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Original Research

Traumatic Brain Injury Rehabilitation Outcome Prediction Using Machine Learning Methods

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KEYWORDS
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Abstract *Objective:* To investigate the performance of machine learning (ML) methods for predicting outcomes from inpatient rehabilitation for subjects with TBI using a dataset with a large number of predictor variables. Our second objective was to identify top predictive features selected by the ML models for each outcome and to validate the interpretability of the models.
Design: Secondary analysis using computational modeling of relationships between patients, injury and treatment activities and 6 outcomes, applied to the large multi-site, prospective, longitudinal observational dataset collected during the traumatic brain injury inpatient rehabilitation study.
Setting: Acute inpatient rehabilitation.
Participants: 1946 patients aged 14 years or older, who sustained a severe, moderate, or complicated mild TBI, and were admitted to 1 of 9 US inpatient rehabilitation sites between 2008 and 2011 (N=1946).
Main Outcome Measures: Rehabilitation length of stay, discharge to home, FIM cognitive and FIM motor at discharge and at 9-months post discharge.
Results: Advanced ML models, specifically gradient boosting tree model, performed consistently better than all other models, including classical linear regression models. Top ranked predictive

List of abbreviations: GBM, gradient boosting tree model; LM, linear model; ML, machine learning; MAE, mean absolute error; MLP, multilayer perceptron; OT, occupational therapy; PBE, practice-based evidence; POC, point-of-care; PT, physical therapy; RMSE, root mean squared error; ST, speech-language therapy; TBI, traumatic brain injury; TBI-PBE, traumatic brain injury practice based evidence.
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features were identified for each of the 6 outcome variables. Level of effort, days to rehabilitation admission, age at rehabilitation admission, and advanced mobility activities were the most frequently top ranked predictive features. The highest-ranking predictive feature differed across the specific outcome variable.

Conclusions: Identifying patient, injury, and rehabilitation treatment variables that are predictive of better outcomes will contribute to cost-effective care delivery and guide evidence-based clinical practice. ML methods can contribute to these efforts.

Optimizing rehabilitation stay of patients with traumatic brain injury (TBI) is critical for achieving desired cognitive and motor improvements and ensuring cost-effective care delivery. Predicting how much functional improvement a patient can achieve or how much care assistance is reduced with a tailored set of activities can inform on the efficacy of the selected therapy activities. Acute inpatient TBI rehabilitation involves multiple professional disciplines selecting therapeutic activities based on varying skilled interventions, lengths of stay, and the medical and functional statuses of patients. Therefore, rehabilitation outcomes for patients with TBI are complex to predict.[1]

Previous research has started to reveal the main therapeutic activities comprising inpatient rehabilitation[2] as well as which therapeutic approaches appear to promote better outcomes.[3] One of the first studies to use treatment session data to predict outcomes was Horn et al.[4] Applying linear model (LM) to large practice-based evidence (PBE) data set, they identified significant associations between patient, injury, and treatment characteristics with outcomes at discharge and at 9-month post discharge. Specifically, Horn et al found that better discharge outcomes were associated with greater effort during therapy sessions, time spent in more complex therapy activities, and use of specific medications (eg, nonnarcotic analgesics).[5] Secondary analysis on the PBE dataset by Bogner et al using propensity score methodology found a greater proportion of time spent in real-life activities during therapy sessions was associated with better functional outcomes at discharge and 9-months post discharge, including increases in community participation.[3]

Horn et al and Bogner et al provided valuable insight into the association of key characteristics during the inpatient stay that are associated with better outcomes.[3,4] A natural next step would be to determine if additional insight or enhanced outcome predictions could be obtained from advanced analytical tools such as machine learning (ML). Compared with LM, advanced ML methods allow greater flexibility for modeling non-linear recovery pattern, interactions between treatments, diminishing returns, ceiling/floor effect, which better reflects real-world settings.[6] A few studies have applied ML methods to rehabilitation data and predict outcomes in different patient populations affected by mild TBI,[7,8] stroke,[9,10] and predict FIM scores at discharge,[11] survival or mortality probability after TBI,[6,12-18] suicidal ideation after TBI.[19] In contrast, Bruschetta et al[20] did not find ML methods to have superiority over LM in predicting outcome after TBI and was limited by quantity of predictor variables.[11,20]

The purpose of the current study was to investigate the predictive performance of ML methods for predicting outcomes at discharge and at 9-month post discharge from inpatient TBI rehabilitation using a dataset with a large set of predictor variables, including patient and injury variables, rehabilitation variables, and daily therapy variables. In addition, the goal of the work was to obtain further insights into which variables are most predictive for each outcome and to validate the interpretability of the models.

