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Factors influencing short-term and long-term survival rates in stroke patients receiving enteral nutrition: a machine learning approach using MIMIC-IV database

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Abstract

Purpose This study aims to evaluate the survival and mortality rates of stroke patients after receiving enteral nutrition, and to explore factors influencing long-term survival. With an aging society, nutritional management of stroke patients has become a focus of clinical attention.

Methods This study is based on the MIMIC-IV database, which contains patient data from healthcare institutions in the United States. We included 81 stroke patients who received enteral nutrition, encompassing various subtypes of stroke, specifically subarachnoid hemorrhage, cerebral infarction, and intracerebral hemorrhage. The exposure variable was the type of enteral nutrition, while the outcome variables were survival rates at 30 days, 1 year, and 3 years. Covariates included age, sex, Charlson Comorbidity Index, and minimum blood glucose levels. We employed Kaplan-Meier survival analysis and machine learning models to assess survival rates and their influencing factors.

Results Results showed a 30-day survival rate of 66.67%, indicating 27 patient deaths within the initial 30 days. The 1-year survival rate decreased to 45.68%, with a cumulative death count of 44 during the follow-up period. The 3-year survival rate was 43.21%, with a total of 46 deaths. Kaplan-Meier survival analysis indicated that low-risk group patients had significantly higher survival rates than the high-risk group ($p = 0.0229$), with higher survival probability in the first 600 days, while the high-risk group showed a significant decline at 400 days. Machine learning model evaluation showed that the XGBoost model had a C-index of 0.80 in predicting survival time, with the Charlson Comorbidity Index being the most important predictor (F score = 12.0). Additionally, factors such as lowest blood glucose, age, and hospital mortality flag significantly influenced survival time.

Conclusion This study highlights the role of early intervention and nutritional management in improving stroke patient outcomes. Our findings suggest that the Charlson Comorbidity Index, age, and in-hospital mortality markers are major predictors of post-stroke survival. These findings underscore the necessity for personalised nutritional strategies, and they call for validation through prospective multicentre studies.

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Keywords Stroke, Enteral nutrition, Survival rate, Charlson comorbidity index, Machine learning

Introduction

Stroke is one of the leading causes of death and disability worldwide, placing a significant burden on public health and healthcare systems. According to the Global Burden of Disease Study, there were approximately 12.8 million new stroke cases globally in 2019, resulting in around 6.2 million deaths [1]. In China, the situation is equally severe. A study by Wang Wei et al. reported that in 2018, the age-standardized incidence rate of stroke in China was 246.8 per 100,000, with a mortality rate of 149.5 per 100,000 [2]. Regarding stroke patient survival rates, a large-scale study based on the China National Stroke Registry reported that the 30-day, 1-year, and 3-year survival rates for ischemic stroke patients were 94.0%, 81.7%, and 71.2%, respectively, while for hemorrhagic stroke patients, the corresponding survival rates were 81.9%, 65.1%, and 57.5% [3]. These statistics highlight the urgency of improving stroke patient outcomes.

Enteral nutrition is an essential means of providing nutritional support for patients who are unable to eat orally, playing a critical role in the treatment of stroke patients. It involves delivering nutrient solutions directly to the gastrointestinal tract via a nasogastric or gastrostomy tube and can be categorized into standard and specialized formulas [4]. Standard formulas typically contain balanced macronutrients and micronutrients, while specialized formulas are tailored to specific diseases or metabolic states, such as those enriched with omega-3 fatty acids or glutamine [5]. Early and appropriate enteral nutrition not only improves patients' nutritional status but also promotes gastrointestinal function recovery, reduces complications, and shortens hospital stays [6]. Research suggests that enteral nutrition may reduce the risk of infections and improve neurological recovery in stroke patients [7]. However, there is still debate within the academic community regarding the long-term effects of different types of enteral nutrition on stroke patient outcomes. A meta-analysis indicated that low-dose n-3 PUFAs could reduce total cholesterol and triglyceride levels, while also lowering cerebrovascular disease-related mortality [8], but other studies have found no significant differences between standard and specialized formulas in improving patient outcomes [9].

