144 triage decision scheme. If they did, the in-depth registry should be recorded, and EMS
55
56
57
58
59
60

1
2
3
4 145 transport protocol recommends that patients are transferred to a near regional trauma center;
5
6 146 but it is not mandatory.
7

8
9 147 The Ministry of Health and Welfare designated three ED levels according to the
10
11 148 resources and functional requirements; level 1 (n = 36) and level 2 (n = 118) EDs have more
12
13 149 resources and better facilities for emergency care and must be staffed by emergency
14
15 150 physicians 24 hours a day/365 days a year; whereas level 3 EDs (n = 248) can be staffed by
16
17 151 general physicians. In accordance with the EMS Act, all EDs participated annually in a
18
19 152 nationwide functional performance evaluation program, which was administered by the
20
21 153 Ministry of Health and Welfare. The three participating hospitals in this study were all level 1
22
23 154 EDs that can perform acute trauma care for patients with TBI 24 hours a day/365 days a
24
25 155 year—including emergency neurosurgical operation and angiographic interventions. The
26
27 156 Ministry of Health and Welfare also designated trauma centers in Korea. Total 16 trauma
28
29 157 centers were designated as trauma centers in 2018. Among them, 15 were Level I EDs.
30
31
32
33
34

35 158 ***Data source***

36
37
38 159 We used an EMS ambulance run-sheet, EMS trauma in-depth registry, and ED administrative
39
40 160 database. The EMS database information, including ambulance run-sheet and trauma in-depth
41
42 161 registry, was collected electronically by EMS providers using tablets. The EMS record
43
44 162 review for each severe trauma has been performed by EMS medical directors of each fire
45
46 163 department since 2012. The ED administrative database contains patients' demographic
47
48 164 characteristics, route of visit, time of visit, and diagnosis and disposition. We merged the
49
50 165 EMS database with the ED administrative database based on patients' arrival time, age, and
51
52 166 sex.
53
54
55
56
57
58
59
60

1
2
3
4 167 ***Study population***
5

6
7 168 We included adult (age ≥ 15) EMS users who were transported to participating hospitals with
8
9 169 severe trauma from January 1, 2014 to December 31, 2018. Severe trauma was assessed by
10
11 170 EMS providers and defined as patients who fulfilled trauma center transport criteria
12
13 (physiologic criteria, anatomic criteria, mechanism of injury criteria, or special patients or
14 171 system consideration criteria) in the field triage decision scheme.²⁰ Patients were excluded if
15
16 172 they had out-of-hospital cardiac arrest or their main cause of EMS call was medical or
17
18 173 nontraumatic injury including choking, drowning, fire, flame, heat, cold, poisoning, chemical,
19
20 174 sexual assault, weather, or natural disaster. Patients with an unknown outcome were also
21
22 175 excluded.
23
24
25
26
27

28
29 177 ***Outcome measure***
30

31
32 178 The primary outcome measure was the diagnosis of TBI. TBI diagnosis was defined as
33
34 179 patients whose diagnostic code, according to the International Statistical Classification of
35
36 180 Diseases and Related Health Problems (ICD-10), was between S06.0 and S06.9.^{21 22}
37
38 181 Although S06.7 is codes for the duration of unconscious, we included S06.7 in our study
39
40 182 outcome according to the previous studies.²¹⁻²³ However, no patients only have S06.7 code
41
42 183 for TBI diagnosis in our study. The ED administrative database has two types of primary
43
44 184 diagnostic codes: the final diagnostic codes at ED discharge and at hospital discharge. We
45
46 185 extracted up to 20 codes for each. We defined the diagnostic code as positive for TBI if a
47
48 186 confirmative diagnostic code was found in any level of the discharge record. Because ICD 10
49
50 187 code is not directly linked to the severity of TBI, we further included a variety of additional
51
52 188 outcome measures to perform analysis that take into account severity. A secondary outcome
53
54 189 measure was TBI diagnosis with intracranial hemorrhage or injury (TBI-I), defined as TBI
55
56
57
58
59
60

1
2
3
4 190 patients excluding concussion (ICD 10 code with S06.0). A tertiary outcome was TBI with
5
6 191 non-discharge (TBI-ND), defined as TBI patients excluding ED discharged patients. Because
7
8 192 TBI-ND patients needed further management by hospitalization or transfer, we thought that
9
10 193 this group of patients had clinically significant severity. A quaternary outcome measure was
11
12 194 TBI with death (TBI-D), defined as TBI patients who died in ED or hospital. Because TBI-D
13
14 195 patients are most severe group, TBI-D patients were also included in TBI-ND.
15
16
17
18

19 196 ***Variables and preprocessing***

20
21
22 197 We collected patients' demographic data, circumstances of trauma, chief complaints, EMS
23
24 198 vital sign assessment, EMS management and hospital outcomes. The detailed descriptions of
25
26 199 each variable are described in Supplementary Table 1. Categorical variables were
27
28 200 preprocessed with the one-hot encoding (dummy variable encoding) method. Continuous
29
30 201 variables were divided into four quantiles and unknown or missing values were categorized
31
32 202 as a fifth category. One-hot encoding was also applied to discretized continuous variables.
33
34 203 Preprocessing measures including discretization results of continuous variables are presented
35
36 204 in Supplementary Table 1.
37
38
39
40

41 42 ***Model development***

43
44
45 206 We developed prediction models for outcomes by using five machine learning algorithms:
46
47 207 traditional logistic regression analyses (LR), extreme gradient boost (XGB), random forest
48
49 208 (RF), support vector machine (SVM), and elastic net (EN). The LR algorithm was chosen as
50
51 209 baseline comparison algorithm because it is widely used in the medical field and has been
52
53 210 used for previous prediction model development in TBI studies.¹² Backward stepwise LR was
54
55 211 selected for feature selection, and we used the default parameter of stepAIC function from
56
57 212 MASS package (version 7.3-53.1) in R for the selection. The other four algorithms were
58
59
60

1
2
3
4 213 selected based on their ability to model nonlinear associations, their relative ease of
5
6 214 implementation, and their general acceptance in the machine learning community.²⁴⁻²⁶ All
7
8
9 215 algorithms have a method to calculate the probability of the outcome occurring and
10
11 216 algorithms other than LR need hyperparameter tuning for proper training and prediction.

12
13 217 The study population was split into training cohorts that included development,
14
15 218 validation, and test cohorts. The development cohort included a training cohort from which
16
17 219 each of the machine learning prediction models were derived and a validation cohort in which
18
19 220 the prediction models were applied to adjust the hyperparameters of the algorithm. The test
20
21 221 cohort was used for the final evaluation of the performance of the prediction models.
22
23 222 Chronological split was used for data split. Patients enrolled from January 1, 2014 to
24
25 223 December 31, 2016 were used as the training cohort; patients from January 1, 2017 to
26
27 224 December 31, 2017 were used as the validation cohort; and patients from January 1, 2018 to
28
29 225 December 31, 2018 were used as the test cohort. Hyperparameter tuning using validation data
30
31 226 was conducted by, first, a random search within 10,000 randomly generated hyperparameters;
32
33 227 then, grid search hyperparameters chosen around from random search with five candidates
34
35 228 per each hyperparameter. Finally, hyperparameter with best area under receiver-operation
36
37 229 curve (AUROC) in validation cohorts were selected. Test data were separated during training
38
39 230 and tuning processes and used to measure algorithm performance.
40
41
42
43
44
45
46

47 231 ***Statistical analysis***

48 232 The demographic findings and outcomes of the study population were described in this study.
49
50 233 Additionally, the baseline characteristics of the training cohort and the validation cohort were
51
52 234 compared. The continuous variables were compared by using Student's T-test or the
53
54 235 Wilcoxon rank sum test, and the categorical variables were compared by using the chi-
55
56 236 squared test or the Fisher exact test, as appropriate.
57
58
59
60

1
2
3
4 237 We assessed discrimination performance by comparing the AUROC for each model
5
6 238 in the test cohort. We considered an AUROC of 0.5 as no discrimination, 0.7 to 0.8 as
7
8
9 239 acceptable, 0.8 to 0.9 as excellent, and more than 0.9 is considered outstanding.²⁷ Area under
10
11 240 the precision-recall curve (AUPRC) was assessed for each model in the test cohort. We
12
13 241 assessed the calibration power by using the Hosmer–Lemeshow test, the scaled Brier score,
14
15 242 and a calibration plot in the test cohort. For the delineation of test characteristics, the
16
17 243 sensitivity, specificity, and positive and negative predictive values with 95% CIs were
18
19
20 244 determined using a cutoff probability at a sensitivity of 80%. Given that poor sensitivity of
21
22 245 clinical predictors for TBI in previous studies,⁷ and almost 75% sensitivity level for other
23
24 246 severe disease prediction in prehospital settings,^{28 29} we thought that 80% sensitivity was an
25
26 247 appropriate target for our prediction model. We calculated false positive rate as 1 –
27
28
29 248 specificity. The added prognostic power of each prediction model compared to the LR model
30
31 249 was also evaluated by continuous net reclassification index (NRI). NRI is a statistical method
32
33 250 to quantify how well a new model correctly reclassifies the study population with the other
34
35 251 models. Details of NRI are described elsewhere.³⁰

36
37
38 252 By using a model-specific metric, the variable importance of each model was
39
40 253 assessed, except for the SVM algorithm. The variable importance was determined by the
41
42 254 coefficient effect sizes for the LR model. The XGB and RF models were ranked by variable
43
44 255 importance on the selection frequency of the variable as a decision node. The absolute value
45
46 256 of the coefficients corresponding to the tuned model were used for the measurement of
47
48 257 variable importance in the EN algorithm. To compare the variable importance of each
49
50
51 258 prediction models efficiently, top 5 variables of each model was presented.
52
53
54
55
56
57
58
59
60

1
2
3
4 259 All statistical analyses were performed with R Statistical Software (version 4.0.1; R
5
6 260 Foundation for Statistical Computing, Vienna, Austria). Packages included caret, e1071,
7
8
9 261 xgboost, randomForest, and glmnet for the analysis of the machine learning algorithms.
10
11

12 262 *Patient and public involvement*

13
14 263 This research was done without patient involvement. Patients were not invited to comment on
15
16
17 264 the study design and were not consulted to develop patient relevant outcomes or interpret the
18
19 265 results. Patients were not invited to contribute to the writing or editing of this document for
20
21 266 readability or accuracy.
22
23

24 267

25 26 27 268 **Result**

28 29 30 269 *Demographic findings*

31
32
33 270 Among the 157,134 EMS users transported to three hospitals from 2014 to 2018, 1,169
34
35 271 patients were included in the final analysis (Figure 1). Patients were split into 2 datasets: data
36
37 272 from 2014 to 2017, consisting of 867 patients (74.2%) in the development cohort; and the
38
39 273 remaining data from 2018 consisting of 302 patients (25.8%) in the test cohort (Figure 1).
40
41

42 274 Among the development cohort, data from 2014 to 2016—consisting of 661 patients—were
43
44 275 used as the training cohort, and 2017 data—consisting of 206 patients—were used as the
45
46 276 validation cohort in the model.
47
48

49 277 Table 1 shows key demographic findings of the development and test cohorts. Median
50
51 278 (IQR) age was 52 years (35–66) in the development cohort and 56 years (40–69) in the test
52
53 279 cohort. Traffic accident was most common mechanism of trauma (43.3% for the development
54
55 280 cohort and 41.4% for the test cohort). The proportion of patients with alert mental status was
56
57
58
59
60

1
2
3
4 281 58.1% for the development cohort and 69.5% in the test cohort. Overall, TBI, TBI-I, TBI-
5
6 282 ND, TBI-D occurred in 215 (24.8%), 195 (22.5%), 192 (22.1%), and 32 (3.7%) in the
7
8 283 development cohort; and 66 (21.9%), 56 (18.5%), 57 (18.9%), and 11 (3.6%) in the test
9
10 284 cohort. All demographic characteristics of the development and test cohorts are described in
11
12 285 Supplementary Table 2.