Methods

Study design

TBI-practice based evidence (TBI-PBE) observational dataset, built from 2008 to 2011 was used for the analyses. Each participant or their proxy gave informed consent. The dataset contains details of abstracted medical records and point-of-care (POC) data on patients with TBI admitted for acute inpatient rehabilitation. Detailed descriptions of the data collection methods and data variables are described in prior studies.[2,5] Institutional review board approval was obtained at the time of data collection from all sites contributing to the dataset. ML methods were selected, applied to the dataset, and compared for each model's ability to predict outcomes.

Setting

The 9 US acute inpatient rehabilitation facilities that participated in TBI-PBE data collection are described in detail in prior studies.[2,5] The facilities provided care as usual, which typically includes a minimum of 3 hours of therapy per day during the weekdays. The primary care in a day includes disciplines of occupational therapy (OT), physical therapy (PT), and speech-language therapy (ST). The mean times per weekday therapy sessions averaged 37.7±7.7 minutes for OT, 38.6±8.7 minutes for PT, and 32.5±6.1 minutes for ST. Each therapy discipline typically scheduled 2 sessions per day.[21]

Regulatory guidelines require a level of therapeutic intensity that is generally defined as a minimum of 3 hours of therapy per day for 5 days or 15 hours across 7 consecutive days. Interdisciplinary therapy and these 3 hours must include PT or OT and 1 other discipline, which is generally speech therapy.[22] These primary therapy disciplines are a requirement for admission to inpatient rehabilitation, while the additional therapies are not typically delivered to all patients. Restricting the dataset to the primary disciplines was done to evaluate outcome predictions based on typical treatment activities delivered to all participants throughout their entire length of stay.

Participants

Participants were enrolled in the TBI-PBE dataset if they were (1) aged 14 years or older; (2) sustained a TBI, defined as damage to brain tissue caused by external force and evidenced by loss of consciousness, posttraumatic amnesia, skull fracture, or objective neurologic findings; (3) TBI diagnostic code was consistent with the Centers for Disease Control and Prevention Guidelines for Surveillance of Central Nervous System Injury at time of the study; (4) received their first inpatient rehabilitation admission at 1 of the participating sites; and (5) consented to follow-up interviews post discharge.[5] From the 2130 originally enrolled (age distribution of 44.5±21.3 years involving 586 women and 1544 men with 113 teenagers), 1946 were included in the current analysis. Participants from the original dataset were excluded from the current analysis if they (1) were enrolled at the Canadian site or (2) were admitted and treated for a disorder of consciousness. Participants from the Canadian site were excluded because of differences in how acute rehabilitation care is delivered in the US compared with Canada. Participants with disorders of consciousness were excluded because of differences in the therapeutic activities employed with this small patient population compared with other participants.

Dataset

Collection of data through the POC forms during the TBI-PBE study provided a very large number of individual therapy activities across 6 professional disciplines—OT, PT, ST, therapeutic recreation, psychology, and social work/case management.[5] Collapsing of the therapy activity data within the original dataset was necessary for manageability and to prevent over-specification of the models during the original logical regression analyses.[4] The features selected for predicting each outcome is presented in the Appendix.

The collapsed therapy activity dataset was analyzed with all therapy activities recorded by all 6 professional disciplines and indicated in the data Tables as *"All"*. A second collapsed dataset was created by eliminating therapies not delivered by the 3 primary disciplines—OT, PT, SLP—and activities not considered interventions. This grouping removed assessment and evaluation activities designed to rate patient performance, and education activity when education did not occur as part of a functional activity (eg, general education about TBI). This dataset is indicated in the data Tables as *"Primary"*. This second dataset was analyzed to evaluate predictions based on the typical therapies provided to all patients during acute inpatient rehabilitation.

The POC forms collected duration of time engaged in therapy activity. The time spent on a particular activity varied over the rehabilitation stay. For simplicity, time spent in a week averaged over the entire rehabilitation stay of the patient was calculated to give a consolidated representation of therapeutic activity. The therapy activities are repetitive and occur in a cycle over the stay of the patient. Hence, by taking average time spent, the effect of each activity on the rehabilitation recovery analysis is still maintained.

Outcome measures

The primary outcome measures for prediction were length of stay, discharge to home, and discharge and 9-month post discharge cognitive and motor function. Length of stay was measured in days and included the days from admission to discharge from rehabilitation. For participants who returned to acute care during the rehabilitation stay, the days in acute care were not included in the final total rehabilitation LOS. Participants were not dropped from analysis if they transferred out to acute care and did not return to rehabilitation. Discharge to home was defined as a private home destination. Cognitive and motor functions were measured using the Rasch-adjusted FIM.[23-26] Cognitive (Range=0 to 100) and motor (Range=0 to 100) FIM sub scores were evaluated each at discharge and at 9-months post discharge.[4] Summary statistics for each outcome metric across the original patient groupings is shown in table 1.