Given the limitations and inconsistencies in existing evidence, further investigation is necessary to explore the relationship between enteral nutrition and stroke patient outcomes. Most current studies focus on short-term outcomes and in-hospital complications, with a lack of systematic assessment of long-term survival rates. Furthermore, many studies have small sample sizes, making it difficult to conduct subgroup analyses and explore potential interactions. Therefore, utilizing large medical databases for retrospective analysis, combined with advanced statistical methods and machine learning techniques, may offer new perspectives in addressing these issues.

This study aims to assess the impact of standard and specialized enteral nutrition on the 30-day, 1-year, and 3-year survival and mortality rates of 81 stroke patients using the MIMIC-IV intensive care database through a retrospective cohort study. This study design has several advantages: first, the MIMIC-IV database contains detailed clinical information and long-term follow-up data, providing a more comprehensive prognosis assessment; second, the application of machine learning models allows us to explore the complex effects of multiple factors on prognosis, offering new ideas for personalized prediction; finally, the retrospective study design enables the acquisition of long-term outcome data in a relatively short period, providing timely references for clinical decision-making.

This study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [10] and aims to provide high-quality evidence for the nutritional management of stroke patients. We hope that this study will not only fill the gaps in current research but also offer references for developing personalized nutrition plans and improving long-term outcomes for patients. Moreover, the application of machine learning models may open new pathways for predicting stroke patient outcomes, promoting the development of precision medicine in this field. Ultimately, we hope the results of this study will contribute to advancements in the field of nutritional support for stroke patients, improving patient quality of life and reducing the burden of the disease.

Methods

Data source

This study is based on data from the MIMIC-IV database, which contains records of patients treated in the intensive care units (ICUs) at Beth Israel Deaconess Medical Center (BIDMC) in Boston, USA, from 2008 to 2019 [11]. This study is a retrospective case-control study. The study included 81 patients with stroke or subarachnoid hemorrhage (SAH), all of whom received enteral nutrition during their hospital stay. The MIMIC database provides detailed clinical data, including patient demographics, medical history, laboratory tests, and treatment information. The enteral nutrition used in this study is divided into two types: standard nutrition and specialized nutrition. Standard nutrition includes general nutritional

support formulas designed to meet the basic nutritional needs of most patients, while specialized nutrition includes formulas tailored for specific diseases and high-calorie, high-protein formulas to meet the clinical needs of particular patients. Enteral nutrition was initiated within 48 h of patient admission to ensure timely fulfillment of the patients' nutritional requirements.

Inclusion and exclusion criteria

Inclusion criteria

1. Adult patients aged ≥ 18 years.
2. Clinically diagnosed with stroke (including ischemic and hemorrhagic stroke) or subarachnoid hemorrhage (SAH).
3. Received enteral nutrition, with relevant nutritional information recorded.
4. ICU stay of ≥ 24 h to ensure sufficient time for treatment and monitoring.
5. Complete mortality outcome data, including 30-day, 1-year, and 3-year mortality.

Exclusion criteria

1. Patients with missing or incomplete key clinical data.
2. Patients who did not receive enteral nutrition or for whom the nutritional method was unclear.
3. Patients who died or were discharged within 24 h of admission.

Study variables and feature selection

To assess the impact of enteral nutrition on the prognosis of stroke and subarachnoid hemorrhage patients, several clinical variables and laboratory indicators were selected. All laboratory data and vital signs are based on the first test results obtained within 24 h of patient admission. These variables encompass the patient's baseline characteristics, severity of illness, and metabolic indicators to build a comprehensive predictive model. The selected variables include:

Demographic characteristics

1. Age.
2. Gender.
3. Categorized Race.

Medical history and scores

1. Charlson Comorbidity Index.
2. Sequential Organ Failure Assessment (SOFA) score: reflecting organ dysfunction severity.
3. AIDS score: an ICU-specific score assessing immune function.

Vital signs

1. Heart rate: minimum, maximum, and mean.
2. Blood pressure (systolic, diastolic, and mean arterial pressure): minimum, maximum, and mean.
3. Respiratory rate, temperature, oxygen saturation (SpO2): minimum, maximum, and mean.

Laboratory results

1. Hemoglobin, platelets, white blood cells, anion gap, bicarbonate, blood urea nitrogen (BUN), calcium, chloride, creatinine, glucose, sodium, potassium: minimum and maximum values for each.
2. Coagulation parameters: International Normalized Ratio (INR), prothrombin time (PT), partial thromboplastin time (PTT).