17 286 ***Main analysis***

20 287 The final hyperparameters of prediction models are described in Supplementary Table 3. The
21
22 288 discrimination and NRI of the prediction models on the test cohort are presented in Table 2.
23
24 289 The AUROC for outcomes were 0.770–0.806 for TBI, 0.820–0.844 for TBI-I, 0.767–0.811
25
26 290 for TBI-ND, and 0.664–0.889 for TBI-D (Table 2 and Supplementary Figure 1). Compared to
27
28 291 LR, XGB performed significantly well in predicting TBI, and RF and EN performed well in
29
30 292 predicting TBI-ND and TBI-D. EN model generally performed well on all outcomes. The
31
32 293 AUROC of the EN model for outcomes were 0.799 (95% CI: 0.732–0.867), 0.844 (95% CI:
33
34 294 0.779–0.910), 0.811 (95% CI: 0.741–0.882), and 0.871 (95% CI: 0.764–0.978) for TBI, TBI-
35
36 295 I, TBI-ND, and TBI-D, respectively. Machine learning models generally resulted in
37
38 296 significant reclassification improvement compared to LR for TBI, TBI-I, and TBI-ND. For
39
40 297 prediction TBI-D, AUROC difference, and reclassification improvement compared to LR
41
42 298 was non-significant in all machine learning models. The precision-recall curve is shown in
43
44 299 Supplementary Figure 2. AUPRC were 0.479–0.564 for TBI, 0.469–0.606 for TBI-I, 0.477–
45
46 300 0.551 for TBI-ND and 0.094–0.140 for TBI-D. EN model showed highest AUPRC among all
47
48 301 prediction models. Supplementary Figure 3 shows the calibration plot of prediction models
49
50 302 according to outcomes. All prediction models generally showed poor calibration. Given the
51
52 303 high AUROC and AUPRC among prediction models, and reclassification improvement
53
54
55
56
57
58
59
60

1
2
3
4 304 compared to LR, we determined EN as a best-performing prediction model in our analysis.

5
6 305 Using cutoff of 80% sensitivity, specificity was 47.5–68.2% for TBI, 71.1–81.3% for
7
8 306 TBI-I, 46.1–74.3% for TBI-ND, and 42.6–49.0 for TBI-D. EN showed the highest specificity
9
10
11 307 and PPV among all outcomes. False positive rate (1 – specificity) was almost 19.7–39.0%
12
13 308 according to outcomes in the EN model. The 95% CI of specificity of the EN model was not
14
15 309 overlapped with LR in TBI, TBI-ND, and TBI-D predictions. NPV was almost 89–99% for
16
17
18 310 all outcomes in the prediction models (Table 3).

19
20 311 Table 4 shows the top 5 variable importance of prediction models according to
21
22 312 outcomes. Variables related to patients' symptom of loss of consciousness, Glasgow Coma
23
24 313 Scale component, and light reflex were the three most important variables to predict all
25
26 314 outcomes. Compared to other outcomes, the difference between variable importance for TBI-
27
28
29 315 D was prominent, and the mechanism of injury, heart rate, and age showed the highest
30
31
32 316 importance for predicting TBI-D.

33 34 35 317 **Discussion**

36
37
38 318 By using prehospital data from EMS users visiting three teaching hospitals, we developed
39
40 319 and validated prediction models for the diagnosis and prognosis of TBI using machine
41
42 320 learning algorithms among patients with severe trauma, identified by EMS providers in South
43
44 321 Korea. We found that 24% of patients were diagnosed with TBI, 22% showed intracranial
45
46 322 injury, 21% could not be discharged from the ED with a TBI diagnosis, and 4% showed TBI-
47
48
49 323 related death. Machine learning models showed acceptable-to-excellent discrimination
50
51 324 performance (AUROCs were 0.799–0.871 according to outcomes in the best-performing EN
52
53 325 model). When identifying 80% of target patients with TBI, the false positive rate was almost
54
55
56 326 19.7–39.0%. Consciousness status related variables ranging from patients' symptom to EMS
57
58
59
60

1
2
3
4 327 providers' assessment showed the highest importance for predicting all outcomes. This study
5
6 328 adds considerably to the understanding of prehospital prediction performance of TBI among
7
8
9 329 patients with severe trauma. Use of comprehensive prehospital information and certain
10
11 330 machine learning approaches led to increased performance with a diminished false positive
12
13 331 rate compared to those of the traditional statistical model.

14
15 332 Several studies reported that EMS providers' assessment using prehospital
16
17 333 information is effective for the identification of patients with severe trauma who require
18
19 334 direct transport to a trauma center.³¹⁻³³ Because TBI accounts for a significant portion of
20
21 335 patients with severe trauma,³² and the majority of patients have poor access to trauma
22
23 336 centers,³⁴ identification of TBI among patients with severe trauma by EMS providers could
24
25 337 contribute to proper prehospital management and destination hospital decisions.³ However,
26
27 338 prehospital identification of TBI is challenging.³⁵ Prehospital clinical signs showed poor
28
29 339 predictive performance for differentiating patients with TBI.⁷, and previous prediction
30
31 340 models related to TBI mostly focused on TBI outcomes.^{8 9 13} One study reported the
32
33 341 predictors for mild TBI with persistent symptoms; but a single-center case-control study
34
35 342 design and ED-based model development lacks applicability to prehospital settings.³⁶ In this
36
37 343 study, we developed and tested TBI prediction models that used prehospital information, and
38
39 344 we found acceptable discrimination power for the prediction of diagnosis and prognosis of
40
41 345 TBI. Uniquely, we incorporated various demographic variables, trauma circumstances,
42
43 346 patients' complaints, and EMS assessment information in the prediction models, and we
44
45 347 adapted the machine learning algorithms.

46
47 348 When using a cutoff for 80% sensitivity for TBI detection, the false positive rate was
48
49 349 19.7–39.0% (Table 2). Those false positive rate levels are plausible for detecting severe
50
51 350 diseases in EMS settings. A previous study reported a 26% of false positive rate of EMS
52
53
54
55
56
57
58
59
60

1
2
3
4 351 triage for myocardial infarction with a sensitivity of 74% and 50% of false positive rate of
5
6 352 EMS recognition of stroke in sensitivity of 74%.^{28 29} Considering the prevalence of outcomes
7
8 353 (24% in TBI, 22% in TBI-I, 21% in TBI-ND, and 4% in TBI-D; Table 1), there would be 16,
9
10 354 9, 12, and 67 false-positive patients for every 10 patients that are accurately identified as TBI,
11
12 355 TBI-I, TBI-ND, and TBI-D, respectively (Supplementary Table 4). Because of the low
13
14 356 prevalence of TBI-D, a similar specificity of the prediction model for outcomes resulted in a
15
16 357 very low positive predictive value and a high proportion of false positive cases, which
17
18 358 suggested the limited applicability of prediction models for TBI-D in prehospital settings.

19
20 359 Consciousness-status-related variables ranging from patients' complaints to EMS
21
22 360 assessment showed the highest importance regardless of models and outcomes in our study.
23
24 361 Consciousness status is closely associated with head trauma. Head trauma can result in
25
26 362 structural brain injury or physiological disruption of brain function, which could result in
27
28 363 altered mental status.³⁷ Mental status is also associated with TBI severity,³⁸ and its
29
30 364 association with TBI outcomes have been reported.^{8 9 13} History taking and physical
31
32 365 examination for altered mental status is key to early diagnosis and proper management of TBI
33
34 366 in prehospital settings.³⁹

35
36 367 We adapted machine learning algorithms for the prediction of TBI-related outcomes
37
38 368 and found an improvement in discrimination and an increase in specificity with the same
39
40 369 sensitivity thresholds. However, the LR model also showed acceptable or similar
41
42 370 performance compared to machine learning models, according to the outcomes. In clinical
43
44 371 prediction models, a previous systematic review reported no performance benefit of the
45
46 372 machine learning model over LR.⁴⁰ The previous study stated that machine learning models
47
48 373 tend to show high performance with a strong signal-to-noise ratio problem like gaming,
49
50 374 image recognition. However, clinical prediction problems often result in a poor signal-to-

1
2
3
4 375 noise ratio.⁴⁰ If we could use unstructured data, which has strong signal-to-noise ratio like
5
6 376 continuous vital sign monitoring data or audiovisual data for patients' appearance, machine
7
8
9 377 learning models might perform better than LR models. In addition, if we analyzed more
10
11 378 patient data, the performance improvement of machine models might be elucidated.

12
13 379 Precise assessment in prehospital field could contribute to improved patient-related
14
15 380 outcomes. High demand of EMS call and response, disparity in accessibility to definitive care
16
17 381 capable hospitals according to regions,³⁴ and the importance of timely management in acute
18
19 382 disease care are the chief reasons behind the necessity for the accurate assessment of EMS
20
21 383 providers. Although information acquisition and processing is quite difficult in prehospital
22
23 384 areas, various instruments and information systems could attribute to diminish those
24
25 385 problems. Complex data acquisition like mobile CT or other unstructured data⁴¹, information
26
27 386 sharing through telemedicine,⁴² and decision support tools in prehospital environments⁴³
28
29 387 could contribute to the accurate assessment of EMS providers. More information acquisition
30
31 388 and real-time processing of those data could improve the clinical prediction models in
32
33 389 prehospital areas, which could lead to the improvement of patients' safety and outcomes.