Modeling methods

Three different ML models of increasing complexity — (1) LM: with regularization (Lasso[27] and Ridge[28]) and without regularization, (2) Multilayer Perceptron (MLP),[29] (3) Gradient Boosting Tree Model (GBM)[30] — were applied to the dataset and the performance of the models were compared. Variations of LMs with lasso and ridge regularization are administered, as regularization reduces overfitting and helps to generate a generalized model which performs well on unseen patients. LM assumes a linear relation between the features and the outcomes, hence making it impossible to learn non-linear recovery pattern, interactions between treatments, diminishing returns of treatments, ceiling/floor effect limitations. MLP handles these problems because it can approximate any arbitrary relation. However, MLP models suffer from limited data, hard to interpret the model, require hyperparameter tuning. Our dataset is noisy and has insufficient data to get useful accuracy from MLP model. Thus, a tree-based gradient boosting model is a suitable choice as it can learn non-linear recovery patterns, ceiling and floor effects and interactions between features. Thus, the advantage of GBM is its ability to generate the importance of features. Details about each ML models and drawbacks of each model are explained in the supplemental section.

Evaluation metrics

F1 score,[31] a performance measure similar to accuracy, is used for analyzing the prediction probability of the discharge location classifier, as it can handle data imbalance. Root mean squared error (RMSE) and mean absolute error (MAE) are used as metrics for the other regression outcome predictions. These 2 metrics can give more interpretable scores for the number of days in the case of length of stay and change in scores in the case of FIM scores. Evaluation to find the best parameters for the model involves 5-fold cross-validation.

Table 1 Outcome variable distribution

Outcome	Total (1946)	Adm cog ≤6 (306)	Adm cog 7-10 (367)	Adm cog 11-15 (481)	Adm cog 16-20 (381)	Adm cog ≥21 (401)
Length of stay	24.81±18.62	40.82±27.92	31.66±17.14	23.44±13.81	18.29±11.24	13.77±7.54
Discharge to home	84.00%	78.00%	78.00%	85.00%	84.00%	91.00%
Discharge FIM cognitive	54.56±13.15	44.31±13.38	47.00±10.40	53.22±8.96	58.13±7.98	67.58±11.32
Discharge FIM motor	54.71±13.23	48.13±13.91	50.58±13.40	55.61±12.07	58.08±12.40	59.51±11.12
9-month FIM cognitive	77.08±17.60	70.56±19.43	72.16±18.67	77.05±16.56	80.39±15.56	83.68±14.71
9-month FIM motor	81.39±18.96	76.85±20.33	77.91±20.44	82.29±19.08	83.33±16.77	85.65±16.63

NOTE. The percentage distribution of "discharge to home" outcome and mean, standard deviation of other outcome variables is shown. "Total" represents the entire patient population. The rest columns represent patient groups where the patients are grouped by "Adm cog" (admission cognitive) score. "Length of stay", "Discharge FIM cognitive", "Discharge FIM motor", "9-month FIM cognitive" and "9-month FIM motor" have the mean and standard deviation of the respective outcomes. "Discharge to home" has the percentage of patients discharged to home.

Models with different combinations of parameters are trialed, followed by calculating corresponding performance metrics for each case. The best model from the combinations was selected based on the lowest RMSE score for regression and the highest F1 score for classification. Mathematical equations for the metrics are detailed in the Appendix.

Results

Table 2 consolidates the results of best-performing models for each outcome in each category. Overall, GBM tended to perform consistently the best across all outcomes and for both datasets. Table 3 lists the top 3 features identified for each outcome. Results for discharge motor function, 9-month cognitive function, and 9-month motor function are available in the supplemental data in the Appendix.

Length of stay prediction

GBM achieved the lowest RMSE and MAE scores of 13.52 and 7.61, respectively, for predicting the length of stay. For *primary* dataset, the GBM model shows an RMSE of 11.45 and an MAE of 6.02. This represented a drop of 18% for the RMSE and a drop of 26% for the MSE score. The assessment and evaluation activities were typically performed at the beginning and at the end of the stay and may have contributed to the length of stay prediction. Hence, removing the details of assessment, evaluation, and education activities in our analysis caused a drop in performance. Feature analysis indicated that the length of stay is highly dependent on the motor abilities of the patient at admission, the severity of brain injury as measured by Comprehensive Severity Index score, and days from injury to rehabilitation admission.

