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Research article

Prediction of mechanical ventilation in Guillain-Barré syndrome at admission: Construction of a nomogram and comparison with the EGRIS model

Yanna Song [a,b,1], Shan Liu [c,1], Wei Qiu [b], Kangding Liu [a,*], Hong-Liang Zhang [d,**]

[a] Department of Neurology, First Hospital of Jilin University, Jilin University, Changchun, China
[b] Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, Guangdong Province, China
[c] Department of Nuclear Medicine, Second Hospital of Jilin University, Jilin University, Changchun, China
[d] Department of Life Sciences, National Natural Science Foundation of China, Beijing, China

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ABSTRACT

Background: Respiratory failure requiring mechanical ventilation (MV) is a common and severe complication of Guillain-Barré syndrome (GBS) with a reported incidence ranging from 20 % to 30 %. Thus, we aim to develop a nomogram to evaluate the risk of MV in patients with GBS at admission and tailor individualized care and treatment.

Methods: A total of 633 patients with GBS (434 in the training set, and 199 in the validation set) admitted to the First Hospital of Jilin University, Changchun, China from January 2010 to January 2021 were retrospectively enrolled. Subjects (n = 71) from the same institution from January 2021 to May 2022 were prospectively collected and allocated to the testing set. Multivariable logistic regression analysis was applied to build a predictive model incorporating the optimal features selected in the least absolute shrinkage and selection operator (LASSO) in the training set. The predictive model was validated using internal bootstrap resampling, an external validation set, and a prospective testing set, and the model's performance was assessed by using the concordance index (C-index), calibration curves, and decision curve analysis (DCA). Finally, we established a multivariable logistic model by using variables of the Erasmus GBS Respiratory Insufficiency Score (EGRIS) and did the same analysis to compare the performance of our predictive model with the EGRIS model.

Results: Variables in the final model selected by LASSO included time from onset to admission, facial and/or bulbar weakness, Medical Research Council sum score at admission, neutrophil-to-lymphocyte ratio, and platelet-lymphocyte ratio. The model presented as a nomogram displaying favorable discriminative ability with a C-index of 0.914 in the training set, 0.903 in the internal validation set, 0.953 in the external validation set, and 0.929 in the testing set. The model was well-calibrated and clinically useful as assessed by the calibration curve and DCA. As compared with the EGRIS model, our predictive model displayed satisfactory performance.

* Corresponding author. Department of Neurology, First Hospital of Jilin University, Xinmin Street 71, 130021, Changchun, China.
** Corresponding author. Department of Life Sciences, National Natural Science Foundation of China, Shuangqing Road 83, 100085, Beijing, China.
E-mail addresses: kangdingliu@163.com (K. Liu), drzhl@hotmail.com, zhanghl@nsfc.gov.cn (H.-L. Zhang).
[1] These authors have contributed equally to this work and share first authorship.

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Conclusions: We constructed a nomogram for early prediction of the risk of MV in patients with GBS. This model had satisfactory performance and appeared more efficient than the EGRIS model in Chinese patients with GBS.

1. Introduction

Guillain-Barré syndrome (GBS) is an immune-mediated polyneuropathy in the peripheral nervous system with an annual incidence of 0.81–1.89 cases per 100,000 persons [1,2]. Some GBS cases may present as a rapidly progressive course with respiratory muscle involvement requiring mechanical ventilation (MV) which is usually associated with unfavorable residual sequelae or mortality [3,4]. Therefore, early prediction of MV in GBS may enable clinicians to administer individualized measures to improve the prognosis of GBS patients.

Multiple clinical parameters have been used as predictors of MV in several studies, including shorter intervals from symptom onset to admission, lower Medical Research Council (MRC) sum score at nadir, neck weakness, facial weakness, bulbar palsy, autonomic dysfunction, elevated neutrophil-to-lymphocyte ratio (NLR), increased platelet-lymphocyte ratio (PLR), positive cerebrospinal fluid (CSF) anti-GQ1b antibody, and electrophysiological features of demyelination [5–14]. Several predictive models have been built for assessing the risk of MV among patients with GBS. Kannan et al. integrated neck weakness, single breath count (SBC), and bulbar paralysis into the NSB score model to assess the risk of MV in GBS patients at admission [9]. However, the sample size of this model was relatively small (only 110 cases of GBS) and calibration was not evaluated. In addition, the measurement of SBC requires patient cooperation, so the NSB model is not suitable for critical patients with GBS. A novel model incorporating hospital stay, glossopharyngeal and vagal nerve deficits, Hughes functional grading scale scores at admission, and NLR has been established [11]. Given the fact that information as to the length of hospital stay is unavailable at admission, the clinical use of the model is limited. Walgaard et al. [8] developed the Erasmus GBS respiratory insufficiency score (EGRIS) to calculate the probability (1%–90 %) of respiratory insufficiency and dependence on MV within the first week after admission for patients with GBS. EGRIS model, based on three predictors including a shorter interval between disease onset and admission, the presence of facial and/or bulbar weakness, and a lower MRC sum score at admission, has been proved applicable to the populations of the Netherlands, Japan, Peru, and Malaysia [8,15–17], whereas it has not yet been validated in Chinese patients with GBS.

With the aim to develop an easy-to-use and effective model which can assist clinicians to evaluate the risk of MV more efficiently in Chinese patients with GBS at admission, we not only enrolled an adequate number of patients and early available and simple clinical and laboratory parameters, but we also performed a systematic assessment and validation of the model's performance.

Hence, we aim to establish a multivariate logistic regression model by using optimal predictors selected by the least absolute shrinkage and selection operator (LASSO) and a predictive model by using three variables in EGRIS. We will then validate the EGRIS model in our external validation set and a prospective testing set to evaluate whether the EGRIS model applies to the Chinese population. We will also compare the performance of our predictive model with the EGRIS model.