34
35 390 Our study had several limitations. First, our data were collected at three teaching
36
37 391 hospitals in urban areas of South Korea. Therefore, external validation for other areas should
38
39 392 be conducted to generalize the developed prediction model. Second, we used retrospective
40
41 393 analysis of electronically collected prehospital and hospital data. There might be various
42
43 394 information loss and missing data. We treated missing status as a separate category for our
44
45 395 analysis;⁴⁴ however, there could be different reasons for missing data. Third, there is a
46
47 396 possibility that the prediction model was overfitted or underfitted. The use of large number of
48
49 397 predictors also can contribute to overfitting. To minimize this issue, we rigorously searched
50
51 398 hyperparameters and carefully chose hyperparameters according to the performance in
52
53
54
55
56
57
58
59
60

1
2
3
4 399 independent validation cohorts. Fourth, we selected our study population using trauma center
5
6 400 transport criteria for EMS providers in Korea. Although those criteria are based on the field
7
8 401 triage decision scheme which is the most widely used prehospital trauma triage protocol,⁶
9
10 402 extrapolation to another EMS setting or general trauma patients would be limited. Fifth,
11
12 403 Abbreviated Injury Scale (AIS) codes were not used to identify our study outcome because of
13
14 404 a lack of information. To compensate for this limitation, we further identified TBI-I, TBI-
15
16 405 ND, and TBI-D patients to consider severity. However, different definitions of clinical
17
18 406 severity, including ICU admission or emergency operation, might be possible. Lastly, this
19
20 407 study was performed in an intermediate-service-level EMS system. The generalization of our
21
22 408 study findings to different EMS settings should be made with caution.

23
24
25
26
27 409 In conclusion, we presented data on TBI among patients with severe trauma assessed
28
29 410 by EMS providers, and our results inform the development of prediction models for the
30
31 411 diagnosis and prognosis of TBI in our population. We used various information that can be
32
33 412 obtained in prehospital settings and showed acceptable outcome performance. The consistent
34
35 413 importance of consciousness-status-related variables emphasizes the importance of
36
37 414 assessment and monitoring of consciousness status in prehospital areas. Although
38
39 415 prospective, and implementation studies are needed for TBI prediction in prehospital areas,
40
41 416 our study outlined a novel method for the precise assessment of EMS providers using a
42
43 417 machine-learning-based prediction model. Further collection of various types of patient-
44
45 418 related data would contribute to the enhanced performance of the clinical prediction model in
46
47 419 prehospital settings.

48
49
50
51
52 420

1
2
3
4 421 **Author Contribution Statement**

5
6
7 422 YHC and JH Park designed and developed the study, analysed and interpreted the data, and
8
9 423 drafted the initial manuscript. KJH, YSR, KJS and SDS were involved in the acquisition of
10
11 424 data, the development of the research question and assisted with analysis and interpretation of
12
13
14 425 data. All authors revised the drafts for intellectual content and edited the manuscript. All
15
16 426 authors reviewed and approved the final draft.

17
18
19 427

20
21
22
23 428 **Funding**

24
25
26 429 This study was supported by grant No. '04-2019-0680' from the Seoul National University
27
28 430 Hospital Research Fund.

29
30 431

31
32
33
34 432 **Competing Interests**

35
36 433 There are no conflicts of interest for all authors in this study.

37
38 434

39
40 435 **Patients consent**

41
42 436 Not required

43
44 437

45
46
47
48
49 438 **Data availability statement**

50
51 439 No data are available. We do not have ethics approval to share data.

52
53 440

1
2
3
4 441 **Ethical statements**

5
6 442 This study complied with the Declaration of Helsinki, and its protocol was approved by the
7
8 443 Institutional Review Board of the Seoul National University Hospital with a waiver of
9
10 444 informed consent (IRB No: E-2006-004-1128).
11
12

13 445

14
15
16
17 446 **References**

- 18
19 447 1. Hsia RY, Markowitz AJ, Lin F, et al. Ten-year trends in traumatic brain injury: a
20
21 448 retrospective cohort study of California emergency department and hospital revisits and
22
23 449 readmissions. *BMJ Open* 2018;8(12):e022297. doi: 10.1136/bmjopen-2018-022297
24
25 450 [published Online First: 2018/12/16]
26
27
28 451 2. Finfer SR, Cohen J. Severe traumatic brain injury. *Resuscitation* 2001;48(1):77-90. doi:
29
30 452 10.1016/s0300-9572(00)00321-x [published Online First: 2001/02/13]
31
32
33 453 3. Spaite DW, Bobrow BJ, Keim SM, et al. Association of Statewide Implementation of the
34
35 454 Prehospital Traumatic Brain Injury Treatment Guidelines With Patient Survival
36
37 455 Following Traumatic Brain Injury: The Excellence in Prehospital Injury Care (EPIC)
38
39 456 Study. *JAMA Surg* 2019;154(7):e191152. doi: 10.1001/jamasurg.2019.1152 [published
40
41 457 Online First: 2019/05/09]
42
43
44 458 4. McHugh GS, Engel DC, Butcher I, et al. Prognostic value of secondary insults in traumatic
45
46 459 brain injury: results from the IMPACT study. *J Neurotrauma* 2007;24(2):287-93. doi:
47
48 460 10.1089/neu.2006.0031 [published Online First: 2007/03/23]
49
50
51 461 5. Pelieu I, Kull C, Walder B. Prehospital and Emergency Care in Adult Patients with Acute
52
53 462 Traumatic Brain Injury. *Med Sci (Basel)* 2019;7(1) doi: 10.3390/medsci7010012
54
55 463 [published Online First: 2019/01/24]
56
57
58 464 6. Sasser SM, Hunt RC, Faul M, et al. Guidelines for field triage of injured patients:
59
60

- 1
2
3
4 465 recommendations of the National Expert Panel on Field Triage, 2011. *Morbidity and*
5
6 466 *Mortality Weekly Report: Recommendations and Reports* 2012;61(1):1-20.
7
8
9 467 7. Ter Avest E, Taylor S, Wilson M, et al. Prehospital clinical signs are a poor predictor of
10
11 468 raised intracranial pressure following traumatic brain injury. *Emerg Med J*
12
13 469 2021;38(1):21-26. doi: 10.1136/emered-2020-209635 [published Online First:
14
15 470 2020/09/20]
16
17
18 471 8. Collaborators MCT, Perel P, Arango M, et al. Predicting outcome after traumatic brain injury:
19
20 472 practical prognostic models based on large cohort of international patients. *BMJ*
21
22 473 2008;336(7641):425-9. doi: 10.1136/bmj.39461.643438.25 [published Online First:
23
24 474 2008/02/14]
25
26
27 475 9. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain
28
29 476 injury: development and international validation of prognostic scores based on
30
31 477 admission characteristics. *PLoS Med* 2008;5(8):e165; discussion e65. doi:
32
33 478 10.1371/journal.pmed.0050165 [published Online First: 2008/08/08]
34
35
36 479 10. Gozt AK, Hellewell SC, Thorne J, et al. Predicting outcome following mild traumatic brain
37
38 480 injury: protocol for the longitudinal, prospective, observational Concussion Recovery
39
40 481 (CREST) cohort study. *BMJ Open* 2021;11(5):e046460. doi: 10.1136/bmjopen-2020-
41
42 482 046460 [published Online First: 2021/05/15]
43
44
45 483 11. Huth SF, Slater A, Waak M, et al. Predicting Neurological Recovery after Traumatic Brain
46
47 484 Injury in Children: A Systematic Review of Prognostic Models. *J Neurotrauma*
48
49 485 2020;37(20):2141-49. doi: 10.1089/neu.2020.7158 [published Online First: 2020/05/29]
50
51
52 486 12. Perel P, Edwards P, Wentz R, et al. Systematic review of prognostic models in traumatic
53
54 487 brain injury. *BMC Med Inform Decis Mak* 2006;6:38. doi: 10.1186/1472-6947-6-38
55
56 488 [published Online First: 2006/11/16]
57
58
59
60

- 1
2
3
4 489 13. Miller PR, Chang MC, Hoth JJ, et al. Predicting Mortality and Independence at Discharge
5
6 490 in the Aging Traumatic Brain Injury Population Using Data Available at Admission. *J*
7
8 491 *Am Coll Surg* 2017;224(4):680-85. doi: 10.1016/j.jamcollsurg.2016.12.053 [published
9
10 492 Online First: 2017/03/07]
11
12
13 493 14. Abujaber A, Fadlalla A, Gammoh D, et al. Prediction of in-hospital mortality in patients
14
15 494 with post traumatic brain injury using National Trauma Registry and Machine Learning
16
17 495 Approach. *Scand J Trauma Resusc Emerg Med* 2020;28(1):44. doi: 10.1186/s13049-
18
19 496 020-00738-5 [published Online First: 2020/05/29]
20
21
22 497 15. Gravesteijn BY, Nieboer D, Ercole A, et al. Machine learning algorithms performed no
23
24 498 better than regression models for prognostication in traumatic brain injury. *J Clin*
25
26 499 *Epidemiol* 2020;122:95-107. doi: 10.1016/j.jclinepi.2020.03.005 [published Online
27
28 500 First: 2020/03/24]
29
30
31 501 16. Roozenbeek B, Lingsma HF, Lecky FE, et al. Prediction of outcome after moderate and
32
33 502 severe traumatic brain injury: external validation of the International Mission on
34
35 503 Prognosis and Analysis of Clinical Trials (IMPACT) and Corticoid Randomisation
36
37 504 After Significant Head injury (CRASH) prognostic models. *Crit Care Med*
38
39 505 2012;40(5):1609-17. doi: 10.1097/CCM.0b013e31824519ce [published Online First:
40
41 506 2012/04/19]
42
43
44 507 17. Wasserman EB, Shah MN, Jones CM, et al. Identification of a neurologic scale that
45
46 508 optimizes EMS detection of older adult traumatic brain injury patients who require
47
48 509 transport to a trauma center. *Prehosp Emerg Care* 2015;19(2):202-12. doi:
49
50 510 10.3109/10903127.2014.959225 [published Online First: 2014/10/08]
51
52
53 511 18. Collins GS, Reitsma JB, Altman DG, et al. Transparent Reporting of a multivariable
54
55 512 prediction model for Individual Prognosis Or Diagnosis (TRIPOD). *Ann Intern Med*
56
57
58
59
60