Weight-related variables

1. Weight at admission.
2. Minimum and maximum weight during hospitalization.

These variables were chosen to reflect the patient's overall condition, organ function, and metabolic status, providing comprehensive data for model training and survival analysis.

Data preprocessing

Before analysis, the raw data underwent several cleaning and preprocessing steps:

1. **Handling Missing Values**: Missing values were filled using the median to ensure data completeness and avoid model instability.
2. **Standardization**: To eliminate the effect of different scales among variables, all continuous variables were standardized using the StandardScaler method, ensuring that each variable contributed equally in the analysis.
3. **Outcome Variables**: The study's primary outcomes were 30-day, 1-year, and 3-year mortality. Each patient's mortality status was clearly recorded in the database, ensuring accurate outcome data.

Model construction and evaluation

Classification models To predict 30-day, 1-year, and 3-year mortality, three machine learning classification models were employed.

1. **Logistic Regression**: Used for linear classification problems.

2. **Random Forest Classifier**: Suitable for handling nonlinear and high-dimensional data, making it ideal for complex medical datasets.
3. **XGBoost Classifier**: A gradient-boosted tree algorithm capable of handling missing data and high-dimensional features.

The dataset was split into training and test sets with an 80:20 ratio. Data were randomly divided using the train_test_split function, and the standardized data were used for model training. Model performance was evaluated using the following metrics:

- **Accuracy**
- **ROC curve**
- **Area under the curve (AUC)**

Survival analysis model To analyze survival time, an XGBoost Cox proportional hazards model was used. Survival time was defined as the number of days from admission to death, and the event status indicated whether death occurred. The survival model was evaluated using the **concordance index (C-index)**, which measures predictive accuracy.

Group survival analysis and Kaplan-Meier curves

To assess the impact of different types of nutrition (standard nutrition and specialized nutrition) on patient survival, Kaplan-Meier survival curves were used for grouped comparisons. Log-rank tests were performed to assess the statistical significance of survival differences between groups. The Kaplan-Meier curves were fitted using the KaplanMeierFitter, and group differences were tested using the logrank_test function.

Feature importance analysis

To explore which clinical variables had the greatest impact on patient prognosis, feature importance analysis was conducted using the XGBoost model [12]. The plot_importance function was used to visualize the top 15 most important features influencing mortality risk. This analysis helped identify the key variables associated with patient outcomes, providing insights for clinical decision-making.

Results

Patient characteristics overview

This study screened 930 patients from the MIMIC database who were admitted to the ICU for the first time and received enteral nutrition, excluding those with subsequent admissions, cases with unclear nutritional components, and patients receiving parenteral nutrition. Among these patients, a final selection of 81 stroke patients was made, including those with ischemic stroke, hemorrhagic stroke, and subarachnoid hemorrhage. To ensure the accuracy and representativeness of the study population, cases with abnormal data, contraindications, and missing data (such as lack of complications, critical clinical features, laboratory tests, and prognostic data) were further excluded. Through these stringent selection criteria, this study aims to provide more reliable clinical data on enteral nutrition in stroke patients. (Supplementary Document - Flowchart)

This study included 81 stroke patients, all of whom received enteral nutrition from the MIMIC-IV database, with a mean age of 70.58 ± 13.46 years. Among these patients, 42 (51.9%) were female, and 39 (48.1%) were male. In terms of racial composition, 38 patients were White (46.9%), 22 were non-White (27.2%), and the race of 21 patients was unknown (25.9%). During hospitalization, a total of 24 patients died, resulting in a mortality rate of 29.6%. The average Charlson Comorbidity Index for the patients was 7.04 ± 2.82, indicating a high prevalence of multiple comorbidities among the patients. Regarding weight, the average weight of the patients was 65.43 ± 39.12 kg, reflecting significant variability in patient weight. Additionally, the incidence of hyperlipidemia among the patients was 58.0% (47 patients), hypertension was 24.7% (20 patients), diabetes was 56.8% (46 patients), and the prevalence of malnutrition reached as high as 86.4% (70 patients). (Table 1)