2. Materials and methods

2.1. Patients

Ethical approval was obtained for this study from the ethics committee of the First Hospital of Jilin University, Changchun, China. Written informed consent was waived by the Institutional Review Board. The records of the patients were anonymized and de-identified prior to analysis. A total of 704 patients who were admitted to the Department of Neurology of the First Hospital of Jilin University from January 2010 to May 2022 and fulfilled the diagnostic criteria of GBS were enrolled [18]. Study participants retrospectively collected from January 2010 to January 2021 were divided into the training set (434 cases, from January 2010 to January 2018) and the external validation set (199 cases, from January 2018 to January 2021) in a 2:1 ratio according to their admission time. We also prospectively recruited 71 patients with GBS from January 2021 to May 2022 and assigned them to the testing set. Exclusion criteria of patients were younger than 16 years, recurrent GBS, Miller-Fisher syndrome, Bickerstaff encephalitis, chronic inflammatory demyelinating polyradiculoneuropathy, spinal cord disease, toxic or metabolic peripheral neuropathy, polyneuropathy, or myopathy [18–20]. Additionally, 38 patients with missing data were excluded and we performed a complete-case analysis.

2.2. Data collection

Clinical data from all subjects were recorded including sex, age, the season of onset, antecedent events, time from onset to admission, facial weakness, bulbar palsy, facial and/or bulbar weakness, autonomic dysfunction, tendon reflex on arms and legs at admission, MRC sum score at admission. The MRC sum score is defined as the sum of MRC scores of 6 different muscles in arms and legs measured bilaterally, resulting in a score ranging from 0 (total paralysis) to 60 (normal strength) [21]. Additional blood tests including NLR and PLR were determined on the day of admission. The baseline NLR was measured by dividing the neutrophil count by the lymphocyte count, and the PLR was measured by dividing the platelet count by the lymphocyte count.

Table 1
Baseline characteristics between MV and non-MV patients with GBS in the training, validation and testing sets.

Variables	Training set (N = 434)			Validation set (N = 199)			Testing set (N = 71)		
	MV N = 75	Non-MV N = 359	*P*	MV N = 46	Non-MV N = 153	*P*	MV N = 15	Non-MV N = 56	*P*
Sex			0.334			0.150			0.747
Male	49 (65.3 %)	213 (59.3 %)		29 (63 %)	78 (51 %)		9 (60 %)	31 (55.4 %)	
Female	26 (34.7 %)	146 (40.7 %)		17 (47 %)	75 (49 %)		6 (40 %)	25 (44.6 %)	
Age (years), median (IQR)	55 (40–61)	49 (33–62)	0.061	57 (46–67)	54 (41–62)	0.306	46 (37–62)	50 (34–61)	0.827
Season of onset			0.902			0.583			0.509
Spring	18 (24.0 %)	83 (23.4 %)		14 (30.4 %)	39 (25.5 %)		2 (13.3 %)	17 (30.4 %)	
Summer	20 (26.7 %)	104 (29.0 %)		14(30.4 %)	39 (25.5 %)		5 (33.3 %)	14 (25 %)	
Autumn	18 (24.0 %)	93 (25.9 %)		11 (23.9 %)	38 (24.8 %)		2 (13.3 %)	9 (16.1 %)	
Winter	19 (25.3 %)	78 (21.7 %)		7 (15.2 %)	37 (24.2 %)		6 (40 %)	16 (28.6 %)	
Antecedent events			0.101			0.666			0.944
None	23 (30.7 %)	128 (35.7 %)		22 (47.8 %)	70 (45.8 %)		4 (26.7 %)	15 (26.8 %)	
Upper respiratory tract infection	25 (33.3 %)	139 (38.7 %)		11 (23.9 %)	46 (30.1 %)		4 (26.7 %)	14 (25 %)	
Diarrhea	18 (24.0 %)	68 (18.9 %)		5 (10.9 %)	20 (13.1 %)		3 (20 %)	14 (25 %)	
Exogenous gangliosides therapy	7 (9.3 %)	11 (3.1 %)		5 (10.9 %)	8 (5.2 %)		0 (0 %)	1 (1.8 %)	
Other	2 (2.7 %)	13 (3.6 %)		3 (6.5 %)	9 (5.9 %)		4 (26.7 %)	12 (21.4 %)	
Time from onset to admission (days)			<0.001*			<0.001*			0.001*
≤3	39 (52.0 %)	69 (19.2 %)		20 (43.5 %)	18 (11.8 %)		7 (46.7 %)	5 (8.9 %)	
4-7	22 (29.3 %)	139 (38.7 %)		14 (30.4 %)	53 (34.6 %)		4 (26.7 %)	18 (32.1 %)	
>7	14 (18.7 %)	151 (42.1 %)		12 (26.1 %)	82 (53.6 %)		4 (26.7 %)	33 (58.9 %)	
Facial weakness			0.002*			0.001*			0.048*
Yes	30 (40 %)	81 (22.6 %)		22 (47.8 %)	36 (23.5 %)		7 (46.7 %)	10 (17.9 %)	
No	45 (60 %)	278 (77.4 %)		24 (52.2 %)	117 (76.5 %)		8 (53.3 %)	46 (82.1 %)	
Bulbar palsy			<0.001*			<0.001*			0.010*
Yes	41 (54.7 %)	69 (19.2 %)		32 (69.6 %)	27 (17.6 %)		7 (46.7 %)	7 (12.5 %)	
No	34 (45.3 %)	290 (80.8 %)		14 (30.4 %)	126 (82.4 %)		8 (53.3 %)	49 (87.5 %)	
Facial and/or bulbar weakness			<0.001*			<0.001*			0.024*
Yes	55 (73.3 %)	116 (32.3 %)		35 (76.1 %)	41 (26.8 %)		9 (60 %)	14 (25 %)	
No	20 (26.7 %)	243 (67.7 %)		11 (23.9 %)	112 (73.2 %)		6 (40 %)	42 (75 %)	
Autonomic dysfunction			<0.001*			<0.001*			0.049*
Yes	24 (32 %)	48 (13.4 %)		26 (56.5 %)	15 (9.8 %)		4 (26.7 %)	3 (5.4 %)	
No	51 (68 %)	311 (86.6 %)		20 (43.5 %)	138 (90.2 %)		11 (73.3 %)	53 (94.6 %)	
Tendon reflex at admission			0.169			0.640			0.152
Normal	1 (1.3 %)	4 (1.1 %)		1 (2.2 %)	8 (5.2 %)		1 (6.7 %)	7 (12.5 %)	
Reduced	19 (25.3 %)	131 (36.5 %)		11 (23.9 %)	35 (22.9 %)		1 (6.7 %)	14 (25 %)	
Absent	55 (73.7 %)	224 (62.4 %)		34 (73.9 %)	110 (71.9 %)		13 (86.7 %)	35 (62.5 %)	
MRC sum score at admission			<0.001*			<0.001*			<0.001*
0-20	27 (36 %)	33 (9.2 %)		28 (60.9 %)	6 (3.9 %)		9 (60 %)	3 (5.4 %)	
21-30	18 (24 %)	39 (10.9 %)		7 (15.2 %)	8 (5.2 %)		2 (13.3 %)	5 (8.9 %)	
31-40	13 (17.3 %)	56 (15.6 %)		5 (10.9 %)	20 (13.1 %)		2 (13.3 %)	8 (14.3 %)	

