Machine learning algorithms to predict 30-day readmission in patients with stroke: a prospective cohort study

Yu-Ching Chen
Kaohsiung Medical University
Jo-Hsuan Chung
Kaohsiung Medical University
Yu-Jo Yeh
Kaohsiung Medical University
Hsiu-Fen Lin
Kaohsiung Medical University Chung Ho Memorial Hospital
Ching-Huang Lin
Kaohsiung Veterans General Hospital
Hong-Hsi Hsien
St. Joseph Hospital
Kuo-Wei Hung
Yuan's General Hospital
Shu-Chuan Jennifer Yeh
Sun Yat-Sen University
HON-YI SHI (hshi@kmu.edu.tw)
Kaohsiung Medical University https://orcid.org/0000-0003-4700-0190

Research

Keywords: Stroke, 30-day readmission, Artificial neural network, Global sensitivity analysis, Post-acute care

Posted Date: June 8th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-33334/v1

Abstract

Background No studies have discussed machine learning algorithms to predict the risk of 30-day readmission in patients with stroke. The objective of the present study was to compare the accuracy of the artificial neural network (ANN), K nearest neighbor (KNN), support vector machine (SVM), naive Bayes classifier (NBC), and Cox regression (COX) models and to explore the significant factors in predicting 30-day readmission after stroke. Methods This study prospectively compared the accuracy of the models using clinical data for 1,476 patients with stroke treated in six hospitals between March, 2014 and September, 2019. A training dataset (n=1,033) was used for model development, a testing dataset (n=443) was used for internal validation, and a validating dataset (n=167) was used for external validation. A global sensitivity analysis was performed to compare the significance of the selected input variables. Results Of all forecasting models, the ANN model had the highest accuracy in predicting 30-day readmission after stroke and had the highest overall performance indices. According to the ANN model, 30-day readmission was significantly associated with post-acute care (PAC) program, patient attributes, clinical attributes, and functional status scores before re-habilitation (all P <0.05). Additionally, PAC program was the most significant variable affecting 30-day readmission, followed by nasogastric tube insertion, and stroke type (P <0.05). Conclusions Comparisons of the five forecasting models indicated that the ANN model had the highest accuracy in predicting 30-day readmission in stroke patients. Before stroke patients are discharged from hospitalization, they should be counseled regarding their potential for recovery and other possible outcomes. These important predictors can also be used to educate candidates for stroke patients who underwent PAC rehabilitation with respect to the course of recovery and health outcomes.

Background

Long-term disabilities after stroke can be enormous physical, mental, and financial burdens for patients, their families, and society [1]. Readmission for any cause after acute care for stroke is associated with increased mortality, increased healthcare costs, and decreased functional status [1–3]. Additionally, high readmission rates negatively affect the profitability of a healthcare institution. Therefore, reducing readmission has become an active area of research in the medical literature.

Although many models for predicting outcomes of stroke treatments have been proposed in recent years, models for predicting 30-day readmission have had major shortcomings: (1) recently proposed forecasting models have shown lower prediction accuracy compared to conventional models [4–9], (2) proposed forecasting models require use of health insurance claims data, which would not be available in a real-time clinical setting [8, 10], (3) predictions of 30-day readmission do not consider post-acute care (PAC) program, patient attributes, clinical attributes and functional status score before rehabilitation [11–15]. In the current study, the best predictors of hospital readmission within 30 days after stroke were identified using artificial neural network (ANN), K nearest neighbor (KNN), support vector machine (SVM), naive Bayes classifier (NBC) and Cox regression (COX) models. Healthcare administrators in Taiwan can use the predictive simulation results obtained in this study not only for developing and improving

healthcare policies as well as support systems for healthcare decision making. In this study, we aimed to compare the five forecasting models in terms of accuracy and to explore the significant variables in predicting hospital readmission within 30 days after stroke.

Methods

Study design and patients

The study population included all patients who had an ICD-9-CM code for stroke (433.01, 433.10, 433.11, 433.21, 433.31, 433.81, 433.91, 434.00, 434.01, 434.11, 434.91and 436 for ischemic stroke; 430 and 431 for hemorrhagic stroke) and had been admitted to the PAC ward at one of four community hospitals (three regional hospitals and one district hospital) or had been admitted to a traditional non-PAC ward at one of two medical centers in south Taiwan between March, 2014 and September, 2019. The enrollment criteria were acute stroke, within 30 days of stroke onset, and a score of 2 to 4 for the Modified Rankin Scale (in this scale, absence of symptoms is scored as 0; significant, slight, moderate, moderately severe, and severe disability are scored as 1, 2, 3, 4 and 5, respectively) [16]. A total of 1,476 patients with stroke were initially recruited in the study and another 167 patients with stroke also were collected from October to December 2019 (Fig. 1). The study protocol was approved by the institutional review board at Kaohsiung Medical University Hospital (KMUH-IRB-20140308), and written informed consent was obtained from each participant.