Discharge to home

GBM achieved the best accuracy for predicted cases and the best F1-score, with an accuracy of 0.86 and an F1-score of 0.92. For *primary* dataset, GBM achieved an accuracy of 0.856 and an F1-score of 0.92. By restricting the dataset to primary therapies, no significant change in performance is noticed. Feature analysis identified level of effort, patient

Table 2 Summary of performance of ML models applied to both data sets on predicting 6 outcomes

Model	Data Set	Length of Stay		Discharge Home		Discharge Cog FIM		Discharge Motor FIM		9-month Cog FIM		9-month Motor FIM	
		RMSE	MAE	Acc	F1	RMSE	MAE	RMSE	MAE	RMSE	MAE	RMSE	MAE
Linear	*All*	14.80	8.67	0.80	0.88	9.10	6.98	8.90	6.69	16.23	13.13	15.00	11.78
	Primary	14.86	8.74	0.79	0.87	9.10	6.97	8.97	6.74	16.32	13.18	15.02	11.76
Lasso	*All*	14.02	7.81	0.84	0.91	9.11	6.90	8.42	6.24	16.24	13.22	14.93	11.79
	Primary	14.82	8.42	0.84	0.91	9.09	6.85	8.38	6.21	16.24	13.20	14.90	11.75
Ridge	*All*	13.99	7.75	0.85	**0.92**	9.07	6.95	8.47	6.29	16.22	13.18	14.92	11.74
	Primary	14.86	8.75	0.84	0.91	9.05	6.92	8.36	6.23	16.25	13.22	14.93	11.71
GBM	*All*	**11.45**	**6.02**	**0.86**	**0.92**	**8.51**	**6.32**	**7.42**	**5.50**	**16.01**	**13.02**	**14.72**	**11.68**
	Primary	**13.52**	**7.61**	**0.85**	**0.92**	**8.45**	**6.30**	**7.37**	**5.51**	**15.97**	**13.00**	**14.61**	**11.59**
MLP	*All*	12.64	6.67	**0.86**	**0.92**	9.22	6.95	8.91	6.72	16.77	13.75	15.23	12.09
	Primary	14.26	8.07	**0.85**	0.91	9.09	6.92	8.80	6.62	16.79	13.78	15.32	12.14

NOTE. Best performing Linear, Lasso, Ridge, GBM and MLP models are listed for each outcome variable prediction. All data set is inclusive of all data; Primary data set eliminated all treatment activities not delivered by OT, PT, F1, accuracy, RMSE, MAE are the scoring metrics used. The best performing results for each dataset (All and Primary) is highlighted in bold. The lowest RMSE and MAE values, and highest F1 and accuracy values across models are shown in bold.

Table 3 Top 3 predictive features selected by the GBM for each outcome

Outcome	Rank	Features	Weight (in %)
Length of stay	1	FIM Rasch Admission Motor	39.80
	2	Maximum BI CSI Component	12.03
	3	Days to Rehab Admission	5.51
Discharge home	1	Age at Rehab Admission	18.80
	2	Level of Effort	14.78
	3	PT Advanced Mobility Activities (gait, community, stairs)	8.29
Discharge FIM Cognitive	1	Level of Effort	36.94
	2	FIM Rasch Admission Cognitive	22.73
	3	Days to Rehab Admission	3.14
Discharge FIM Motor	1	FIM Rasch Admission Motor	27.24
	2	Level of Effort	16.99
	3	PT Advanced Mobility Activities (gait, community, stairs)	14.57
9-month FIM Cognitive	1	Level of Effort	15.52
	2	Age at Rehab Admission	10.47
	3	Days to Rehab Admission	8.72
9-month FIM Motor	1	Days to Rehab Admission	9.80
	2	Age at Rehab Admission	8.88
	3	Level of Effort	6.96

NOTE. Top 3 most predictive features selected by the GBM is shown along with its rank and weight.
Abbreviations: BI, brain injury; CSI, Comprehensive Severity Index.

age at admission to inpatient rehabilitation, and advanced PT activities (advanced gait training, community locomotion, stairs) as the top predictive features for returning home at discharge.

Discharge cognitive function

As with the preceding predictions, GBM achieved the best performance relative to other models. For the total dataset, GBM produced an RMSE of 8.51 and an MAE of 6.32. GBM remained the best-performing model for the *Primary* dataset, with an RMSE of 8.45 and an MAE of 6.30. Performance of GBM did not differ significantly between the 2 datasets, with only a 0.7% and 0.3% improvement in RMSE and MAE, respectively, and likely attributable to a reduction of noise in the primary therapy activity dataset. The most predictive features identified were level of effort during OT, PT, and ST sessions, admission Rasch-adjusted FIM cognitive score, and days from injury to rehabilitation admission.