- 1
2
3
4 513 2015;162(10):735-6. doi: 10.7326/L15-5093-2 [published Online First: 2015/05/20]
5
6 514 19. Sasser SM, Hunt RC, Sullivent EE, et al. Guidelines for field triage of injured patients:
7
8 515 recommendations of the National Expert Panel on Field Triage. 2009
9
10 516 20. Sasser SM, Hunt RC, Faul M, et al. Guidelines for field triage of injured patients:
11
12 517 recommendations of the National Expert Panel on Field Triage, 2011. *MMWR Recomm*
13
14 518 *Rep* 2012;61(RR-1):1-20. [published Online First: 2012/01/13]
15
16 519 21. Andelic N, Anke A, Skandsen T, et al. Incidence of hospital-admitted severe traumatic
17
18 520 brain injury and in-hospital fatality in Norway: a national cohort study.
19
20 521 *Neuroepidemiology* 2012;38(4):259-67. doi: 10.1159/000338032 [published Online
21
22 522 First: 2012/06/09]
23
24 523 22. Ro YS, Shin SD, Holmes JF, et al. Comparison of clinical performance of cranial computed
25
26 524 tomography rules in patients with minor head injury: a multicenter prospective study.
27
28 525 *Acad Emerg Med* 2011;18(6):597-604. doi: 10.1111/j.1553-2712.2011.01094.x
29
30 526 [published Online First: 2011/06/17]
31
32 527 23. Chan V, Thurairajah P, Colantonio A. Defining pediatric traumatic brain injury using
33
34 528 International Classification of Diseases Version 10 Codes: a systematic review. *BMC*
35
36 529 *Neurol* 2015;15:7. doi: 10.1186/s12883-015-0259-7 [published Online First:
37
38 530 2015/02/05]
39
40 531 24. Zou H, Hastie T. Regularization and variable selection via the elastic net. *Journal of the*
41
42 532 *Royal Statistical Society: Series B (Statistical Methodology)* 2005;67(2):301-20. doi:
43
44 533 10.1111/j.1467-9868.2005.00503.x
45
46 534 25. Hearst MA, Dumais ST, Osuna E, et al. Support vector machines. *IEEE Intelligent Systems*
47
48 535 *and their Applications* 1998;13(4):18-28. doi: 10.1109/5254.708428
49
50 536 26. Chen T, Guestrin C. XGBoost: A Scalable Tree Boosting System. Proceedings of the 22nd
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 537 ACM SIGKDD International Conference on Knowledge Discovery and Data Mining.
5
6 538 San Francisco, California, USA: Association for Computing Machinery, 2016:785–94.
7
8
9 539 27. Menard S. Applied logistic regression analysis: Sage 2002. pp. 162.
10
11 540 28. Oostema JA, Konen J, Chassee T, et al. Clinical predictors of accurate prehospital stroke
12
13 541 recognition. *Stroke* 2015;46(6):1513-7. doi: 10.1161/STROKEAHA.115.008650
14
15 542 [published Online First: 2015/04/30]
16
17
18 543 29. Swan PY, Nighswonger B, Boswell GL, et al. Factors associated with false-positive
19
20 544 emergency medical services triage for percutaneous coronary intervention. *West J*
21
22 545 *Emerg Med* 2009;10(4):208-12. [published Online First: 2010/01/05]
23
24
25 546 30. Park JH, Shin SD, Song KJ, et al. Prediction of good neurological recovery after out-of-
26
27 547 hospital cardiac arrest: A machine learning analysis. *Resuscitation* 2019;142:127-35.
28
29 548 doi: 10.1016/j.resuscitation.2019.07.020 [published Online First: 2019/07/31]
30
31
32 549 31. Esposito TJ, Offner PJ, Jurkovich GJ, et al. Do prehospital trauma center triage criteria
33
34 550 identify major trauma victims? *Arch Surg* 1995;130(2):171-6. doi:
35
36 551 10.1001/archsurg.1995.01430020061010 [published Online First: 1995/02/01]
37
38
39 552 32. Ocak G, Sturms LM, Hoogeveen JM, et al. Prehospital identification of major trauma
40
41 553 patients. *Langenbecks Arch Surg* 2009;394(2):285-92. doi: 10.1007/s00423-008-0340-
42
43 554 4 [published Online First: 2008/06/27]
44
45
46 555 33. Fries GR, McCalla G, Levitt MA, et al. A prospective comparison of paramedic judgment
47
48 556 and the trauma triage rule in the prehospital setting. *Ann Emerg Med* 1994;24(5):885-
49
50 557 9. doi: 10.1016/s0196-0644(94)70207-1 [published Online First: 1994/11/01]
51
52
53 558 34. Branas CC, MacKenzie EJ, Williams JC, et al. Access to trauma centers in the United States.
54
55 559 *JAMA* 2005;293(21):2626-33. doi: 10.1001/jama.293.21.2626 [published Online First:
56
57 560 2005/06/02]
58
59
60

- 1
2
3
4 561 35. Whiting MD, Dengler BA, Rodriguez CL, et al. Prehospital Detection of Life-Threatening
5
6 562 Intracranial Pathology: An Unmet Need for Severe TBI in Austere, Rural, and Remote
7
8 563 Areas. *Front Neurol* 2020;11:599268. doi: 10.3389/fneur.2020.599268 [published
9
10 564 Online First: 2020/11/17]
- 11
12
13 565 36. Wojcik SM. Predicting mild traumatic brain injury patients at risk of persistent symptoms
14
15 566 in the Emergency Department. *Brain Inj* 2014;28(4):422-30. doi:
16
17 567 10.3109/02699052.2014.884241 [published Online First: 2014/02/26]
- 18
19
20 568 37. Management of Concussion/m TBIWG. VA/DoD Clinical Practice Guideline for
21
22 569 Management of Concussion/Mild Traumatic Brain Injury. *J Rehabil Res Dev*
23
24 570 2009;46(6):CP1-68. [published Online First: 2010/01/30]
- 25
26
27 571 38. Grote S, Bocker W, Mutschler W, et al. Diagnostic value of the Glasgow Coma Scale for
28
29 572 traumatic brain injury in 18,002 patients with severe multiple injuries. *J Neurotrauma*
30
31 573 2011;28(4):527-34. doi: 10.1089/neu.2010.1433 [published Online First: 2011/01/27]
- 32
33
34 574 39. Badjatia N, Carney N, Crocco TJ, et al. Guidelines for prehospital management of traumatic
35
36 575 brain injury 2nd edition. *Prehosp Emerg Care* 2008;12 Suppl 1:S1-52. doi:
37
38 576 10.1080/10903120701732052 [published Online First: 2008/09/06]
- 39
40
41 577 40. Christodoulou E, Ma J, Collins GS, et al. A systematic review shows no performance
42
43 578 benefit of machine learning over logistic regression for clinical prediction models. *J*
44
45 579 *Clin Epidemiol* 2019;110:12-22. doi: 10.1016/j.jclinepi.2019.02.004 [published Online
46
47 580 First: 2019/02/15]
- 48
49
50 581 41. Nakada TA, Masunaga N, Nakao S, et al. Development of a prehospital vital signs chart
51
52 582 sharing system. *Am J Emerg Med* 2016;34(1):88-92. doi: 10.1016/j.ajem.2015.09.048
53
54 583 [published Online First: 2015/10/29]
- 55
56
57 584 42. Kim Y, Groombridge C, Romero L, et al. Decision Support Capabilities of Telemedicine
58
59
60

- 1
2
3
4 585 in Emergency Prehospital Care: Systematic Review. *J Med Internet Res*
5
6 586 2020;22(12):e18959. doi: 10.2196/18959 [published Online First: 2020/12/09]
7
8
9 587 43. Reisner AT, Khitrov MY, Chen L, et al. Development and validation of a portable platform
10
11 588 for deploying decision-support algorithms in prehospital settings. *Appl Clin Inform*
12
13 589 2013;4(3):392-402. doi: 10.4338/ACI-2013-04-RA-0023 [published Online First:
14
15 590 2013/10/25]
16
17
18 591 44. Maslove DM, Podchiyska T, Lowe HJ. Discretization of continuous features in clinical
19
20 592 datasets. *J Am Med Inform Assoc* 2013;20(3):544-53. doi: 10.1136/amiajnl-2012-
21
22 593 000929 [published Online First: 2012/10/13]
23
24
25
26 594
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 595 **Figure legends**
5

6
7 596 Figure 1. Population flow. EMS, emergency medical service; OHCA, out-of-hospital cardiac
8
9 597 arrest; TBI, traumatic brain injury.
10

11 598
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

599 Table 1. Key characteristics of the development and test cohorts.

	n (%) or Median (IQR)			P
	Total	Development cohort	Test cohort	
Total	N = 1169	n = 867	n = 302	
Demographics				
Age, years	53 (36–66)	52 (35–66)	56 (40–69)	< 0.01
Male	809 (69.2)	592 (68.3)	217 (71.9)	0.25
Job, unemployed	299 (25.6)	197 (22.7)	102 (33.8)	< 0.01
Diabetes	62 (5.3)	35 (4.0)	27 (8.9)	< 0.01
Hypertension	105 (9.0)	61 (7.0)	44 (14.6)	< 0.01
Circumstances of trauma				
Location, road/highway	444 (38.0)	326 (37.6)	118 (39.1)	0.65
Season, summer	336 (28.7)	253 (29.2)	83 (27.5)	0.57
Weekday, weekend	811 (69.4)	599 (69.1)	212 (70.2)	0.72
Time, 6 p.m. to midnight	361 (30.9)	265 (30.6)	96 (31.8)	0.69
Mechanism of injury, TA	500 (42.8)	375 (43.3)	125 (41.4)	0.57
Chief complaint				
Fracture/abrasion/laceration	302 (25.8)	204 (23.5)	98 (32.5)	< 0.01
EMS vital sign assessment				
SBP, mmHg	130 (109–150)	130 (104–146)	131 (115–150)	< 0.01
DBP, mmHg	80 (70–91)	80 (69–90)	80 (70–92)	0.21
RR, /min	18 (16–20)	18 (16–20)	18 (16–20)	0.33
HR, /min	86 (75–99)	86 (74–99)	86 (76–100)	0.40
SpO ₂ , %	98 (95–99)	98 (95–99)	98 (96–99)	0.67
AVPU scale, Alert	714 (61.1)	504 (58.1)	210 (69.5)	< 0.01
EMS management				
Intravenous route	176 (15.1)	129 (14.9)	47 (15.6)	0.77
Hemorrhage control	586 (50.1)	426 (49.1)	160 (53.0)	0.25
Spinal motion restriction	811 (69.4)	606 (69.9)	205 (67.9)	0.51
Oxygen supply	233 (19.9)	176 (20.3)	57 (18.9)	0.59
In-hospital mortality	90 (7.7)	74 (8.5)	16 (5.3)	0.07
Outcomes				
TBI	281 (24.0)	215 (24.8)	66 (21.9)	0.30
TBI with intracranial injury	251 (21.5)	195 (22.5)	56 (18.5)	0.15
TBI-related non-discharge	249 (21.3)	192 (22.1)	57 (18.9)	0.23
TBI-related death	43 (3.7)	32 (3.7)	11 (3.6)	0.95

600 IQR, interquartile range; TA, traffic accident; SBP, systolic blood pressure; DBP, diastolic
601 blood pressure; RR, respiratory rate; AVPU, mental status in alert, verbal, pain, and
602 unresponsive scale; ED, emergency department; TBI, traumatic brain injury.