(*continued on next page*)

Table 1 (*continued*)

Variables	Training set (N = 434)			Validation set (N = 199)			Testing set (N = 71)		
	MV N = 75	Non-MV N = 359	*P*	MV N = 46	Non-MV N = 153	*P*	MV N = 15	Non-MV N = 56	*P*
41-50	11 (14.7 %)	112 (31.2 %)		5 (10.9 %)	59 (38.6 %)		1 (6.7 %)	15 (26.8 %)	
51-60	6 (8.0 %)	119 (33.1 %)		1 (2.2 %)	60 (39.2 %)		1 (6.7 %)	25 (44.6 %)	
NLR			<0.001*			<0.001*			<0.001*
< 4.11	19 (25.3 %)	285 (79.4 %)		10 (21.7 %)	131 (85.6 %)		3 (20 %)	42 (75 %)	
≥4.11	56 (74.7 %)	74 (20.6 %)		36 (78.3 %)	22 (14.4 %)		12 (80 %)	14 (25 %)	
PLR			<0.001*			<0.001*			<0.001*
< 163.2	28 (37.3 %)	277 (77.2 %)		14 (30.4 %)	109 (71.2 %)		3 (20 %)	38 (67.9 %)	
≥163.2	47 (62.7 %)	82 (22.83 %)		32 (69.6 %)	44 (22.8 %)		12 (80 %)	18 (32.1 %)	

Data are presented as n (%) or median (IQR) unless stated otherwise. * Significant difference.
Other antecedent events: vaccination, surgery, biological drugs, and malignancy.
Abbreviations: GBS, Guillain-Barré syndrome; MV, mechanical ventilation; IQR, interquartile range; MRC, Medical Research Council; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-lymphocyte ratio.

2.3. Evaluation and grouping criteria of potential predictors

Time from onset to admission, MRC sum score at admission, NLR, and PLR were categorized to facilitate the applicability in clinical practice (Table 1). The optimal cutoff values of the NLR and PLR for patients with GBS were calculated via receiver operating characteristic (ROC) curves.

2.4. Criteria for MV

The decision of MV was based on the existence of one major criterion or two minor criteria [7]. Main criteria: 1) Unbearable respiratory distress; 2) $PaCO_2$ greater than 6.4 kPa; 3) PaO_2 less than 7.5 kPa. Minor criteria: 1) Inefficient cough reflex; 2) Bronchial secretions still cannot be cleared after intensive chest physical therapy; 3) Severe dysfunction of the medulla oblongata, repeated cough, and aspiration after swallowing; 4) Atelectasis on a chest radiograph.

2.5. Variable selection

The LASSO regression algorithm was applied to the training set to determine which clinical parameters and biomarkers had non-zero coefficients while being cross-validated 10 times by the penalty parameter. LASSO, as a statistical analysis method for variable selection and model regularization, can select optimal variables and enhance prediction accuracy. The optimal predictors selected by the LASSO regression equation were used to develop a predictive model for assessing the risk of MV.

2.6. Development, validation, and testing of a nomogram

A clinical model based on multivariate logistic regression analysis of candidate predictors selected by LASSO was developed. The features were quantified as odds ratio (OR) with 95 % confidence interval (CI) and as *P*-value. In order to visually present the predictive model, a nomogram was then constructed to provide clinicians with a simple tool through the use of the selected covariates. We calculated the concordance index (C-index) of the ROC curve to evaluate the discrimination performance of the established model. Calibration and the clinical utility of the established model were assessed using a calibration curve, and DCA, respectively. Furthermore, we performed bootstrapping validation with 1000 bootstrap resamples to obtain a relatively corrected C-index. Also, the predictive capability of the model was then validated through an external validation set. Finally, we did the same analysis in a prospective testing set and further evaluated the performance of the model.

2.7. Validation of the EGRIS model

In order to evaluate the capacity of the EGRIS model to predict the risk of MV in Chinese patients with GBS, we established a multivariable logistic model by using variables of EGRIS in our training set and validated the performance of EGRIS in our external validation set and the prospective testing set. We assessed the discriminative ability, calibration, and clinical application of the EGRIS model through the C-index, calibration curve, and DCA, respectively. Importantly, given that the application value of the EGRIS model in Chinese patients with GBS is still unknown, we also compared the performance of our predictive model with that of the EGRIS model.

2.8. Statistical analysis

In the first part of our study, we performed univariate analysis to present the baseline characteristics between MV and non-MV patients with GBS and to ascertain the predictors related to the risk of MV. In the second part, we developed a predictive model by using optimal predictive variables selected by LASSO in the training set. The model was presented as a nomogram and validated in the external validation set and the prospective testing set. The performance of the model was evaluated by discriminative ability, calibration, and clinical application. Finally, we constructed a model by using three variables of EGRIS and performed the same analysis to compare the performance of the EGRIS model with the predictive model we developed.

Statistical analysis was performed using SPSS 24 (IBM, Armonk, NY, USA), and R software (Version 4.0.2; https://www.R-project.org). Categorical data were presented as proportions, while continuous data were presented as means and standard deviations or median and interquartile ranges depending on the distribution of the data. We compared two groups using the Student's t-test or Mann-Whitney *U* test for continuous variables and the Chi-square test for categorical variables. All statistical tests were two-sided and $P < 0.05$ was considered significant.