The Sequential Organ Failure Assessment (SOFA) score averaged 6.49 ± 4.07, suggesting moderate organ dysfunction. Laboratory findings revealed an average minimum hemoglobin value of 10.21 ± 2.81 g/dL and a maximum value of 11.62 ± 2.62 g/dL, suggesting possible mild anemia. The average minimum white blood cell count was 10.06 ± 5.19 × 10^9/L, with a maximum of 13.41 ± 6.12 × 10^9/L, slightly above the normal range. Renal function indicators showed an average minimum blood urea nitrogen (BUN) of 25.49 ± 23.58 mg/dL and a maximum of 30.20 ± 25.03 mg/dL; the average minimum creatinine was 1.31 ± 1.16 mg/dL, and the maximum was 1.59 ± 1.35 mg/dL, indicating mild elevations. Blood glucose levels exhibited large fluctuations, with an average minimum of 128.19 ± 41.26 mg/dL and a maximum of 189.00 ± 134.02 mg/dL. Vital signs showed an average heart rate of 85.84 ± 14.19 beats per minute, average systolic blood pressure of 123.17 ± 20.77 mmHg, and average diastolic blood pressure of 65.02 ± 13.39 mmHg. The average respiratory rate was 19.90 ± 3.88 breaths per minute. The average body temperature was 36.71 ± 4.16 °C, with a maximum of 38.26 °C. The average oxygen saturation was 97.78 ± 1.82%, indicating good overall oxygenation (Table 2).

Table 1 Demographic data characteristics

	age	charlson_comorbidity_index	hospital_expire_flag	weight
count	81.00	81.00	81.00	81.00
mean	70.58	7.04	0.30	65.43
std	13.46	2.82	0.46	39.12
min	28.99	0.00	0.00	0.00
0.25	62.69	5.00	0.00	53.80
0.50	72.47	7.00	0.00	75.60
0.75	80.04	9.00	1.00	87.70
max	91.08	14.00	1.00	161.00
	Female, **Male**	**White**, **Non-White**, **Unknown**	**Death**, **Survive**	**No**, **Yes**
Gender	42,39			
Race		38,22,21		
Hospital Expire			24,57	
Hyperlipidemia				47,34
Hypertensive				20,61
Diabetes				46,35
Malnutrition				70,11

Overall survival analysis

We conducted an analysis of patient survival at 30 days, 1 year, and 3 years. The results indicated that the 30-day survival rate was 66.67%, which means that 27 patients died within the first 30 days. By 1 year, the survival rate had decreased to 45.68%, with a cumulative death toll of 44 patients. At 3 years, the survival rate was 43.21%, with a total of 46 deaths (Table 3).

These data reveal a temporal pattern of mortality risk. The first 30 days represent the period of highest risk, during which approximately one-third of patients died. Between 30 days and 1 year, there were 17 new deaths, resulting in a mortality rate of 20.9%. In contrast, from 1 year to 3 years, only 2 new deaths occurred, leading to a mortality rate of 2.4%. This indicates that the mortality rate actually declines over time. This pattern suggests that early intervention and treatment may be crucial for improving patient outcomes, particularly during the first 30 days and the subsequent 11 months. Additionally, patients who survive beyond 1 year exhibit a relatively optimistic long-term prognosis, potentially reflecting stability or adaptation to their condition.

Kaplan-Meier survival analysis (Fig. 1A) demonstrates survival curves for patients receiving enteral nutrition post-stroke, stratified by risk level. The low-risk group maintained relatively stable survival probabilities for the first 600 days, followed by a gradual decline. In contrast, the high-risk group showed a rapid decline in survival probability around 400 days, with significantly lower survival compared to the low-risk group. The 95% confidence intervals (CIs) suggest precise survival estimates for the low-risk group, while the high-risk group exhibited greater uncertainty beyond 400 days. The Log-rank test showed a statistically significant difference between the survival curves of the high- and low-risk groups ($p = 0.0229$), indicating a significant association between risk stratification and survival outcomes for stroke patients receiving enteral nutrition.