Instruments and potential predictors

Functional disability was measured using the Barthel Index (BI) [17], Functional Oral Intake Scale (FOIS) [18], Mini-mental State Examination (MMSE) [19], Instrumental Activities of Daily Living (IADL) [20], EuroQoL Quality of Life Scale (EQ-5D-3L) [21], and Berg Balance Scale (BBS) [22]. The Chinese versions of all instruments used in this study have been validated and used extensively in both clinical practice and research [17, 22, 23].

A research assistant collected the following data from medical records: PAC program (PAC group or non-PAC group), patient attributes (age, gender, education, and body mass index (BMI)), clinical attributes (stroke type, nasogastric (NG) tube, Foley catheter, hypertension, diabetes mellitus (DM), hyperlipidemia, atrial fibrillation, previous stroke, acute care length of stay (LOS), rehabilitation ward LOS), and functional status score before rehabilitation. In multivariate analysis, the potential predictors were the independent variables, and 30-day readmission was the dependent variable.

Statistical analysis

The unit of analysis in this study was the individual patient with stroke. Statistical analysis was performed in the following steps. In the first step, the statistical significance of continuous variables was tested by one-way analysis of variance, and the statistical significance of categorical variables was tested by Fisher exact analysis. Univariate analyses were performed to identify significant predictors ($P<$

0.05). In the second step of the statistical analysis, the cases in the overall database were randomly divided into two datasets: a training dataset including 1,033 cases was used for model development and a testing dataset including 443 cases was used for internal validation. Additionally, a validating dataset including 167 new cases was used for external validation. The independent variables fitted to the forecasting models were the significant predictors, and the dependent variable was 30-day readmission. After model training, model outputs were collected for each testing dataset. In the third step of statistical analysis, 1,000 pairs of forecasting models with 95% confidence intervals were compared in terms of accuracy in predicting 30-day readmission in patients with stroke. Statistical significance between the differences of the two models and performance indices are calculated using a Chi-squared test, since this test is nonparametric and does not require a normal distribution of either the data or the variances. Indices used for performance comparisons included sensitivity, specificity, positive and negative predictive value (PPV and NPV), accuracy, and area under the receiver operating characteristics (AUROC) curve.

In the fourth and final step of statistical analysis, global sensitivity analysis was performed to assess the importance of variables in the prediction model, to assess the relative significance of input variables in the forecasting model, and to rank the importance of the variables. The global sensitivity of the input variables against the output variable was expressed as the ratio of the network error (sum of squared residuals) [24]. Variables with a sensitivity ratio (VSR) of 1 or lower were assumed to diminish performance and were removed.

All statistical analyses were performed using the STATISTICA 13.0 software package (StatSoft, Inc., Tulsa, OK, USA). All statistical tests were two-sided; a *p* value less than 0.05 was considered statistically significant.

Results

Study characteristics

Table 1 shows that 1,283 patients (86.9%) joined the per-diem PAC program and the remaining patients selected the fee-for-service non-PAC program. The stroke patients had a mean age of 65.5 years (standard deviation, SD 13.0 years) and most patients were male (62.5%). During the study period, 120 patients with stroke were readmission within 30 days. In univariate analysis, PAC program, age, gender, education, BMI, stroke type, NG tube, Foley, hypertension, DM, hyperlipidemia, atrial fibrillation, previous stroke, acute care LOS, rehabilitation LOS and functional status score before rehabilitation are significantly associated with 30-day readmission ($P < 0.05$) and these significant predictors were included in the forecasting models (Table 2).

Table 1

Baseline characteristics of the study population (N = 1,476)*

Variables		Mean ± SD or N (%)
Post-acute care	No	193(13.1)
	Yes	1,283(86.9)
Patient attributes		
Age (years)		65.5 ± 13.0
Gender	Female	554(37.5)
	Male	922(62.5)
Education (years)		8.9 ± 2.1
Body mass index (kg/m^2)		24.0 ± 2.6
Clinical attributes		
Stroke type	Ischemic	1,224(82.9)
	Hemorrhagic	252(17.1)
Nasogastric tube	No	1,187(80.4)
	Yes	289(19.6)
Foley catheter	No	1,342(90.9)
	Yes	134(9.1)
Hypertension	No	449(30.4)
	Yes	1,027(69.6)
Diabetes mellitus	No	906(61.4)
	Yes	570(38.6)
Hyperlipidemia	No	967(65.5)
	Yes	509(34.5)
Atrial fibrillation	No	1,354(91.7)
	Yes	122(8.3)

SD standard deviation, *BI* Barthel Index, *FOIS* Functional Oral Intake Scale, *EQ-5D* EuroQoL Quality of Life Scale, *IADL* Instrumental activities of Daily Living Scale, *BBS* Berg Balance Scale, *MMSE* Mini-Mental State Examination, *BDI* Beck Depression Inventory, *BAI* Beck Anxiety Inventory.

*Data are reported as mean ± SD or n (%).