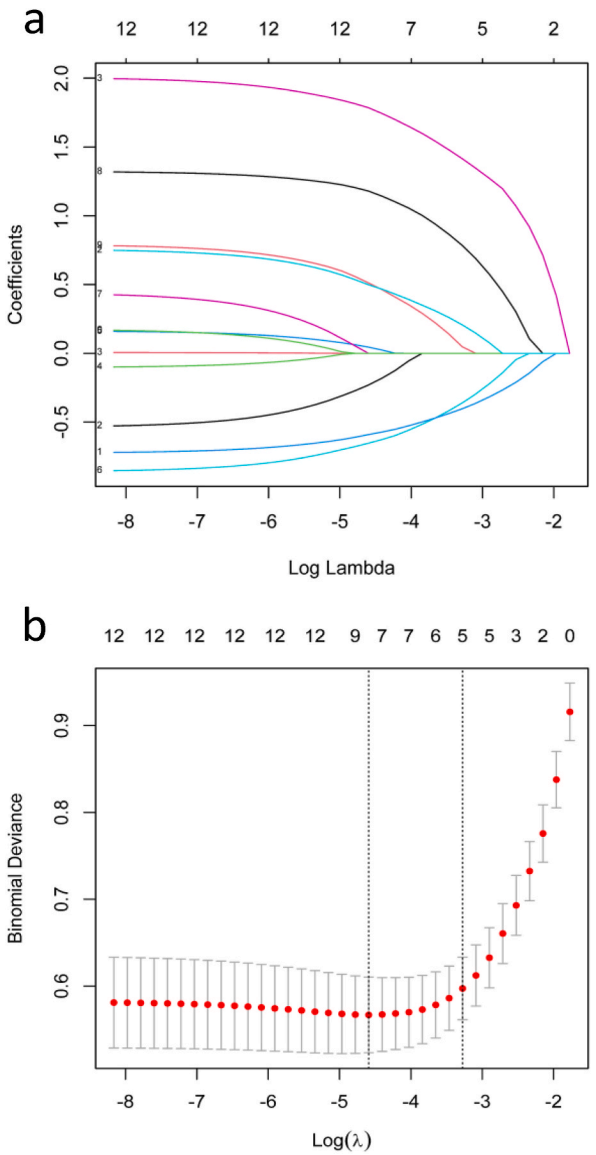

Fig. 1. LASSO regression model for feature selection. **a**: LASSO coefficient profiles of the 13 features. **b**: Optimal parameter (lambda) selection in the LASSO model used 10-fold cross-validation via minimum criteria. Vertical line was drawn at the value selected using 10-fold cross-validation, where optimal lambda resulted in five features with nonzero coefficients. Abbreviations: LASSO, least absolute shrinkage and selection operator.

3. Results

3.1. Baseline characteristics of patients

The baseline characteristics of 704 patients with GBS classified by the need for MV are summarized in Table 1. The optimal cut-off values of NLR and PLR to assess the risk of ventilation dependence were determined by ROC curves analysis in the training set. The cut-off values of NLR and PLR were 4.11 and 163.2, respectively, and the corresponding areas under the ROC curves were 0.770 (95 % CI 0.708–0.832) and 0.699 (95 % CI 0.630–0.768), respectively. Overall, Males had a slightly higher risk of GBS in our study, with a male-to-female ratio of about 1.4:1. Of the 704 patients with GBS, 19 % of patients (136 cases) developed respiratory failure requiring MV. The ratio of patients requiring MV was 17 % (75 cases) in the training set, 23 % (46 cases) in the validation set, and 21 % (15 cases) in the testing set. About 52 % of patients with GBS had antecedent symptoms of respiratory or gastrointestinal infection before the onset of the disease. Upper respiratory tract infection was more common than gastrointestinal infection (34 % vs. 18 %, respectively). Seasonal changes did not increase the hazard of ventilation dependence in patients with GBS. In univariable analysis, there were no statistically significant differences in gender, age, season of onset, antecedent events, and tendon reflex on arms and legs at admission between the MV group and the non-MV group ($P > 0.05$). Notably, variables significantly associated with the risk of MV in the training, validation, and testing sets were time from onset to admission, facial weakness, bulbar palsy, facial and/or bulbar weakness, autonomic dysfunction, MRC sum score at admission, NLR, and PLR (Table 1).

3.2. Development of a risk prediction nomogram for MV

Five optimal predictors associated with the risk of MV, including time from onset to admission, facial and/or bulbar weakness, MRC sum score at admission, NLR, and PLR, were selected by the LASSO regression model from the 13 variables identified in the training set (Fig. 1a and b). Based on the five predictors above, a multivariate logistic regression model to estimate the risk of MV was developed, which further indicated that time from onset to admission, facial and/or bulbar weakness, MRC sum score at admission, and NLR were the independent predicting risk factors of MV among GBS patients (Table 2). Besides, the predictive model was presented as the nomogram, a more intuitive and convenient manner (Fig. 2).

3.3. Performance of the nomogram in the training set

The performance of the nomogram was evaluated from two aspects: discrimination and calibration. The model exhibited satisfactory discriminative ability in the training set with a C-index of 0.914 (95 % CI 0.878–0.949) (Fig. 3). As shown in Fig. 4a, in the training set, the predicted probability of the risk of MV was largely close to the actual proportion of patients who required MV, indicating excellent calibration of the nomogram.

3.4. Validation of the predictive nomogram

3.4.1. Internal validation

To further assess the performance of the nomogram, we performed an internal validation using the bootstrap validation method in the training set, which achieved good discriminative ability with the corrected C-index of 0.903.

3.4.2. External validation

The nomogram was externally validated with 199 patients in the external validation set, which showed similar performance to that of the training set. The predictive nomogram yielded a high C-index of 0.953 (95 % CI 0.925–0.981), reflecting excellent discriminative ability in assessing the risk of MV among patients with GBS (Fig. 3). Similarly, the calibration curve of the predictive model exhibited favorable agreement between prediction and actual observation in the validation set (Fig. 4c).