603 Table 2. Discrimination and reclassification of prediction models for outcomes on test
604 cohort.

Outcome	Model	AUROC (95% CI)	p ^a	NRI (95% CI)	p ^b	AUPRC
TBI						
	LR	0.770 (0.698, 0.841)	NA	NA	NA	0.492
	XGB	0.809 (0.743, 0.876)	0.04	0.689 (0.427, 0.951)	< 0.01	0.552
	SVM	0.776 (0.708, 0.844)	0.77	0.339 (0.072, 0.607)	0.01	0.479
	RF	0.800 (0.735, 0.865)	0.13	0.308 (0.047, 0.569)	0.02	0.532
	EN	0.799 (0.732, 0.867)	0.06	0.698 (0.441, 0.954)	< 0.01	0.564
TBI-I						
	LR	0.820 (0.751, 0.890)	NA	NA	NA	0.551
	XGB	0.838 (0.775, 0.901)	0.28	0.539 (0.258, 0.821)	< 0.01	0.554
	SVM	0.812 (0.748, 0.875)	0.66	0.729 (0.464, 0.994)	< 0.01	0.469
	RF	0.836 (0.772, 0.899)	0.38	0.333 (0.058, 0.607)	0.02	0.552
	EN	0.844 (0.779, 0.910)	0.15	1.093 (0.845, 1.342)	< 0.01	0.606
TBI-ND						
	LR	0.767 (0.690, 0.844)	NA	NA	NA	0.482
	XGB	0.800 (0.727, 0.873)	0.07	0.605 (0.326, 0.884)	< 0.01	0.496
	SVM	0.778 (0.704, 0.852)	0.56	0.285 (-0.001, 0.572)	0.05	0.477
	RF	0.809 (0.739, 0.880)	0.03	0.194 (-0.059, 0.448)	0.13	0.535
	EN	0.811 (0.741, 0.882)	0.02	0.768 (0.496, 1.039)	< 0.01	0.551
TBI-D						
	LR	0.664 (0.490, 0.838)	NA	NA	NA	0.138
	XGB	0.714 (0.512, 0.917)	0.64	-0.026 (-0.605, 0.553)	0.93	0.094
	SVM	0.814 (0.718, 0.910)	0.09	0.209 (-0.325, 0.742)	0.44	0.140
	RF	0.889 (0.801, 0.976)	< 0.01	-0.204 (-0.742, 0.334)	0.46	0.196
	EN	0.871 (0.764, 0.978)	0.01	0.119 (-0.415, 0.654)	0.66	0.293

605 ^aComparing the AUROC and the logistic regression model.

606 ^bComparing the NRI and the logistic regression model.

607 AUROC, area under the receiver operating characteristic curve; CI, confidence interval;

608 NRI, net reclassification index; AUPRC, area under precision-recall curve; TBI,

609 traumatic brain injury, TBI-I, traumatic brain injury with intracranial injury; TBI-ND;

610 traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with death;

611 LR, logistic regression analysis; XGB, extreme gradient boosting; SVM, support vector

612 machine; RF, random forest; EN, elastic net

613

614

615

616 Table 3. Test characteristics of prediction models for outcomes on test cohort.

Outcome	Model	Specificity (95% CI)	Sensitivity (95% CI)	PPV (95% CI)	NPV (95% CI)	Cutoff
TBI						
	LR	47.5 (40.9, 54.0)	80.3 (68.7, 89.1)	29.9 (23.3, 37.3)	89.6 (82.9, 94.3)	0.136
	XGB	72.5 (66.3, 78.1)	80.3 (68.7, 89.1)	44.9 (35.7, 54.3)	92.9 (88.2, 96.2)	0.268
	SVM	64.8 (58.4, 70.9)	80.3 (68.7, 89.1)	39.0 (30.7, 47.7)	92.2 (87.0, 95.8)	0.191
	RF	68.2 (61.9, 74.1)	80.3 (68.7, 89.1)	41.4 (32.8, 50.4)	92.5 (87.6, 96.0)	0.185
	EN	61.0 (54.5, 67.3)	80.3 (68.7, 89.1)	36.6 (28.7, 44.9)	91.7 (86.3, 95.5)	0.205
TBI-I						
	LR	71.1 (65.0, 76.7)	80.4 (67.6, 89.8)	38.8 (29.9, 48.3)	94.1 (89.7, 97.0)	0.164
	XGB	74.0 (68.0, 79.4)	80.4 (67.6, 89.8)	41.3 (31.9, 51.1)	94.3 (90.0, 97.1)	0.143
	SVM	71.1 (65.0, 76.7)	80.4 (67.6, 89.8)	38.8 (29.9, 48.3)	94.1 (89.7, 97.0)	0.172
	RF	76.0 (70.2, 81.2)	80.4 (67.6, 89.8)	43.3 (33.6, 53.3)	94.4 (90.3, 97.2)	0.205
	EN	81.3 (75.9, 86.0)	80.4 (67.6, 89.8)	49.5 (38.8, 60.1)	94.8 (90.9, 97.4)	0.204
TBI-ND						
	LR	46.1 (39.8, 52.6)	80.7 (68.1, 90.0)	25.8 (19.6, 32.9)	91.1 (84.7, 95.5)	0.090
	XGB	66.5 (60.2, 72.4)	80.7 (68.1, 90.0)	35.9 (27.7, 44.9)	93.7 (89.0, 96.8)	0.242
	SVM	59.2 (52.7, 65.4)	80.7 (68.1, 90.0)	31.5 (24.1, 39.7)	92.9 (87.7, 96.4)	0.147
	RF	60.4 (54.0, 66.6)	80.7 (68.1, 90.0)	32.2 (24.6, 40.5)	93.1 (88.0, 96.5)	0.138
	EN	74.3 (68.3, 79.6)	80.7 (68.1, 90.0)	42.2 (32.8, 52.0)	94.3 (90.0, 97.1)	0.201
TBI-D						
	LR	42.6 (36.9, 48.5)	81.8 (48.2, 97.7)	5.1 (2.4, 9.5)	98.4 (94.4, 99.8)	0.005
	XGB	57.7 (51.8, 63.5)	81.8 (48.2, 97.7)	6.8 (3.2, 12.5)	98.8 (95.8, 99.9)	0.002
	SVM	74.2 (68.8, 79.2)	81.8 (48.2, 97.7)	10.7 (5.0, 19.4)	99.1 (96.7, 99.9)	0.039
	RF	74.9 (69.5, 79.8)	81.8 (48.2, 97.7)	11.0 (5.1, 19.8)	99.1 (96.8, 99.9)	0.005
	EN	79.0 (73.9, 83.6)	81.8 (48.2, 97.7)	12.9 (6.1, 23.0)	99.1 (96.9, 99.9)	0.033

617 TBI, traumatic brain injury; TBI-I, traumatic brain injury with intracranial injury; TBI-
618 ND; traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with
619 death; LR, logistic regression analysis; XGB, extreme gradient boosting; SVM, support
620 vector machine; RF, random forest; EN, elastic net.

621

622 Table 4. Top 5 important variables for outcomes in descending order using model
 623 specific metrics

Outcome	Rank	LR	XGB	RF	EN
TBI					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	Loss of consciousness
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	GCS, Motor, 1
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 2
	4	Light reflex	Other mechanism	Light reflex	GCS, Eye, 1
	5	GCS, Motor, 1	GCS, Verbal, 2	GCS, Motor, 1	GCS, Verbal, 1
TBI-I					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	GCS, Eye, 1
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	Loss of consciousness
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 1
	4	Light reflex	GCS, Verbal, 2	Light reflex	GCS, Verbal, 1
	5	GCS, Motor, 1	Other mechanism	GCS, Motor, 1	Light reflex
TBI-ND					
	1	Loss of consciousness	Loss of consciousness	Loss of consciousness	Loss of consciousness
	2	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1	GCS, Eye, 1
	3	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 1
	4	Light reflex	GCS, Verbal, 2	GCS, Verbal, 2	GCS, Verbal, 1
	5	GCS, Motor, 1	GCS, Motor, 1	GCS, Motor, 4	Light reflex
TBI-D					
	1	Loss of consciousness	GCS, Verbal, 1	GCS, Verbal, 1	GCS, Motor, 2
	2	GCS, Verbal, 1	Oxygen saturation<96%	Light reflex	GCS, Verbal, 1
	3	GCS, Eye, 1	Fall mechanism	Loss of consciousness	Loss of consciousness
	4	Light reflex	Afternoon	GCS, Eye, 1	Age over 80
	5	GCS, Motor, 1	Light reflex	GCS, Motor, 1	HR 87-99

624 TBI, traumatic brain injury; TBI-I, traumatic brain injury with intracranial injury; TBI-
 625 ND; traumatic brain injury with non-discharge; TBI-D, traumatic brain injury with
 626 death; LR, logistic regression; XGB, extreme gradient boosting; RF, random forest; EN,
 627 elastic net; GCS, Glasgow coma scale; HR, heart rate.

628

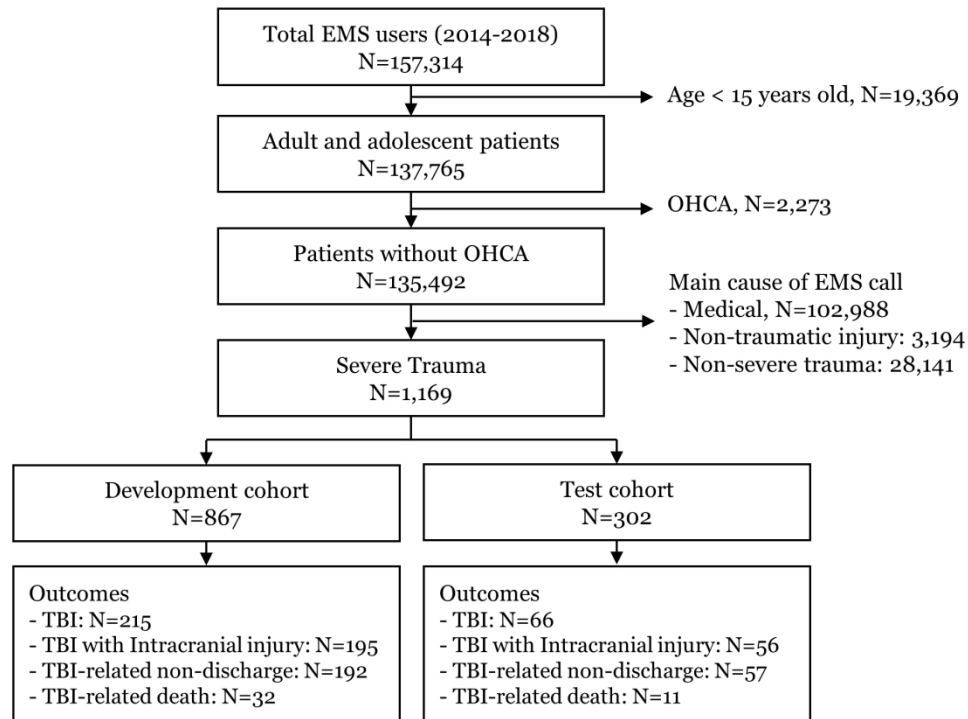


Figure 1. Population flow. EMS, emergency medical service; OHCA, out-of-hospital cardiac arrest; TBI, traumatic brain injury.