Mortality prediction using machine learning models

We evaluated the performance of Logistic Regression, Random Forest, and XGBoost models in predicting 30-day, 1-year, and 3-year mortality for stroke patients following enteral nutrition. The Logistic Regression model showed moderate performance in predicting 30-day mortality, with an accuracy of 76% and an ROC-AUC of 0.76. However, its performance for predicting 1-year and 3-year mortality was weaker, with accuracies of 65% and 59%, and ROC-AUCs of 0.71 and 0.67, respectively.

The Random Forest model performed well in predicting 30-day mortality, achieving 94% accuracy, though the ROC-AUC was 0.74, indicating high accuracy for survival prediction. For 1-year and 3-year mortality, the model maintained an accuracy of 71%, with an ROC-AUC of 0.71, demonstrating consistency in mid- to long-term predictions.

The XGBoost model excelled in predicting 30-day mortality, with 94% accuracy and an ROC-AUC of 0.81. However, it underperformed in 1-year and 3-year mortality prediction, with accuracies of 59% and ROC-AUCs of 0.81 and 0.82, respectively, highlighting limitations in long-term mortality prediction (Supplementary Fig. 1B).

Overall, Random Forest and XGBoost showed better performance for short-term mortality predictions, while Logistic Regression was weaker in long-term predictions. Future research should focus on optimizing models to improve long-term mortality prediction accuracy.

Table 2 Vitals and labs

Variable	Count	Mean	Std	Min	25%	50%	75%	Max	F Score
age	81	70.58	13.46	28.99	62.69	72.47	80.04	91.08	14.72
charlson_comorbidity_index	81	7.04	2.82	0	5	7	9	14	2.78
sofa	81	6.49	4.07	0	4	6	8	17	2.68
hematocrit_min	81	31.83	8.25	0	26.8	32.8	37.2	48.4	0.03
hematocrit_max	81	36.15	7.63	0	30.9	36.3	41.6	52.8	0.02
hemoglobin_min	81	10.21	2.81	0	8.7	10.3	12.1	15.8	0.01
hemoglobin_max	81	11.62	2.62	0	9.9	11.4	13.3	17.2	0.1
platelets_min	81	174.1	86.06	0	113	179	219	453	0.04
platelets_max	81	206.09	86.71	0	145	196	246	482	0.01
wbc_min	81	10.06	5.19	0	7	8.7	13.4	31.3	8.51
wbc_max	81	13.41	6.12	0	9.4	12.8	16.5	33.3	6.44
aniongap_min	81	14.22	5.01	0	12	14	17	40	2.1
aniongap_max	81	18.04	6	0	15	17	19	46	5.68
bicarbonate_min	81	20.41	4.48	0	19	21	22	31	0.03
bicarbonate_max	81	23.1	4.48	0	22	23	25	35	0.81
bun_min	81	25.49	23.58	0	12	17	30	153	1.68
bun_max	81	30.2	25.03	0	16	22	36	157	2.32
calcium_min	81	8.08	1.5	0	7.8	8.2	8.8	10.2	0.22
calcium_max	81	8.6	1.6	0	8.2	8.7	9.3	11.6	0.36
chloride_min	81	100.49	12.69	0	99	103	105	115	0.08
chloride_max	81	105.11	13.62	0	103	106	110	130	0
creatinine_min	81	1.31	1.16	0	0.7	0.9	1.5	5.6	2.25
creatinine_max	81	1.59	1.35	0	0.8	1.1	2	7	1.79
glucose_min	81	128.19	41.26	0	100	120	146	253	1.01
glucose_max	81	189	134.02	0	122	160	213	1182	1.57
sodium_min	81	136.95	15.94	0	136	139	141	150	0.52
sodium_max	81	140.73	16.55	0	140	142	144	163	0.46
potassium_min	81	3.88	0.7	0	3.6	3.9	4.2	5.7	0.8
potassium_max	81	4.57	1.06	0	4.1	4.4	4.7	8.3	0.16
inr_min	81	1.24	0.64	0	1	1.1	1.3	3.9	1.2
inr_max	81	1.51	0.92	0	1.1	1.2	1.7	4.9	2.5
pt_min	81	13.47	6.95	0	11.3	12.1	14.1	42.3	1.17
pt_max	81	16.44	10.14	0	12.1	13.2	18.4	54.8	2.61
ptt_min	81	27.77	15.9	0	23.9	26.2	30.6	125.4	0
ptt_max	81	41.22	34.82	0	26.2	29.6	44.9	150	0
urineoutput	81	1554.38	1068.78	0	1050	1397	2080	7150	2.43
heart_rate_min	81	69.95	13.94	38	60	70	82	99	0.37
heart_rate_max	81	106.96	18	70	94	106	118	156	0
heart_rate_mean	81	85.84	14.19	49.32	76.36	83.89	95.04	117.54	0.04
sbp_min	81	93.12	19.73	0	84	92	103	148	0
sbp_max	81	159.07	35.75	0	145	155	174	321.01	2.12
sbp_mean	81	123.17	20.77	0	113.29	122.96	133.73	172.5	0.22
dbp_min	81	47.59	12.59	0	40	48	57	81	1.46
dbp_max	81	93.73	25.21	0	77	92	104	181	1.41
dbp_mean	81	65.02	13.39	0	57.5	64.83	73.97	91.19	0
mbp_min	81	62.14	12.89	7	56	61	69	101	0.36
mbp_max	81	114.96	29.06	85	97	109	124	256	0.52
mbp_mean	81	83.24	10.47	63.68	74.45	81.48	89.92	113.44	0.16
resp_rate_min	81	12.78	3.65	2	10	13	15	25.5	1.19
resp_rate_max	81	29.51	8.16	19	24	28	35	69	2.72
resp_rate_mean	81	19.9	3.88	12.64	17.19	19.22	22.56	35.77	3.24
temperature_min	81	36.08	4.11	0	36.44	36.61	36.89	37.67	0.18
temperature_max	81	37.38	4.28	0	37.28	37.78	38.28	40	0.43