Variables		Mean ± SD or N (%)
Previous stroke	No	1,250(84.7)
	Yes	226(15.3)
Acute care length of stay(days)		15.2 ± 9.0
Rehabilitation length of stay (days)		44.9 ± 21.2
Readmission in 30 days	No	1,356(91.9)
	Yes	120(8.1)
Functional status scores before rehabilitation		
BI score		39.0 ± 23.7
FOIS score		5.5 ± 2.1
EQ5D score		10.4 ± 1.9
IADL score		1.2 ± 1.1
BBS score		15.6 ± 15.8
MMSE score		19.4 ± 8.9
BDI score		1.9 ± 0.8
BAI score		1.9 ± 0.6

SD standard deviation, *BI* Barthel Index, *FOIS* Functional Oral Intake Scale, *EQ-5D* EuroQoL Quality of Life Scale, *IADL* Instrumental activities of Daily Living Scale, *BBS* Berg Balance Scale, *MMSE* Mini-Mental State Examination, *BDI* Beck Depression Inventory, *BAI* Beck Anxiety Inventory.

*Data are reported as mean ± SD or n (%).

Table 2

Univariate analysis of selected risk factors for 30-day readmission in patients with stroke (N = 1,476)*

Variables	Statistics	*P* value
Post-acute care (yes vs. no)	52.074	< 0.001
Patient attributes		
Age (years)	7.890	0.005
Gender (female vs. male)	23.657	< 0.001
Education (years)	10.870	< 0.001
Body mass index (kg/m^2)	7.944	0.005
Clinical attributes		
Stroke type (ischemic vs. hemorrhagic)	32.053	< 0.001
Nasogastric tube (yes vs. no)	49.361	< 0.001
Foley catheter (yes vs. no)	5.590	0.018
Hypertension (yes vs. no)	4.564	0.033
Diabetes mellitus (yes vs. no)	7.324	0.007
Hyperlipidemia (yes vs. no)	5.777	0.016
Atrial fibrillation (yes vs. no)	6.114	0.013
Previous stroke (yes vs. no)	6.899	0.009
Acute care length of stay, days	30.008	< 0.001
Rehabilitation length of stay, days	26.508	< 0.001
Functional status score before rehabilitation		
BI score	37.494	< 0.001
FOIS score	26.508	< 0.001
EQ5D score	16.712	< 0.001
IADL score	22.726	< 0.001
BBS score	14.903	< 0.001

SD standard deviation, *BI* Barthel index, *FOIS* functional oral intake scale, *EQ-5D* EuroQoL quality of life scale, *IADL* instrumental activities of daily living scale, *BBS* Berg balance scale, *MMSE* mini-mental state examination, *BDI* Beck depression inventory, *BAI* Beck anxiety inventory.

*One-way analysis of variance or Fisher exact analysis was used for statistical analysis.

Variables	Statistics	*P* value
MMSE score	34.665	< 0.001
BDI score	13.555	< 0.001
BAI score	14.087	< 0.001

SD standard deviation, *BI* Barthel index, *FOIS* functional oral intake scale, *EQ-5D* EuroQoL quality of life scale, *IADL* instrumental activities of daily living scale, *BBS* Berg balance scale, *MMSE* mini-mental state examination, *BDI* Beck depression inventory, *BAI* Beck anxiety inventory.

*One-way analysis of variance or Fisher exact analysis was used for statistical analysis.

Comparison of the forecasting models

The training and testing datasets did not significantly differ in the significant predictors and 30-day readmission (data not shown); therefore, samples were compared between the training and testing datasets to increase reliability in the validation results. The data in the Table 3 showed that sensitivity, specificity, PPV, NPV, accuracy, and AUROC were all significantly superior in the ANN model in comparison with other forecasting models ($P < 0.001$).

Table 3
Comparison of 1,000 pairs of forecasting models for predicting 30-day readmission in patients with stroke (N = 1,476)

Model	Sensitivity	Specificity	PPV	NPV	Accuracy	AUROC
Training dataset (n = 1,033)						
ANN (95% CI)	0.73 (0.65, 0.82)	0.98 (0.96, 0.99)	0.88 (0.84, 0.92)	0.77 (0.70, 0.84)	0.92 (0.89, 0.95)	0.94 (0.91,0.97)
KNN (95% CI)	0.59 (0.50, 0.68)	0.86 (0.82, 0.90)	0.56 (0.47, 0.65)	0.64 (0.56, 0.72)	0.83 (0.78, 0.88)	0.76 (0.68, 0.84)
SVM (95% CI)	0.49 (0.39, 0.59)	0.96 (0.93, 0.99)	0.76 (0.68, 0.84)	0.62 (0.54, 0.70)	0.89 (0.85, 0.93)	0.74 (0.66, 0.82)
NBC (95% CI)	0.48 (0.38, 0.59)	0.96 (0.93, 0.99)	0.50 (0.40, 0.60)	0.69 (0.61, 0.77)	0.81 (0.75, 0.87)	0.73 (0.65, 0.81)
COX (95% CI)	0.51 (0.42, 0.61)	0.97 (0.95, 0.99)	0.77 (0.69, 0.85)	0.71 (0.63, 0.79)	0.85 (0.80, 0.90)	0.88 (0.83, 0.93)
P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Testing dataset (n = 443)						
ANN (95% CI)	0.70 (0.62, 0.78)	0.97 (0.95, 0.99)	0.89 (0.85, 0.93)	0.82 (0.76, 0.88)	0.93 (0.90, 0.96)	0.89 (0.85, 0.93)
KNN (95% CI)	0.53 (0.44, 0.62)	0.88 (0.84, 0.92)	0.60 (0.51, 0.69)	0.71 (0.63, 0.79)	0.71 (0.63, 0.79)	0.81 (0.75, 0.87)
SVM (95% CI)	0.53 (0.44, 0.62)	0.93 (0.90, 0.96)	0.75 (0.67, 0.82)	0.78 (0.71, 0.85)	0.82 (0.73, 0.89)	0.80 (0.74, 0.86)