3.5. Testing of the predictive nomogram

To further confirm the predictive value of our established model, we applied it to a prospective testing set of 71 patients with GBS.

Table 2
Multivariable logistic regression analysis to predict the risk of MV in GBS patients based on five predictors selected by LASSO.

Intercept and Variable	Coefficient	Odds Ratio (95%CI)	*P*-value
Intercept	−2.4706		0.003865*
Time from onset to admission	−0.8092	0.445 (0.282–0.702)	0.00505*
Facial and or bulbar paralysis	1.8064	6.089 (2.976–12.456)	7.54e-07*
MRC sum score at admission	−0.7782	0.459 (0.355–0.595)	3.81e-09*
NLR	1.9194	6.817 (3.083–15.073)	2.13e-06*
PLR	0.7493	2.116 (0.973–4.601)	0.058698

Abbreviations: MV, mechanical ventilation; GBS, Guillain-Barré syndrome; LASSO, least absolute shrinkage and selection operator; CI, confidence interval; MRC, Medical Research Council; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-lymphocyte ratio.

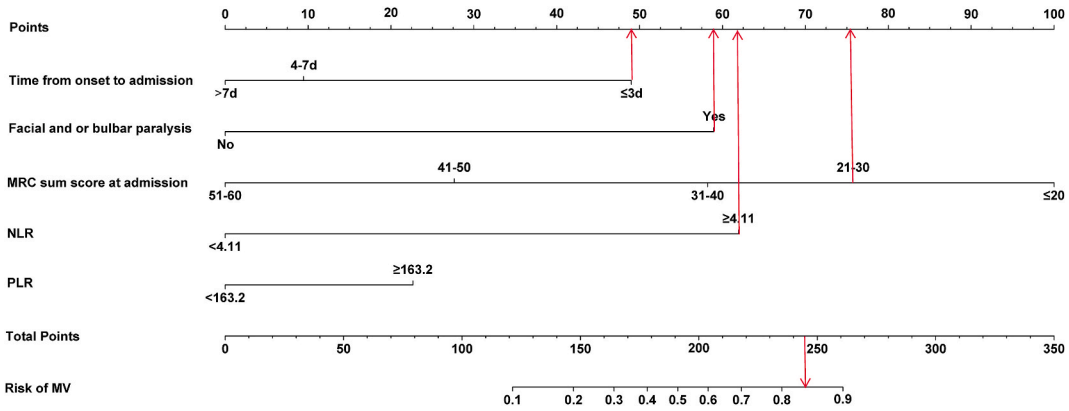

Fig. 2. Nomogram for predicting the risk of MV in patients with GBS. The nomogram was generated to depict the potential predictive ability of the model for each patient in the training set, incorporating time from onset to admission, facial and/or bulbar paralysis, MRC sum score at admission, NLR, and PLR. For example, a patient admitted to hospital 2 days after symptoms onset (49 points), with facial and/or bulbar paralysis (59 points), with MRC sum score at admission 25 (75 points), with NLR >4.11 (62 points) and PLR <163.2 (0 points), had a total points of 245, corresponding to MV probability of 84 %. Abbreviations: MV, mechanical ventilation; GBS, Guillain-Barré syndrome; MRC, Medical Research Council; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-lymphocyte ratio.

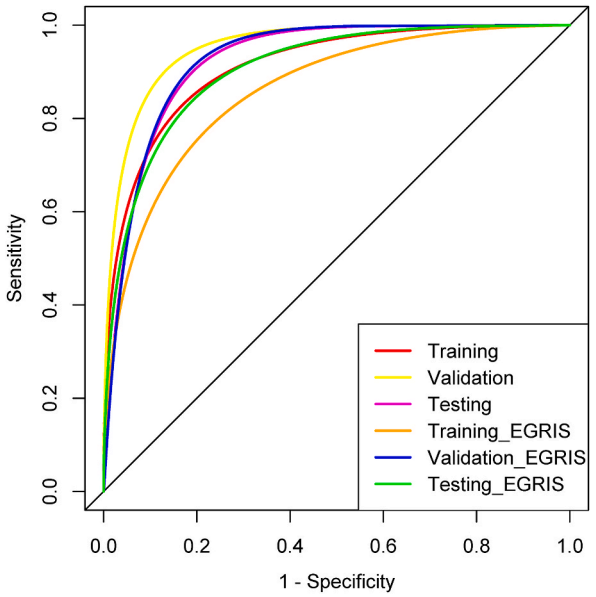

Fig. 3. ROC curve analysis of our nomogram and the EGRIS model predicting the risk of MV in the training, validation, and testing sets. ROC curves of our nomogram showed AUCs of 0.914 (95 % CI 0.878–0.949) in the training set (Red curve), 0.953 (95 % CI 0.925–0.981) in the validation set (Yellow curve), and 0.929 (95 % CI: 0.8647–0.9936) in the testing set (Magenta curve). Besides, ROC curves of the EGRIS model showed AUCs of 0.860 (95 % CI 0.816–0.905) in the training set (Orange curve), 0.929 (95 % CI 0.895–0.963) in the validation set (Blue curve), and 0.902 (95 % CI: 0.7828–1) in the testing set (Green curve). Abbreviations: ROC, receiver operating characteristic; EGRIS, Erasmus GBS respiratory insufficiency score; MV, mechanical ventilation; AUC, area under the ROC curve; CI, confidence interval. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

The C-index of the testing set (0.929, 95 % CI 0.8647–0.9936) was slightly higher than that of the training set (0.914, 95 % CI 0.878–0.949), demonstrating better discriminative ability (Fig. 3). The calibration curve of the testing set depicted that the predicted probability of the risk of MV was generally close to the observed frequency of actual need for MV (Fig. 4e). Overall, the performance of our predictive nomogram in the testing set was comparable to that in the training set and the validation set.