Overall, GBM exhibited consistent and best performance for outcome prediction relative to the other ML methods for both datasets. The top features were both different and similar depending on the outcome variable predicted. Level of effort during OT, PT, and ST sessions was the most consistently noted top feature. The only outcome for which the level of effort was not a top feature was the length of stay. Age at rehabilitation admission was also found as a top feature for discharge to home and 9-month cognitive and motor function. Days to rehabilitation admission was a top feature for the length of stay and discharge cognitive function. Advanced PT activities were among the top features for discharge to home and discharge motor function.

Discussion

An initial goal of this study was to determine if ML models perform better than classical or traditional LM at predicting outcomes, which was shown. Mostly previous studies show the use of models such as neural networks, tree based model, and LM. The application and the subdomain they have tackled is different. In this study, the GBM variant of the tree model is shown to be the best model for TBI outcome prediction at discharge and 9 months from discharge. The GBM model gives a picture on importance of features and specifies which combinations of features is significant. Clinical datasets contain variation in relation between input and outcome variable at different cognitive levels. Complex combination of different activities may affect the outcome in different ways. Thus, GBM, which model interactions between features, is a suitable ML method. An additional advantage of GBM is its ability to generate the importance of features. Thus, the second goal of this study was achieved—obtaining further insights into which patient, injury, and treatment variables were most predictive for each outcome. Level of effort was a frequently noted top predictive feature and it was the highest-ranked feature in 3 of the 6 outcomes. Days to rehabilitation admission was a predictive feature for length of stay, discharge cognitive FIM, 9-month cognitive and motor FIM. Age at rehabilitation admission was a predictive feature for discharge to home, and 9-month cognitive and motor FIM. These results indicate that no 1 feature is relevant to all outcomes and outcome selection may determine which variables are necessary for better prediction. Therefore, in line with past research, the availability and robustness of large sets of predictive variables are needed to accommodate predictions of different outcomes.[20]

Current findings bear similarities to past analyses using the TBI-PBE dataset. Horn et al using ordinal least squares and logistic regression analyses found greater effort demonstrated during therapy sessions, time spent in more complex therapy activities, and select medications were associated with better outcomes. Unlike the regression analyses conducted in the Horn et al study, which could only identify the percent of variance accounted for by a dependent variable, the current study was able to rank order the importance of variables per outcome with the help of GBM model. This has therefore added further insight into the predictive value of these features for the different outcome variables. For example, the level of effort was consistently found to be a top-performing predictive feature in the current study, and it was an identified variable in the Horn et al study associated with better outcomes. Thus, these results indicate rehabilitation therapists should carefully monitor level of effort and take it into consideration during treatment planning. However, level of effort was not a top performing predictive feature for length of stay and motor function prediction. These nuanced findings exemplify the added advantage that ML methods may have over classical LM in outcome prediction.

Study limitations

Several limitations in the current study are worth noting. The TBI-PBE dataset used in the current study is relatively aged as data were last collected in 2011; however, the dataset contains intricate and valuable details on each activity the patient undertook. It is also possible that the TBI-PBE dataset missed essential therapeutic features (eg, patient familiarity, patient preference, treatment target, etc) that could affect treatment as well as confounding variables (eg, bowel and bladder management, social determinants of health, etc) that could affect outcome. Future studies should consider capturing additional therapeutic features and confounding variables. By taking the weekly average time, even though the temporal information about the activities is lost becomes a vital trade-off to reduce the dimensionality but still preserve the activity details. The FIM is also only a proxy measure of cognitive and motor function. FIM measures the burden of care by assessing the level of assistance needed to perform functional activities. It is possible that with greater specificity in metrics assessing motor (eg, gait quality, walking speed) and cognition (eg, frequency of applied compensatory strategy), the predictive value of these functional variables may change the current findings.

Conclusions

There is an increasing need to identify what leads to greater levels of recovery and better outcomes and the role inpatient TBI rehabilitation has in effecting those improvements. Past and ongoing research is identifying critical and essential inpatient rehabilitation components and their relation to various outcomes. The newer methods of data analysis, including ML, appear to have value in this discovery process. The current study built upon 2 prior studies examining which variables are associated with better outcomes. The current study adds to these findings by demonstrating the utility of ML methods in analyzing a dataset with a large set of predictive variables and in identifying the top predictive features specific to each outcome variable.

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