ANN artificial neural network, *KNN* K nearest neighbor, *SVM* support vector machine, *NBC* naive Bayes classifier, *COX* Cox regression, *PPV* positive predictive value, *NPV* negative predictive value, *AUROC* area under the receiver operating characteristic, *CI* confidence interval.

Model	Sensitivity	Specificity	PPV	NPV	Accuracy	AUROC
NBC (95% CI)	0.50 (0.40, 0.60)	0.93 (0.90, 0.96)	0.63 (0.54, 0.72)	0.79 (0.72, 0.86)	0.83 (0.76, 0.90)	0.84 (0.78, 0.90)
COX (95% CI)	0.54 (0.45, 0.64)	0.96 (0.94, 0.98)	0.88 (0.83, 0.93)	0.61 (0.53, 0.69)	0.87 (0.82, 0.92)	0.87 (0.82, 0.92)
P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

ANN artificial neural network, *KNN* K nearest neighbor, *SVM* support vector machine, *NBC* naive Bayes classifier, *COX* Cox regression, *PPV* positive predictive value, *NPV* negative predictive value, *AUROC* area under the receiver operating characteristic, *CI* confidence interval.

Significant predictors in the ANN model

Next, the training dataset was used for calculating VSRs for the ANN model. In global sensitivity analysis, PAC program had the highest VSR (1.61) for predicting 30-day readmission in stroke patients followed by NG tube (VSR = 1.52) and stroke type (VSR = 1.48) (Table 4). The VSR values for the ANN model were all higher than 1, which indicated that network performance improved when all variables were considered.

Table 4
Global sensitivity analysis of artificial neural network model in predicting 30-day readmission in patients with stroke (N = 1,033)

	Rank 1st	Rank 2nd	Rank 3rd
Variables	Post-acute care	Nasogastric tube	Stroke type
Variable sensitivity ratio (VSR)	1.61	1.52	1.48

Sensitivity analysis

Additionally, to verify the predictive accuracy of the models, the 167 new data sets were collected. Table 5 compares the performance indices values obtained by ANN, KNN, SVM, NBC and COX models for external validation. Compared to other forecasting models, the ANN model also consistently and significantly obtained better performance indices values to predict 30-day readmission ($P < 0.001$).

Table 5
Comparative performance indices of forecasting models when using 167 new validation datasets to predict 30-day readmission in patients with stroke

Models	Sensitivity	Specificity	PPV	NPV	Accuracy	AUROC
ANN (95% CI)	0.74 (0.66, 0.82)	0.97 (0.95, 0.99)	0.89 (0.85, 0.94)	0.87 (0.82, 0.92)	0.93 (0.90, 0.96)	0.94 (0.91, 0.97)
KNN (95% CI)	0.50 (0.40, 0.49)	0.87 (0.83, 0.91)	0.61 (0.52, 0.70)	0.70 (0.62, 0.78)	0.80 (0.74, 0.86)	0.83 (0.78, 0.88)
SVM (95% CI)	0.51 (0.41, 0.61)	0.96 (0.94, 0.98)	0.76 (0.69, 0.83)	0.79 (0.72, 0.87)	0.88 (0.84, 0.92)	0.81 (0.76, 0.86)
NBC (95% CI)	0.50 (0.40, 0.60)	0.93 (0.90, 0.96)	0.61 (0.52, 0.70)	0.80 (0.73, 0.87)	0.84 (0.79, 0.89)	0.80 (0.75, 0.85)
COX (95% CI)	0.58 (0.49, 0.67)	0.92 (0.89, 0.95)	0.84 (0.78, 0.90)	0.69 (0.61, 0.77)	0.88 (0.84, 0.92)	0.88 (0.84, 0.92)
P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

ANN artificial neural network, *KNN* K nearest neighbor, *SVM* support vector machine, *NBC* naive Bayes classifier, *COX* Cox regression, PPV positive predictive value, *NPV* negative predictive value, *AUROC* area under the receiver operating characteristic.