3.6. Clinical utility of the predictive nomogram

The DCAs of the predictive nomogram in the training, validation, and testing sets were shown in Fig. 5 (a, c, e). Apparently, the

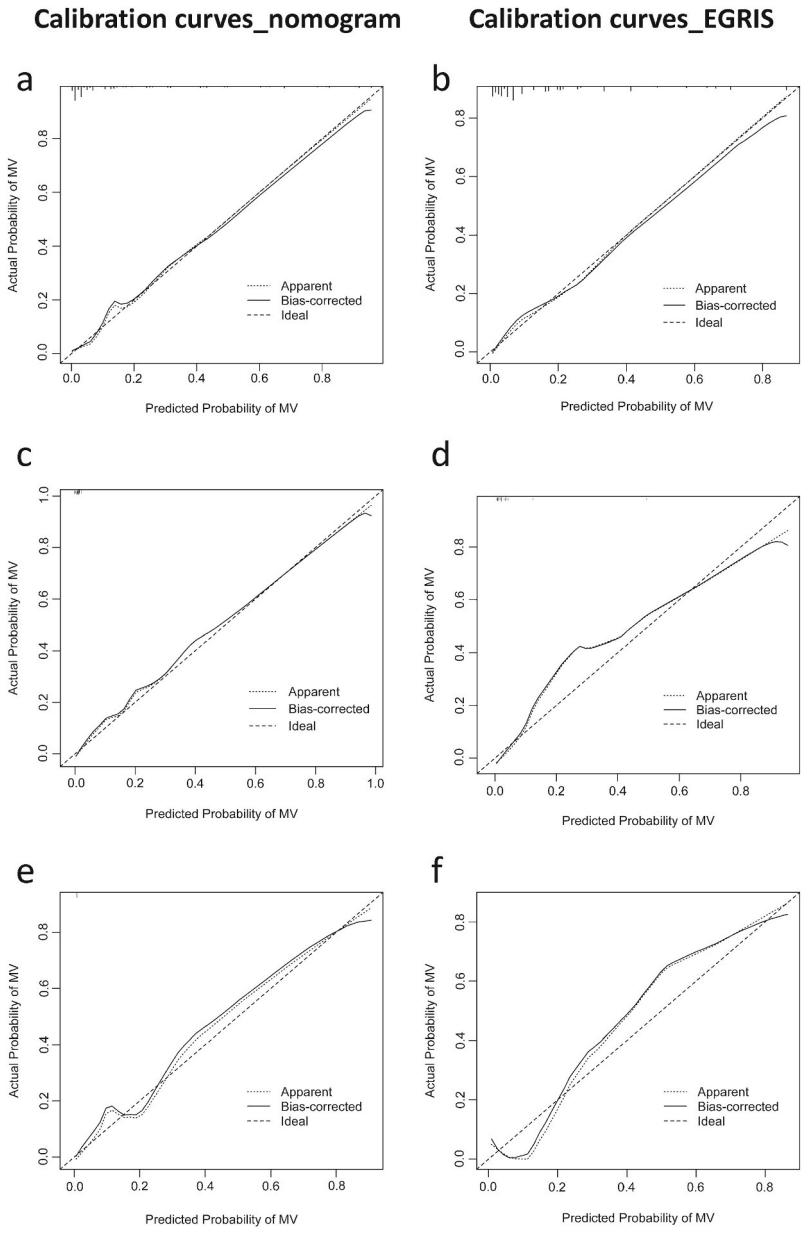

Fig. 4. Calibration plots of our nomogram and the EGRIS model predicting the risk of MV in the training **(a, b)**, validation **(c, d)**, and testing sets **(e, f)**. X-axes represent the predicted MV risk probability. Y-axes represent the actual MV probability. The 45-degree diagonal line represents a perfect prediction. Solid line represents the performance of the present nomogram or the EGRIS model. Abbreviations: EGRIS, Erasmus GBS respiratory insufficiency score; MV, mechanical ventilation.

DCAs demonstrated that using this nomogram to predict the risk of MV in patients with GBS could add more benefit than treat-all or treat-none strategies, which indicated that the nomogram had significant clinical application value.

3.7. EGRIS model validation

Based on three variables of the EGRIS model, we constructed a multivariate logistic regression model in our training set (Table 3). The model displayed strong discriminative ability with C-index of 0.860 (95%CI: 0.816–0.905), 0.929 (95%CI: 0.895–0.963), and 0.902 (95%CI: 0.7828–1) in the training, validation, and testing sets, respectively (Fig. 3). By comparison, the C-index of the EGRIS model was slightly lower than that of the nomogram we developed. The calibration curves of the EGRIS model showed great fit in the training set, whereas it exhibited poorly fitting performance in the validation and testing sets (Fig. 4b, d, and f). The DCAs of the EGRIS model were comparable to that of the nomogram we developed (Fig. 5b, d, and f). Therefore, compared with the EGRIS model, the