165x119mm (300 x 300 DPI)

Supplementary Table 1. List of analyzed variables.

Variables	Descriptions	Type of raw data	Category	Preprocessing
Gender	Sex of the patients	Binary	Male, Female	
Age	Age of patients	Continuous	15-39 years, 40-59 years, 60-79 years, and 80- years	Discretization and one hot encoding
Job	Job of patients	Categorical	Unemployed, Student/Housewife; Office/Commercial/Service workers; Industrial/Agricultural/Fishery/Miner worker; Others	One hot encoding Missing data were classified into others
Diabetes	History of diabetes mellitus	Binary	Yes, No	Missing data were classified into no
Hypertension	History of hypertension	Binary	Yes, No	Missing data were classified into no
Location of injury	Location of injury	Categorical	home/residential area/medical facility/school/gym; Road/highway; Off-road traffic area; Others	One hot encoding Missing data were classified into others
Season	Season when injury occurred	Categorical	Spring, Summer, Fall, Winter	One hot encoding
Weekend	Whether Injury occurred on weekday or weekend	Binary	Weekday, Weekend	
Daytime	When injury was occurred	Categorical	Night (Midnight to 5AM), Morning (6AM to 11AM), Afternoon (Midday to 5PM), Evening (6PM to 11PM)	One hot encoding Missing time were imputed using EMS call time
Mechanism of injury	Mechanism of injury	Categorical	Slip down, Fall down, Traffic accident, Other	One hot encoding Missing data were classified into others
Glasgow coma scale eye	Eye element of Glasgow coma scale	Categorical	1;2;3;4;Unknown	One hot encoding
Glasgow coma scale Verbal	Verbal element of Glasgow coma scale	Categorical	1;2;3;4;5;Unknown	One hot encoding
Glasgow coma scale Motor	Motor element of Glasgow coma scale	Categorical	1;2;3;4;5;6;Unknown	One hot encoding
Light Reflex any Abnormal	Any abnormality of light reflex on any side	Categorical	No, Yes, Unknown	One hot encoding Missing data were classified into unknown

Systolic blood pressure	blood	Systolic blood pressure	Continuous	-107 mmHg, 108-130 mmHg, 131-145 mmHg, 146- mmHg, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Diastolic blood pressure	blood	Diastolic blood pressure	Continuous	-69 mmHg, 70-80 mmHg, 81-91 mmHg, 92- mmHg, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Heart rate		Heart rate	Continuous	-74/min, 75-86/min, 87-99/min, 100-/min, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Respiratory rate		Respiratory rate	Continuous	-16/min, 17-18/min, 19-20/min, 21-/min, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Oxygen saturation		Oxygen saturation	Continuous	-95%, 96-98%, 99%, 100%, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Body temperature		Body temperature	Continuous	-36°C, 36.1-36.3°C, 36.4-36.8°C, 36.9-°C, Unknown	Discretization and one hot encoding Cutoff values for categories were calculated from median and interquartile range of training cohort Missing data were classified into unknown
Chest pain or abdominal pain		Symptom of chest pain or abdominal pain	Binary	Yes, No	

Fracture, abrasion, or laceration	Symptom of fracture, abrasion, or laceration	Binary	Yes, No	
Loss of consciousness	Symptom of loss of consciousness (whether patients had loss of consciousness between injury and EMS provider's assessment)	Binary	Yes, No	
Dyspnea	Symptom of dyspnea	Binary	Yes, No	
Nose bleeding	Symptom of nose bleeding	Binary	Yes, No	
Nausea or vomiting	Symptom of nausea or vomiting	Binary	Yes, No	
Headache, paralysis or dizziness	Symptom of headache, paralysis or dizziness	Binary	Yes, No	

Supplementary Table 2. Demographic characteristics of development and test cohorts

Characteristics	N (%) or Median (IQR)			P-value
	Total	Development	Test	
Total	1169	867	302	
Demographics				
Male	809 (69.2)	592 (68.3)	217 (71.9)	0.25
Age, years	53 (36-66)	52 (35-66)	56 (40-69)	<0.01
Job of patients				<0.01
Unemployed	299 (25.6)	197 (22.7)	102 (33.8)	
Student/Housewife	161 (13.8)	129 (14.9)	32 (10.6)	
Office/Commercial/Service worker	283 (24.2)	176 (20.3)	107 (35.4)	
Industrial/Agricultural/Fishery/Minery worker	36 (3.1)	25 (2.9)	11 (3.6)	
Others	390 (33.4)	340 (39.2)	50 (16.6)	
Past medical history				
Diabetes	62 (5.3)	35 (4.0)	27 (8.9)	<0.01
Hypertension	105 (9.0)	61 (7.0)	44 (14.6)	<0.01
Circumstances of Trauma				
Location of trauma				0.52
Residential/Nursing/Education/Exercise facility	303 (25.9)	218 (25.1)	85 (28.1)	
Road/Highway	444 (38.0)	326 (37.6)	118 (39.1)	
Off-road traffic area	181 (15.5)	140 (16.1)	41 (13.6)	
Others	241 (20.6)	183 (21.1)	58 (19.2)	
Season of trauma				<0.01
Spring	249 (21.3)	167 (19.3)	82 (27.2)	
Summer	336 (28.7)	253 (29.2)	83 (27.5)	
Fall	304 (26.0)	242 (27.9)	62 (20.5)	
Winter	280 (24.0)	205 (23.6)	75 (24.8)	
Weekday	811 (69.4)	599 (69.1)	212 (70.2)	0.72
Time of trauma				0.83
6A-MD	281 (24.0)	206 (23.8)	75 (24.8)	
MD-6P	266 (22.8)	203 (23.4)	63 (20.9)	
6P-MN	361 (30.9)	265 (30.6)	96 (31.8)	
MN-6A	261 (22.3)	193 (22.3)	68 (22.5)	
Mechanism of Trauma				
Traffic accident	500 (42.8)	375 (43.3)	125 (41.4)	0.60
Slip down	325 (27.8)	232 (26.8)	93 (30.8)	
Fall down	171 (14.6)	129 (14.9)	42 (13.9)	
Others	173 (14.8)	131 (15.1)	42 (13.9)	
Chief complaint				
Altered mentality	279 (23.9)	223 (25.7)	56 (18.5)	0.01
Fracture/Abrasion/Laceration	302 (25.8)	204 (23.5)	98 (32.5)	<0.01
Chest/Abdominal pain	47 (4.0)	31 (3.6)	16 (5.3)	0.19
Dyspnea	25 (2.1)	20 (2.3)	5 (1.7)	0.50

1					
2					
3					
4					
5	Epistaxis	44 (3.8)	30 (3.5)	14 (4.6)	0.36
6	Headache/Paralysis/Dizziness/Vertigo	95 (8.1)	64 (7.4)	31 (10.3)	0.11
7	Nausea/Vomiting	32 (2.7)	20 (2.3)	12 (4.0)	0.13
8	EMS Vital sign assessment				
9		130 (109-		131 (115-	
10	SBP, mmHg	150)	130 (104-146)	150)	<0.01
11	Missing	65 (5.6)	56 (6.5)	9 (3.0)	0.02
12	DBP, mmHg	80 (70-91)	80 (69-90)	80 (70-92)	<0.01
13	Missing	75 (6.4)	65 (7.5)	10 (3.3)	0.01
14	HR, /min	86 (75-99)	86 (74-99)	86 (76-100)	<0.01
15	Missing	31 (2.7)	28 (3.2)	3 (1.0)	0.04
16	RR, /min	18 (16-20)	18 (16-20)	18 (16-20)	<0.01
17	Missing	36 (3.1)	33 (3.8)	3 (1.0)	0.01
18	SpO2, %	98 (95-99)	98 (95-99)	98 (96-99)	<0.01
19	Missing	38 (3.3)	33 (3.8)	5 (1.7)	0.07
20	Temperature, °C	36.5 (36-		36.5 (36-	
21		36.8)	36.5 (36-36.8)	36.7)	<0.01
22	Missing	94 (8.0)	65 (7.5)	29 (9.6)	0.25
23	AVPU scale				<0.01
24	Alert	714 (61.1)	504 (58.1)	210 (69.5)	
25	Verbal	168 (14.4)	136 (15.7)	32 (10.6)	
26	Pain	199 (17.0)	158 (18.2)	41 (13.6)	
27	Unresponsive	88 (7.5)	69 (8.0)	19 (6.3)	
28	Abnormal light reflex	165 (14.1)	132 (15.2)	33 (10.9)	<0.01
29	Missing	66 (5.6)	57 (6.6)	9 (3.0)	
30	GCS scale component				
31	Glasgow coma scale eye				<0.01
32	4	558 (47.7)	380 (43.8)	178 (58.9)	
33	3	128 (10.9)	109 (12.6)	19 (6.3)	
34	2	110 (9.4)	82 (9.5)	28 (9.3)	
35	1	174 (14.9)	141 (16.3)	33 (10.9)	
36	Unknown	199 (17.0)	155 (17.9)	44 (14.6)	
37	Glasgow coma scale Verbal				0.01
38	5	520 (44.5)	359 (41.4)	161 (53.3)	
39	4	118 (10.1)	88 (10.1)	30 (9.9)	
40	3	25 (2.1)	19 (2.2)	6 (2.0)	
41	2	132 (11.3)	105 (12.1)	27 (8.9)	
42	1	174 (14.9)	141 (16.3)	33 (10.9)	
43	Unknown	200 (17.1)	155 (17.9)	45 (14.9)	
44	Glasgow coma scale Motor				<0.01
45	6	499 (42.7)	333 (38.4)	166 (55.0)	
46	5	124 (10.6)	103 (11.9)	21 (7.0)	
47	4	158 (13.5)	123 (14.2)	35 (11.6)	
48	3	47 (4.0)	39 (4.5)	8 (2.6)	
49	2	17 (1.5)	15 (1.7)	2 (0.7)	
50	1	125 (10.7)	99 (11.4)	26 (8.6)	
51	Unknown	199 (17.0)	155 (17.9)	44 (14.6)	
52					
53					
54					
55					
56					
57					
58					
59					
60					