Discussion

To the best of our knowledge, this study is the first to use forecasting models to analyze 30-day readmission in patients with stroke. Accuracy in predicting 30-day readmission in patients with stroke was compared among the five forecasting models. When all models were constructed using a given set of clinical inputs, the ANN model was clearly superior to other forecasting models. Additionally, unlike previous works in which the analyses were performed using a dataset for a single medical center, our study used prospective and longitudinal data from multiple medical institutions, which provides a more accurate depiction of current treatment for patients with stroke [10–13]. Additionally, unlike single-center series studies, our use of registry data provides more accurately depicts stroke treatment in large populations. Using registry data also minimizes referral bias or bias caused by the practices of a single physician or a single institution [25, 26].

Recent works have repeatedly demonstrated the superior performance of the ANN model compared to other models [9, 13]. The advantages offered by the unique characteristics of the ANN model have been

confirmed by statistical analyses. For example, using an ANN model can enable more appropriate and more accurate processing of inputs that are incomplete or inputs that introduce noise [9, 27]. Another advantage is that linear and non-linear ANN models with good potential for use in large-scale medical databases can be constructed using data that are highly correlated but not normally distributed. Prognosis prediction is only one of the many applications of ANN models in clinical research in the medical field [27].

The comparisons of various models in the present study suggest that, by expanding the number of potential predictors, the ANN model facilitates systematic analysis of various diseases and facilitates comparisons of the effectiveness of research methods. Additionally, the proposed model can be extended to outcome prediction for treatments other than PAC and in patients other than patients with stroke.

The global sensitivity analysis of the weights of significant predictors of 30-day readmission in the patients with stroke in this study revealed that the best predictor was PAC. This finding is consistent with earlier reports that, compared to all other stroke treatment variables, PAC has the largest effect on outcome in terms of overall treatment cost, functional status after stroke, and duration of hospital stay before transfer to rehabilitative ward [25, 28]. Wang et al. coupled a natural experimental design with propensity score matching to assess the impact of PAC in stroke patients and to examine the longitudinal effects of PAC on functional status [25]. The study concluded that intensive rehabilitative PAC delivered on a per-diem basis substantially improves functional status in patients with stroke. Another recent study compared a wide range of functional domains between a stroke PAC group and a well-matched nationwide cohort of patients with stroke who did not receive PAC [29]. The authors similarly reported that the stroke PAC group had significantly better outcomes in terms of restoration of functional impairments, 90-day clinical outcomes, and healthcare utilization.

The present study found that, before rehabilitation, NG tube insertion was significantly associated with 30-day readmission ($P < 0.001$). During the study period, no patient with stroke required NG tube insertion after rehabilitation. Previous works indicate that an NG tube insertion may be beneficial in acute stroke. However, prolonged use is associated with poor prognosis [30, 31]. A large clinical trial recently reported that, at 6 months after stroke, survival and other medical outcomes are better in patients who have had NG tubes removed compared to those who still require NG tubes at 6 months [30]. As reported previously in Ho et al., our study found that removal of NG tube early after stroke is associated with reduced rate of readmission, reduced incidence of pneumonia, and reduced mortality [31].

Hemorrhagic stroke is associated with a higher readmission rate and higher mortality compared to ischemic stroke [32, 33]. It is generally more severe in hemorrhagic stroke than in ischemic stroke. In the first 3 months after stroke, readmission and mortality are higher in hemorrhagic stroke, and both readmission and mortality are independently associated with the hemorrhagic of the stroke lesion. In the present study, 30-day readmission was higher in the hemorrhagic patients with stroke compared to ischemic patients with stroke.

This prospective observational study of a cohort of patients with stroke in Taiwan analyzed data for patients treated at multiple healthcare institutions. The ANN model developed in this study improves accuracy in identifying correlations between predictors and 30-day readmission in patients with stroke. However, the proposed predictive model has many other potential clinical applications. For example, healthcare institutions can improve care quality by using the methods developed in this study to evaluate the effectiveness of medical treatment. Since the proposed ANN model accurately predicts 30-day readmission, healthcare administrators at other institutions can use the model to demonstrate the need for prompt and appropriate PAC for patients with stroke. A broader application of the model is in facilitating the formulation and promotion of healthcare policies and the development of decision-support systems in Taiwan, which would ultimately enhance the health of all citizens. However, further studies are needed to determine the true clinical relevance of the ANN model and to clarify whether clinicians can effectively use the model to predict prognosis and to optimize medical management for patients with stoke.

To confirm our data for the PAC program significantly associated with 30-day readmission in patients with stroke, Table 6 presents an international data comparison. The comparison includes this and three other selected studies of similar population in the United States and Taiwan [34–36]. These studies all shared the following features: 1) sample size was relatively large, 2) mean age of study sample was similar to that in the present study, 3) data sources from the State or National datasets, and, most importantly, 4) to explore 30-day readmission measures in patients with stroke. All of these previous studies are consistent with reported findings in the present study that multidiscipline PAC program can significantly reduce 30-day readmission in patients with stroke compared with the non-PAC program ($P < 0.001$).