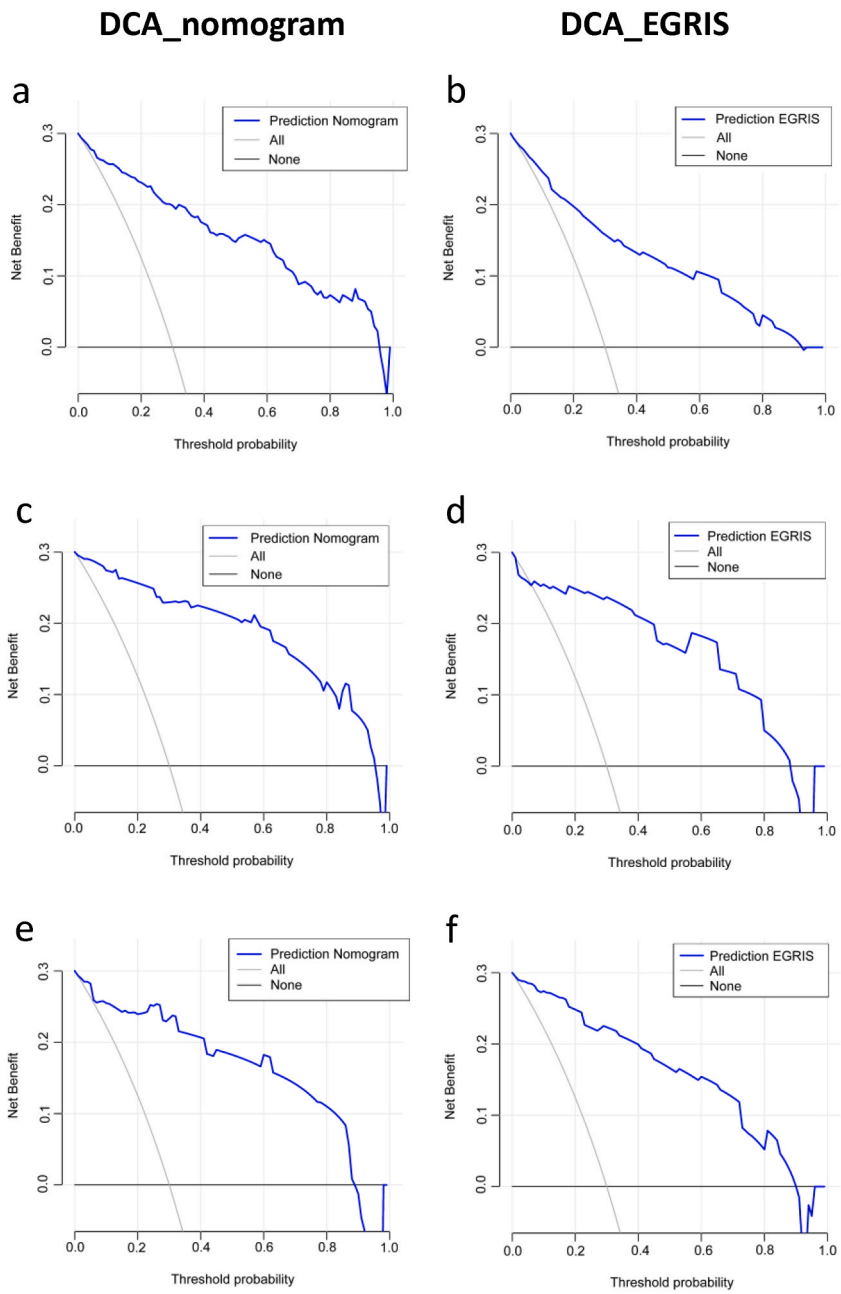

Fig. 5. The DCA for our nomogram and the EGRIS model predicting the risk of MV in the training **(a, b)**, validation **(c, d)**, and testing sets **(e, f)**. The x-axis represents the threshold probability. The y-axis measures the net benefit. The grey line depicts the net benefit of the strategy that all patients accept the treatment of MV. The black line represents the assumption that no patients accept the treatment of MV. The blue line represents the nomogram for predicting the risk of MV. The DCAs showed using our nomogram or the EGRIS model to predict the risk of MV could benefit patients with GBS more. Abbreviations: DCA, decision curve analysis; EGRIS, Erasmus GBS respiratory insufficiency score; MV, mechanical ventilation; GBS, Guillain-Barré syndrome. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

predictive model we built had better discriminative ability and higher prediction accuracy in both the validation and testing sets.

4. Discussion

Respiratory failure is the leading hazard factor of mortality in patients with GBS [22]. Early prediction of respiratory failure and MV can improve the prognosis of patients with GBS. Our previous retrospective study revealed that shorter intervals between onset of GBS and admission, facial weakness, bulbar paralysis, and lower MRC sum score at nadir were independent predictors of the risk of MV in

Table 3
Multivariable logistic regression model based on three variables of EGRIS.

Intercept and Variable	Coefficient	Odds Ratio (95%CI)	*P*-value
Intercept	1.3992		0.0107*
Time from onset to admission	−0.8258	0.438 (0.294–0.652)	4.82e-05*
Facial and/or bulbar paralysis	1.8729	6.507 (3.452–12.265)	6.98e-09*
MRC sum score at admission	−0.7693	0.463 (0.370–0.581)	2.51e-11*

Abbreviations: EGRIS, Erasmus GBS respiratory insufficiency score; CI, confidence interval; MRC, Medical Research Council.

patients with GBS [10]. Different from the previous study, we herein focused more on integrating optimal and early available predictors into a predictive model, and represented the model in a visual form, so as to help clinicians assess the risk of MV in patients with GBS in the early phase of the disease.

In our study, approximately 19 % of patients with GBS developed respiratory insufficiency requiring MV, which is consistent with the proportion of ventilatory dependence reported in the International GBS Outcome Study (IGOS) cohort [23]. Herein, we found shorter intervals between disease onset and admission, the presence of facial and/or bulbar weakness, autonomic dysfunction, lower MRC sum score at admission, elevated NLR, and increased PLR were associated with the risk of MV in patients with GBS. In order to facilitate clinical application, we developed and validated a novel predictive model using five easily available variables selected by the LASSO regression model, which could reliably estimate the probability of GBS patients relying on MV at admission. Multivariate analysis showed that several variables including shorter intervals between symptom onset and admission, the presence of facial and/or bulbar weakness, lower MRC sum score at admission, and elevated NLR were independent predictors of the risk of MV in patients with GBS. The model was presented as a nomogram, which was an easy-to-use tool for clinicians to assess the possibility of ventilatory dependence among patients with GBS. Of note, the model displayed excellent performance with favorable discriminative ability and calibration as well as high clinical application value.

Similar to previous findings, covariates such as shorter intervals from symptoms onset to admission, the presence of facial and/or bulbar weakness, and lower MRC sum score at admission have been confirmed to be related to the risk of MV [4,5,8–11,24]. Notably, our model incorporated new, inexpensive, and easily available blood tests in routine hospital examinations, such as NLR and PLR. NLR and PLR are simple and cost-effective peripheral biomarkers available in routine blood count analysis, which are considered to be closely associated with GBS severity and the risk of MV at admission [11,25,26]. Luo et al. [27] found that NLR may be a useful marker for predicting weaning failure in GBS patients, especially NLR >11 should be carefully considered, which indicated that GBS patients with elevated NLR were more likely to develop ventilator dependence. In our study, we selected optimal variables of NLR and PLR by using LASSO and constructed a novel predictive model, which enabled clinicians to more objectively assess the risk of MV in patients with GBS at admission.