1					
2					
3					
4					
5	EMS management				
6	Intravenous route	176 (15.1)	129 (14.9)	47 (15.6)	0.77
7	Hemorrhage control	586 (50.1)	426 (49.1)	160 (53.0)	0.25
8	Spinal motion restriction	811 (69.4)	606 (69.9)	205 (67.9)	0.51
9	Advanced airway management	4 (0.3)	2 (0.2)	2 (0.7)	0.28
10	Oxygen supply	233 (19.9)	176 (20.3)	57 (18.9)	0.59
11					
12	Field triage decision scheme criteria*				
13	Physiological criteria				
14	SBP<90 mmHg	58 (5.0)	42 (4.8)	16 (5.3)	0.75
15	RR<10 or >29 /min	11 (0.9)	11 (1.3)	0 (0.0)	0.08
16	Non-Alert	429 (36.7)	343 (39.6)	86 (28.5)	<0.01
17					
18	Anatomic criteria				
19	All penetrating injuries to head, neck,				
20	torso and extremities proximal to elbow				
21	or knee	34 (2.9)	23 (2.7)	11 (3.6)	0.38
22	Chest wall instability or deformity	4 (0.3)	4 (0.5)	0 (0.0)	0.58
23	Two or more proximal long bone				
24	fractures	19 (1.6)	13 (1.5)	6 (2.0)	0.60
25	Crush, degloved, mangled or				
26	pulseless extremity	15 (1.3)	13 (1.5)	2 (0.7)	0.38
27	Amputation proximal to wrist or ankle	9 (0.8)	9 (1.0)	0 (0.0)	0.12
28	Pelvic fractures	8 (0.7)	6 (0.7)	2 (0.7)	>0.95
29	Open or depressed skull fracture	17 (1.5)	9 (1.0)	8 (2.6)	0.05
30	Paralysis	21 (1.8)	11 (1.3)	10 (3.3)	0.02
31					
32	Mechanism of injury criteria				
33	Fall > 6 meter	113 (9.7)	84 (9.7)	29 (9.6)	>0.95
34	High-risk auto crash	96 (8.2)	73 (8.4)	23 (7.6)	0.66
35	Auto vs pedestrian/bicyclist thrown,				
36	run over, or with significant (>30km/h)				
37	impact	119 (10.2)	83 (9.6)	36 (11.9)	0.25
38	Motorcycle crash > 30 km/hour	105 (9.0)	70 (8.1)	35 (11.6)	0.07
39					
40	ED disposition				0.11
41					
42	Discharge	320 (27.4)	241 (27.8)	79 (26.2)	
43	Transfer	444 (38.0)	316 (36.4)	128 (42.4)	
44	Admitted	366 (31.3)	276 (31.8)	90 (29.8)	
45	In-hospital mortality	90 (7.7)	74 (8.5)	16 (5.3)	0.07
46					
47	Outcomes				
48					
49	TBI	281 (24.0)	215 (24.8)	66 (21.9)	0.30
50	TBI with intracranial injury	251 (21.5)	195 (22.5)	56 (18.5)	0.15
51	TBI-related non-discharge	249 (21.3)	192 (22.1)	57 (18.9)	0.23
52	TBI-related death	43 (3.7)	32 (3.7)	11 (3.6)	>0.95

*EMS providers check specific criteria orderly from physiologic, anatomical, and mechanism of injury. If the preceding criteria are satisfied, the information of the latter criteria is not collected.

1
2
3
4 IQR, interquartile range; SBP, systolic blood pressure; RR, respiratory rate; ED, emergency department; TBI,
5
6 traumatic brain injury.
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

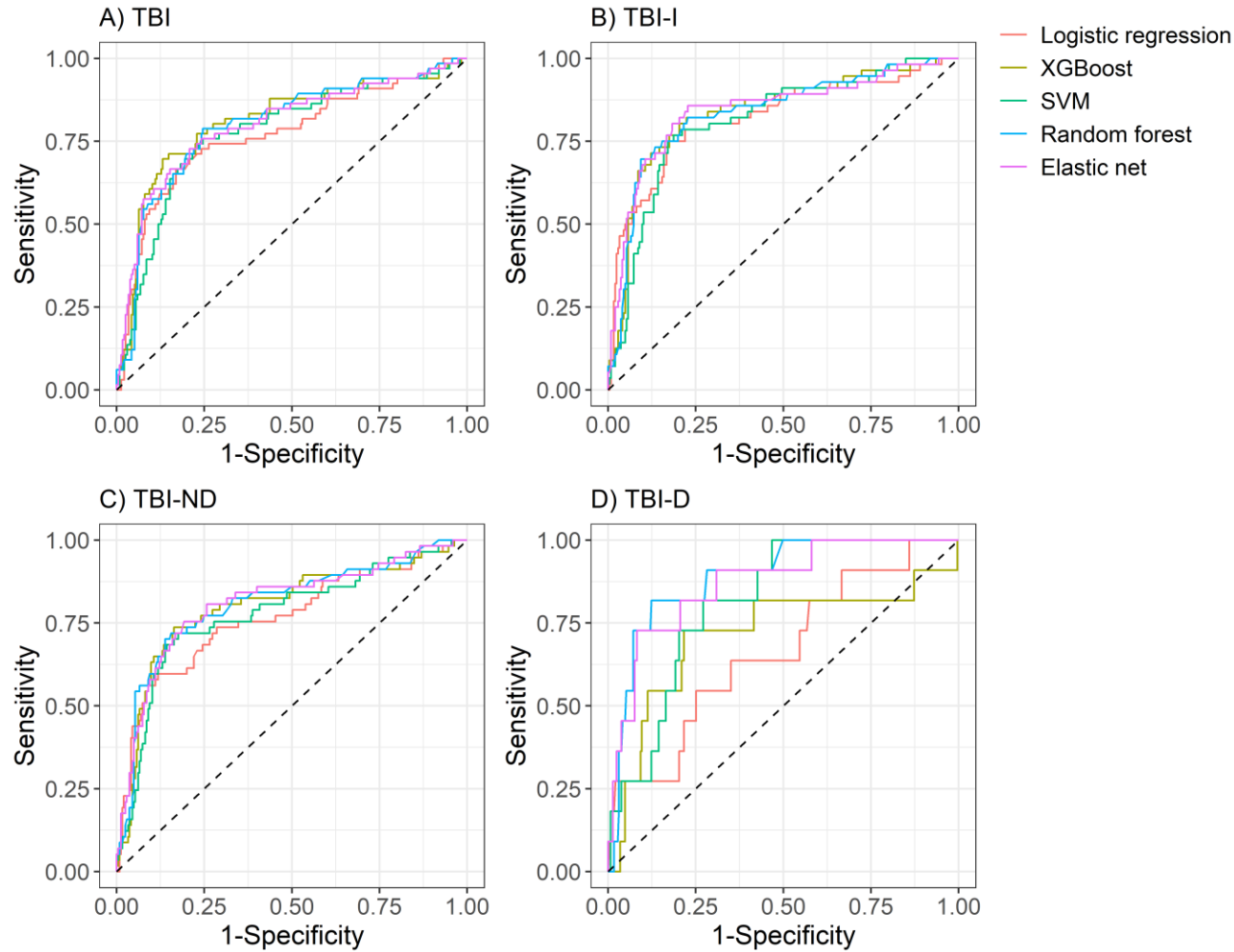
Supplementary Table 3. Hyperparameters of the final prediction models*

Model	Outcome	Hyperparameters
Elastic net	TBI	alpha: 0.325, lambda: 0.07506346
	TBI-I	alpha: 0.325, lambda: 0.07506346
	TBI-ND	alpha: 0.325, lambda: 0.07017153
	TBI-D	alpha: 0.325, lambda: 0.01565599
Random forest	TBI	ntree:500, mtry: 18
	TBI-I	ntree:500, mtry: 18
	TBI-ND	ntree:500, mtry: 18
	TBI-D	ntree:500, mtry: 15
Support vector machine	TBI	sigma: 0.008047; C: 4
	TBI-I	sigma: 0.008047; C: 4
	TBI-ND	sigma: 0.008047; C: 4
	TBI-D	sigma: 0.008047; C: 4
Extreme gradient boosting	TBI	nrounds: 299; max_depth: 1; eta: 0.4807096; gamma: 2.336623; colsample_bytree: 0.3657893; min_child_weight: 8; subsample: 0.8182623
	TBI-I	nrounds: 299; max_depth: 1; eta: 0.4807096; gamma: 2.336623; colsample_bytree: 0.3657893; min_child_weight: 8; subsample: 0.8182623
	TBI-ND	nrounds: 301; max_depth: 1; eta: 0.02154674; gamma: 4.696105; colsample_bytree: 0.590754; min_child_weight: 1; subsample: 0.5070866
	TBI-D	nrounds: 50; max_depth: 0.3; eta: 0.3; gamma: 0; colsample_bytree: 0.8; min_child_weight: 1; subsample: 0.5510204

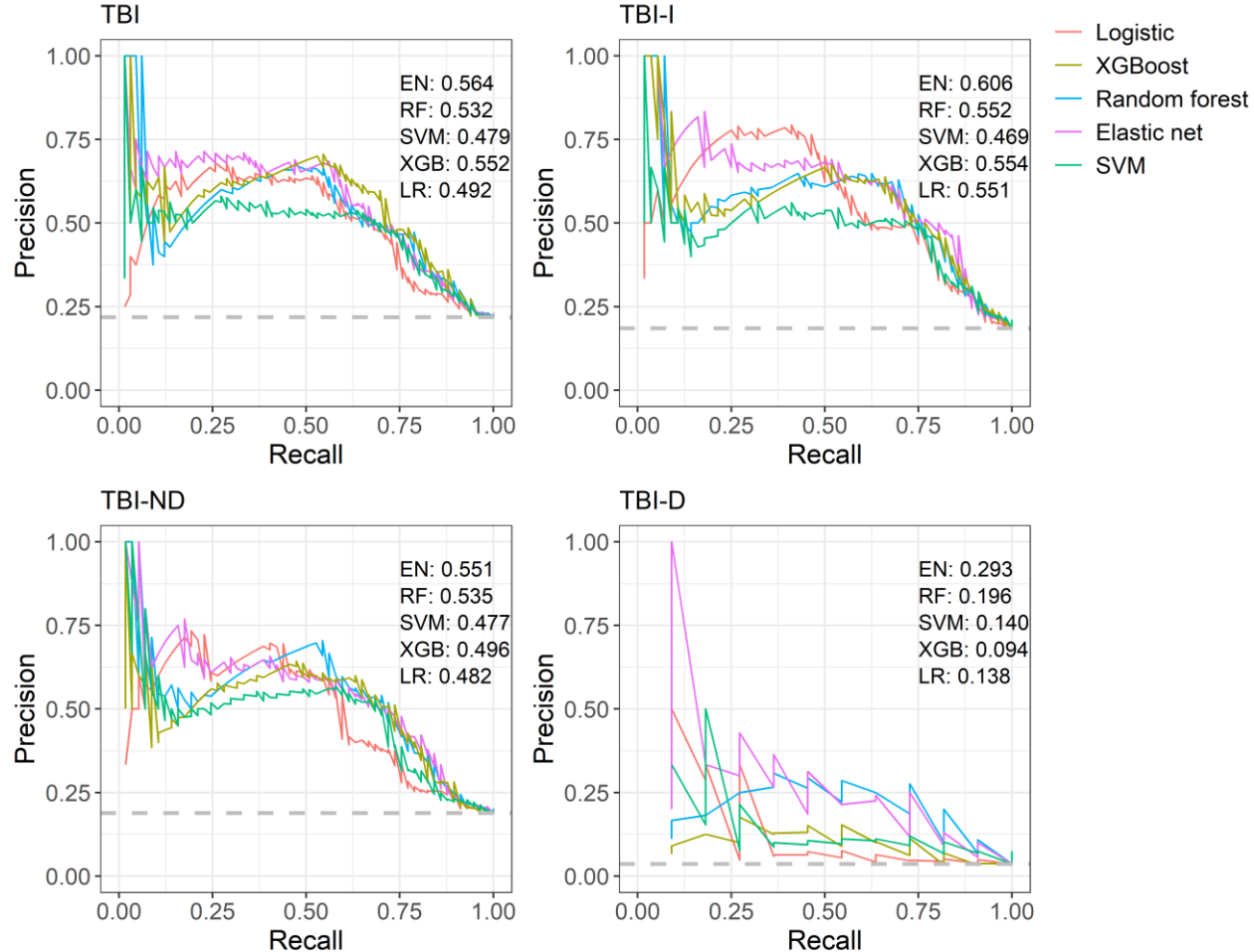
*Aside from the hyperparameters mentioned, all other hyperparameters are used as the default value.

TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death.

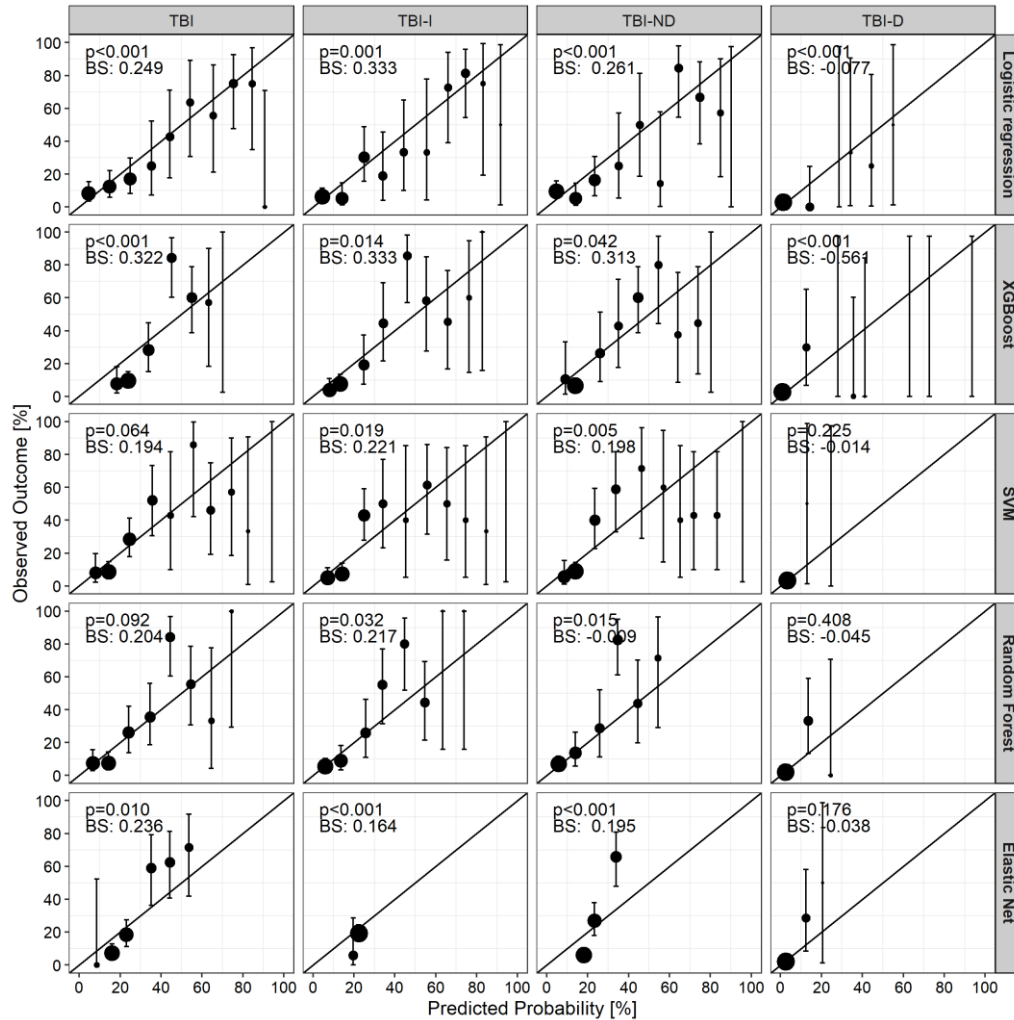
Supplementary Figure 1. Receiver operating characteristics of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death.



Supplementary Figure 2. Precision-recall curve of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death; LR, logistic regression analysis; XGB, extreme gradient boosting; RF, random forest, EN, elastic net.



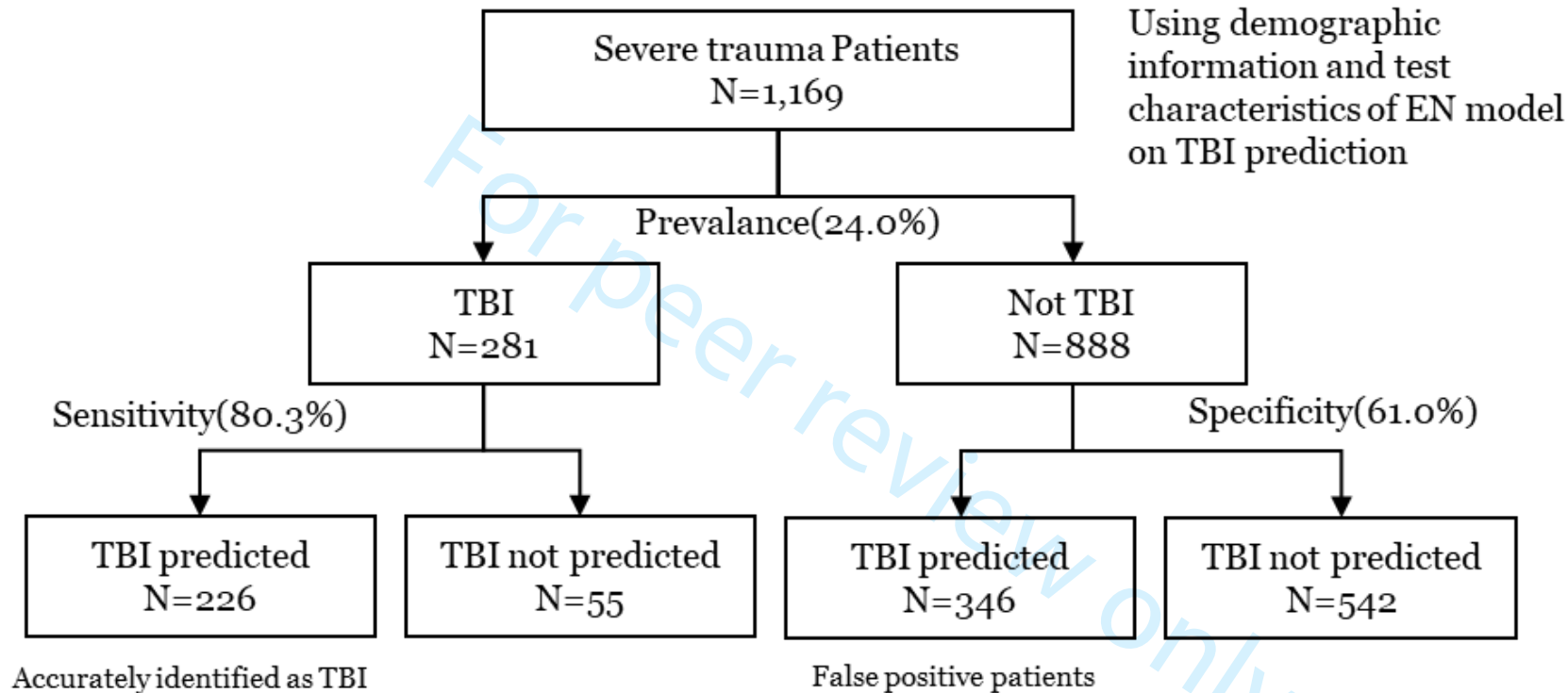
Supplementary Figure 3. Calibration plot of prediction models according to outcomes. TBI, traumatic brain injury; TBI-I, TBI with intracranial hemorrhage or injury; TBI-ND, TBI non-discharge; TBI-D, TBI with death; p, p-value of Hosmer-Lemeshow test; BS, scaled Brier score.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

For peer review only

Supplementary Table 4. Example of calculating false-positive patients for accurately identified patients. TBI, traumatic brain injury; EN, elastic net.



False-positive patients for every 10 patients that are accurately identified as TBI :
 $346/226 \times 10 = 15.3$, rounded up to 16 patients

TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	D;V Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	4
Introduction			
Background and objectives	3a	D;V Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	7
	3b	D;V Specify the objectives, including whether the study describes the development or validation of the model or both.	8
Methods			
Source of data	4a	D;V Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	8-9
	4b	D;V Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	9
Participants	5a	D;V Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	8-9
	5b	D;V Describe eligibility criteria for participants.	10
	5c	D;V Give details of treatments received, if relevant.	N/A
Outcome	6a	D;V Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	10-11
	6b	D;V Report any actions to blind assessment of the outcome to be predicted.	N/A
Predictors	7a	D;V Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	11
	7b	D;V Report any actions to blind assessment of predictors for the outcome and other predictors.	N/A
Sample size	8	D;V Explain how the study size was arrived at.	14
Missing data	9	D;V Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	11
Statistical analysis methods	10a	D Describe how predictors were handled in the analyses.	11
	10b	D Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	11-12
	10c	V For validation, describe how the predictions were calculated.	12-13
	10d	D;V Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12-13
	10e	V Describe any model updating (e.g., recalibration) arising from the validation, if done.	N/A
Risk groups	11	D;V Provide details on how risk groups were created, if done.	N/A
Development vs. validation	12	V For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	12
Results			
Participants	13a	D;V Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	14
	13b	D;V Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	14
	13c	V For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	14
Model development	14a	D Specify the number of participants and outcome events in each analysis.	14
	14b	D If done, report the unadjusted association between each candidate predictor and outcome.	N/A
Model specification	15a	D Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	N/A
	15b	D Explain how to use the prediction model.	14-15
Model performance	16	D;V Report performance measures (with CIs) for the prediction model.	14-15
Model-updating	17	V If done, report the results from any model updating (i.e., model specification, model performance).	N/A
Discussion			
Limitations	18	D;V Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	19-20
Interpretation	19a	V For validation, discuss the results with reference to performance in the development data, and any other validation data.	16-17
	19b	D;V Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	20	D;V Discuss the potential clinical use of the model and implications for future research.	18-19
Other information			
Supplementary information	21	D;V Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Suppl
Funding	22	D;V Give the source of funding and the role of the funders for the present study.	20

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.