Table 6
Post-acute care (PAC) program predictor significantly associated with 30-day readmission in patients with stroke

Authors (area)	No. of subjects	Age (range)	Data source	Findings
Present Study (Taiwan)	1,476	65.5	PAC ward at one of four community hospitals (three regional hospitals and one district hospital) or a traditional non-PAC ward at one of two medical centers.	PAC program was the most significant variable affecting 30-day readmission.
Kosar CM, et al. (2020) (U.S.)	2,044,231	80.2	The Medicare Provider Analysis and Review database.	For patients from the most rural counties, adjusted 30-day readmission rates were 0.3 (95% CI, -0.6 to -0.1) percentage points lower than those of patients receiving postacute care.
Raman N, et al. (2020) (U.S.)	1,613	74.4	The State Inpatient Database in California.	Clinical predictors of 30-day readmissions included several comorbidities (i.e. liver disease, hypertension), and discharge to a postacute care facility.
Hsieh CY, et al. (2018) (Taiwan)	6,839	69.4	Taiwan National Health Insurance claims datasets.	The 30-day readmission rates were 15.5% for the PAC group, compared to 30.4% for the non-PAC group.

Limitations

This study has several limitations inherent in any large database analysis. First, the validity of the comparisons in the study is limited by the exclusion of complications associated with stroke rehabilitation outcomes. Second, the analysis was limited to 30-day readmission, which reduces the subset of patients with stroke in which the ANN model is clinically applicable. Third, this study only compared ANN, KNN, SVM, NBC and COX models. Further studies are needed to compare other forecasting models. A final limitation is that this study did not compare other outcomes, e.g., patient-reported quality of life, because the database did not contain these outcome data. Nevertheless, the results can still be considered valid given the robustness and statistical significance of the results.

Conclusions

Based on the comparison results in this study, we conclude that the ANN model is superior to the other forecasting models in terms of accuracy in predicting 30-day readmission in patients with stroke after hospital discharge. Overall performance indices for the ANN model were also superior. These important predictors can also be used to educate candidates for stroke patients who underwent PAC rehabilitation with respect to the course of recovery and health outcomes. Although the practical applicability of database studies such as this have been convincingly demonstrated, future studies can expand the range of clinical variables included in the analysis, which could obtain further novel results and could also improve precision. Such data could be vital for developing, promoting, and improving health policies for treating patients with stroke.

Abbreviations

ANN: artificial neural network; KNN: K nearest neighbor; SVM: support vector machine; NBC: naive Bayes classifier; COX: Cox regression; PAC: post-acute care; BI: Barthel Index; FOIS: Functional Oral Intake Scale; MMSE: Mini-mental State Examination; IADL: Instrumental Activities of Daily Living; EQ-5D-3L: EuroQoL Quality of Life Scale; BBS: Berg Balance Scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; BMI: body mass index; NG: nasogastric; DM: diabetes mellitus; LOS: length of stay; PPV: positive predictive value; NPV: negative predictive value; AUROC: area under the receiver operating characteristic; VSR: variables with a sensitivity ratio.

Declarations

Acknowledgments

We thank all stroke cohort participants, medical staff, and investigators for their contribution to the study.

Funding

This study was supported by funding from the NSYSU-KMU JOINT RESEARCH PROJECT (NSYSUKMU 109-P001) and the Ministry of Science and Technology (MOST 104-2410-H-037-006-SS2 & MOST 106-2410-B-037 -076) in Taiwan.

Availability of data and materials

Dataset used during the current study is available from the corresponding author on request.