Unlike previous studies, we excluded several variables like vital capacity (VC), electrophysiological results, and CSF anti-GQ1b antibody, mainly due to the limited statistical data on these predictors. Also, the test of VC is volitional which requires patients' cooperation and is hence relatively insensitive, so it is not suitable for critical patients with GBS. Moreover, both electrophysiological and CSF tests are routinely performed about 2 weeks after the onset of GBS, making it difficult for us to obtain complete electrophysiological and CSF results at admission. Similarly, we also excluded several variables that have been proved to correlate with ventilation dependence, such as fasting blood glucose, serum albumin, and C-reactive protein. On the one hand, considering that these variables are non-urgent examination items at admission, the examination results cannot be obtained early. On the other hand, the larger the number of predictors included in the model, the more challenging the nomogram is to interpret [28]. Accordingly, the inclusion of the above three covariables would increase the complexity of the model to some extent. Herein, the variables inclusion of our model follows the principle of less variable inclusion, convenient calculation, and early availability, so as to promote the popularization of the model.

Several clinical predictive models for evaluating the risk of MV have been reported over the past 20 years. Remarkably, the EGRIS model incorporating variables of MRC sum score at admission, the interval from symptom onset to admission, and the presence of facial and/or bulbar paralysis has been widely validated in the Netherlands, Japan, Peru, and Malaysia [8,15–17]. Recently, the EGRIS model was validated in the IGOS cohort, showing satisfactory performance and application value in GBS patients from Europe, North America, and Asia [29]. Nevertheless, it is unclear whether the EGRIS model is applicable to Chinese patients with GBS. Hence, we also built a model with the variables in EGRIS and evaluated the performance of EGRIS using GBS patients from the external validation and testing sets. We found the model based on three variables of EGRIS exhibited high discriminative ability in both validation and testing sets, whereas it displayed moderate discriminative ability in the training set. Besides, the EGRIS model showed favorable calibration in the training set, but it showed poor calibration performance in the validation and testing sets. Compared with the EGRIS model, the model we developed displayed better discriminative ability and calibration. Therefore, the model we developed may be more suitable for assessing the risk of MV in Chinese patients with GBS. Notably, our model added variables NLR and PLR, which further demonstrated the predictive value of NLR and PLR in the risk assessment of MV. Herein, given the regional variation in the GBS subtype, the generalization of EGRIS model to other regions is uncertain. Prospective studies in more diverse populations of patients with GBS are required to determine the general validity of the EGRIS model for evaluating the risk of MV.

Our study has some strengths. Firstly, our model integrated several routine blood parameters available at admission, which not only increased the objectivity of the model in predicting the risk of MV, but also improved the predictive ability of the model as evidenced by comparison to the EGRIS model. Secondly, we presented the model as a nomogram-a relatively straightforward form with a clear

digital interface. The nomogram allows for individualized and evidence-based risk estimation, facilitating better treatment stratification and individualized management. Finally, in addition to validation in an external validation set, our model was validated in a prospective testing set to further identify the predictive value of the model. As expected, the predictive model displayed satisfactory performance which favors clinical application.

Our study bears some limitations. Firstly, although the addition of routine blood parameters NLR and PLR improved the predictive ability of the model we developed, the inclusion of more variables also increased the complexity and computation burden of the model. Additionally, several studies have indicated a correlation between specific GBS subtypes and the likelihood of requiring MV, such as the Miller-Fisher variant or acute motor axonal neuropathy, may carry a higher risk of respiratory failure necessitating mechanical ventilation compared to other GBS subtypes [7,12,30,31]. The subtypes of GBS vary geographically, axonal GBS is more common in Asia in comparison to Europe and the United States [23,32]. The present model was developed and validated predominantly in Northern China cohorts, raising concerns about its generalizability to other regions and populations. Prospective studies in more diverse populations of patients with GBS are required to determine the general validity of the predictive model for evaluating the risk of MV. Moreover, the model did not account for other factors that might influence the requirement for MV, such as comorbidities, incorporating additional clinical information and refining the model could further enhance its predictive accuracy and applicability in diverse patient populations.

5. Conclusions

We developed a model based on five variables selected by LASSO and assessed its predictive ability in an external validation set and a prospective testing set to predict the risk probability of MV in patients with GBS at admission. The model was presented as a nomogram-a straightforward and reliable complementary decision-making tool. We featured that NLR and PLR were important predictors of risk of MV in patients with GBS, which were simple, inexpensive, and readily available at admission. Notably, compared with the model based on the three variables of EGRIS, our model showed better discriminative ability and predictive accuracy in Chinese patients with GBS. Notwithstanding, this model, derived from a single center sample in China, should be further evaluated in larger independent populations.

Abbreviations: GBS, Guillain-Barré syndrome; MV, mechanical ventilation; LASSO, least absolute shrinkage and selection operator; C-index, concordance index; DCA, decision curve analysis; MRC, Medical Research Council; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-lymphocyte ratio; EGRIS, Erasmus GBS respiratory insufficiency score; ROC, receiver operating characteristic; OR, odds ratio; CI, confidence interval; AUCs, area under the ROC curves; VC, vital capacity; SBC, single breath count; CSF, cerebrospinal fluid; IGOS, International GBS Outcome Study.

Declarations

Hong-Liang Zhang is affiliated with the National Natural Science Foundation of China. The views expressed are his own and do not necessarily represent the views of the National Natural Science Foundation of China or the Chinese government.

Ethics declarations

This study approved by the institutional ethics committee of the First hospital of Jilin University, with the approval number **(AF-IRB-032–04).** The committee waived the requirement for informed consent because the data were analyzed anonymously.

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None.

Data availability statement

Data will be made available upon reasonable request.

CRediT authorship contribution statement

Yanna Song: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis. **Shan Liu:** Writing – review & editing, Methodology. **Wei Qiu:** Methodology, Investigation. **Kangding Liu:** Validation, Supervision, Data curation. **Hong-Liang Zhang:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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