Authors’ contributions

YCC and HYS contributed to the design of the study. JHC, YJY, HFL, CHL,

HHH, KWH and SCY collected the data. YCC and HYS analyzed and interpreted the data, and drafted the manuscript. JHC, YJY, HFL, CHL, HHH, KWH and SCY reviewed the manuscript. All authors read, commented, and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the institutional review board at Kaohsiung Medical University Hospital (KMUH-IRB-20140308), and written informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Ottenbacher KJ, Karmarkar A, Graham JE, Kuo YF, Deutsch A, Reistetter TA, et al. Thirty-day hospital readmission following discharge from postacute rehabilitation in fee-for-service Medicare patients. JAMA. 2014;311:604–14.
2. Timm FP, Houle TT, Grabitz SD, Lihn A-L, Stokholm JB, Eikermann-Haerter K, et al. Migraine and risk of perioperative ischemic stroke and hospital readmission: hospital based registry study. BMJ. 2017;356:i6635.
3. Association of US Centers for Medicare and Medicaid Services Hospital 30-Day Risk-Standardized Readmission Metric With Care Quality and Outcomes After Acute Myocardial Infarction: Findings From the National Cardiovascular Data Registry/Acute
   Pandey A, Golwala H, Hall HM, Tracy Y, Wang, Di Lu, Y, Xian, et al. Association of US Centers for Medicare and Medicaid Services Hospital 30-Day Risk-Standardized Readmission Metric With Care Quality and Outcomes After Acute Myocardial Infarction: Findings From the National Cardiovascular Data Registry/Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines. JAMA Cardiol. 2017;2:723–31.
4. Gil-Pita R, Yao X. Evolving edited k-nearest neighbor classifiers. Int J Neural Syst. 2008;18:459–67.
5. Marie Bruun KS, Frederiksen, Hanneke FM, Rhodius-Meester M, Baroni L, Gjerum J, Koikkalainen, et al. Impact of a clinical decision support tool on prediction of progression in early-stage dementia: a prospective validation study. Alzheimers Res Ther. 2019;11:25.
6. Anette Hall T, Pekkala T, Polvikoski M, van Gils M, Kivipelto J, Lötjönen, et al. Prediction models for dementia and neuropathology in the oldest old: the Vantaa 85 + cohort study. Alzheimers Res Ther. 2019;11:11.
7. Kickingereder P, Isensee F, Tursunova I, Petersen J, Neuberger U, Bonekamp D, et al. Automated quantitative tumour response assessment of MRI in neuro-oncology with artificial neural networks: a multicentre, retrospective study. Lancet Oncol. 2019;20:728–40.
8. Beam AL, Kohane IS. Big Data and Machine Learning in Health Care. JAMA. 2018;319:1317–8.

9. Alfredo Madrid-García, Judit Font-Urgelles, Mario Vega-Barbas, Leticia León-Mateos, Dalifer Dayanira Freites, Cristina Jesus Lajas, et al. Outpatient Readmission in Rheumatology: A Machine Learning Predictive Model of Patient's Return to the Clinic. J Clin Med. 2019;8(8):1156.
10. Todorov MI, Paetzold JC, Schoppe O, Tetteh G, Shit S, Efremov V, et al. Machine learning analysis of whole mouse brain vasculature. Nat Methods. 2020;17:442–9.
11. Latourelle JC, Beste MT, Hadzi TC, Miller RE, Oppenheim JN, Valko MP, et al. Large-scale identification of clinical and genetic predictors of motor progression in patients with newly diagnosed Parkinson's disease: a longitudinal cohort study and validation. Lancet Neurol. 2017;16:908–16.
12. Khera S, Kolte D, Gupta T, Goldsweig A, Velagapudi P, Kalra A, et al. Association Between Hospital Volume and 30-Day Readmissions Following Transcatheter Aortic Valve Replacement. JAMA Cardiol. 2017;2:732–41.
13. Ottenbacher KJ, Smith PM, Illig SB, Linn RT, Fiedler RC, Granger CV. Comparison of logistic regression and neural networks to predict rehospitalization in patients with stroke. J Clin Epidemiol. 2001;54:1159–65.
14. Collins SP, Jenkins CA, Harrell FE Jr, Liu D, Miller KF, Lindsell CJ, et al. Identification of Emergency Department Patients With Acute Heart Failure at Low Risk for 30-Day Adverse Events: The STRATIFY Decision Tool. JACC Heart Fail. 2015;3:737–47.
15. Kumar A, Rahman M, Trivedi AN, Resnik L, Gozalo P, Vincent Mor. Comparing post-acute rehabilitation use, length of stay, and outcomes experienced by Medicare fee-for-service and Medicare Advantage beneficiaries with hip fracture in the United States: A secondary analysis of administrative data. PLoS Med. 2018;15:e1002592.
16. Quinn TJ, McArthur K, Dawson J, Walters MR, Lees KR. Reliability of structured modified rankin scale assessment. Stroke. 2010;41:e602.
17. Leung SO, Chan CC, Shah S. Development of a Chinese version of the Modified Barthel Index–validity and reliability. Clin Rehabil. 2007;21:912–22.
18. Crary MA, Mann GD, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil. 2005;86:1516–20.
19. Agrell B, Dehlin O. Mini mental state examination in geriatric stroke patients. Validity, differences between subgroups of patients, and relationships to somatic and mental variables. Aging (Milano). 2000;12:439–44.
20. Vittengl JR, White CN, McGovern RJ, Morton BJ. Comparative validity of seven scoring systems for the instrumental activities of daily living scale in rural elders. Aging Ment Health. 2006;10:40–7.
21. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol group. Ann Med. 2001;33:337–43.
22. Chou CY, Chien CW, Hsueh IP, Sheu CF, Wang CH, Hsieh CL. Developing a short form of the Berg Balance Scale for people with stroke. Phys Ther. 2006;86:195–204.

23. Tseng MC, Lin HJ. Health-related quality of life after stroke: review of the literature and implications for future research. Acta Neurol Taiwan. 2007;16:7–12.
24. Saltelli A, Ratto M, Andres T, Campolongo F, Cariboni J, Gatelli D, et al. Global Sensitivity Analysis: The Primer. Chichester: Wiley & Sons; 2008.
25. Wang CY, Hsien HH, Hung KW, Lin HF, Chiou HY, Yeh SC, et al. Multidiscipline Stroke Post-Acute Care Transfer System: Propensity-Score-Based Comparison of Functional Status. J Clin Med. 2019;8:1233.
26. Jahan R, Saver JL, Schwamm LH, Fonarow GC, Liang L, Matsouaka RA, et al. Association Between Time to Treatment With Endovascular Reperfusion Therapy and Outcomes in Patients With Acute Ischemic Stroke Treated in Clinical Practice. JAMA. 2019;322:252–63.
27. Baxt WG. Application of artificial neural networks to clinical medicine. Lancet. 1995;346:1135–8.
28. Wang CY, Chen YR, Hong JP, Chan CC, Chang LC, Shi HY. Rehabilitative post-acute care for stroke patients delivered by per-diem payment system in different hospitalization paths: A Taiwan pilot study. Int J Qual Health Care. 2017;29:779–84.
29. Peng LN, Lu WH, Liang CK, Chou MY, Chung CP, Tsai SL, et al. Functional Outcomes, Subsequent Healthcare Utilization, and Mortality of Stroke Postacute Care Patients in Taiwan: A Nationwide Propensity Score-matched Study. J Am Med Dir Assoc. 2017;18:990.e7-990.e12.
30. Dennis MS, Lewis SC, Warlow C, FOOD Trial Collaboration. Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial. Lancet. 2005;365:764–72.
31. Ho CH, Lin WC, Hsu YF, et al. One-Year Risk of Pneumonia and Mortality in Patients with Poststroke Dysphagia: A Nationwide Population-Based Study. J Stroke Cerebrovasc Dis. 2018;27:1311–7.
32. Andersen KK, Olsen TS, Dehlendorff C, Lee IH, Hung YC. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. Stroke. 2009;40:2068–72.
33. Roth GA, Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, Morozoff C, Naghavi M, et al. Trends and Patterns of Geographic Variation in Cardiovascular Mortality Among US Counties, 1980–2014. JAMA. 2017;317:1976–92.
34. Kosar CM, Loomer L, Ferdows NB, Trivedi AN, Panagiotou OA, Momotazur Rahman. Assessment of Rural-Urban Differences in Postacute Care Utilization and Outcomes Among Older US Adults. JAMA Netw Open. 2020;3:e1918738.
35. Raman N, Al-Robaidi K, Jadhav A, Thirumala PD. Perioperative Stroke and Readmissions Rates in Noncardiac Non-Neurologic Surgery. J Stroke Cerebrovasc Dis. 2020;29:104792.
36. Hsieh CY, Tsao WC, Lin RT, Chao AC. Three years of the nationwide post-acute stroke care program in Taiwan. J Chin Med Assoc. 2018;8187–8.

Figures

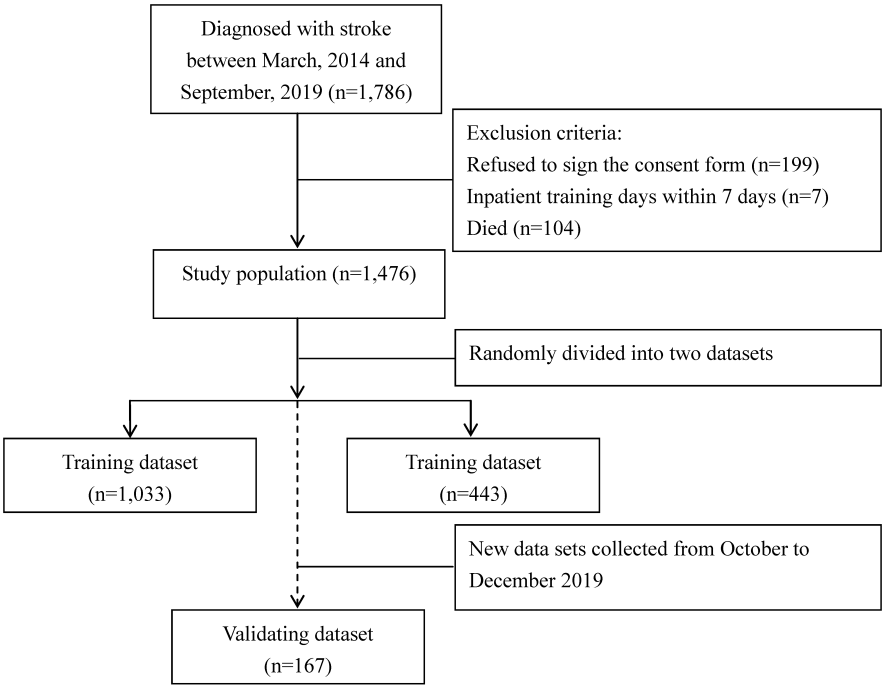

Figure 1

Flowchart of the study.