Table 2 (continued)

Variable	Count	Mean	Std	Min	25%	50%	75%	Max	F Score
temperature_mean	81	36.71	4.16	0	36.83	37.16	37.52	38.26	0.34
spo2_min	81	93.2	4.51	72	91	94	96	100	0
spo2_max	81	99.81	0.55	97	100	100	100	100	0.06
spo2_mean	81	97.78	1.82	92.54	96.71	98.15	99.27	100	0
glucose_min_vitalsign	81	112.02	37.59	0	89	107	125	253	1.16
glucose_max_vitalsign	81	184.46	102.09	0	126	159	207	822	1.53
glucose_mean	81	144.89	48.46	0	112	134.5	174.17	285.88	1.21
weight_admit	81	73.03	29	0	60	74.7	87.2	140	1.94
weight	81	75.4	26.54	0	61.4	75.6	87.3	140	1.22
weight_min	81	74.9	26.69	0	60.4	75.6	87.3	140	1.07
weight_max	81	76.04	26.61	0	64.3	76.9	88	140	1.37

Table 3 Descriptive statistics of 30-Day, 1-Year, and 3-Year mortality rates

Timepoint	Survival Rate (%)	Deaths
30 Days	66.67	27.00
1 Year	45.68	44.00
3 Years	43.21	46.00

Survival analysis results

Survival time prediction using XGBoost Cox regression model

We developed and evaluated an XGBoost-based survival analysis model to predict survival times for stroke patients receiving enteral nutrition. The model's performance was assessed using the concordance index (C-index), which reached 0.80, indicating good predictive performance in ranking survival times. This result demonstrates that the model could accurately predict which patients had longer survival times in 80% of cases. This high level of predictive accuracy suggests that the XGBoost survival model is a useful tool for exploring factors influencing long-term survival in stroke patients, providing valuable insights for clinical decision-making to improve stroke patient care and prognosis management.

Comparison of survival curves for patients with different nutrition types (Standard vs. Specialized nutrition)

We compared the effects of Specialized and Standard nutrition types on survival time in stroke patients receiving enteral nutrition from the MIMIC-IV database. Kaplan-Meier survival curves and the C-index were used to evaluate the predictive performance of the model. The results showed a C-index of 0.81 for the Specialized group, indicating good predictive ability, while the C-index for the Standard group was 1.00, demonstrating perfect predictive accuracy.

Kaplan-Meier survival curves (Fig. 2A and B) showed similar patterns for both nutrition groups, but the predictive capability of the Standard nutrition model was more prominent. The survival curves revealed the dynamic changes in survival probability over time for both groups

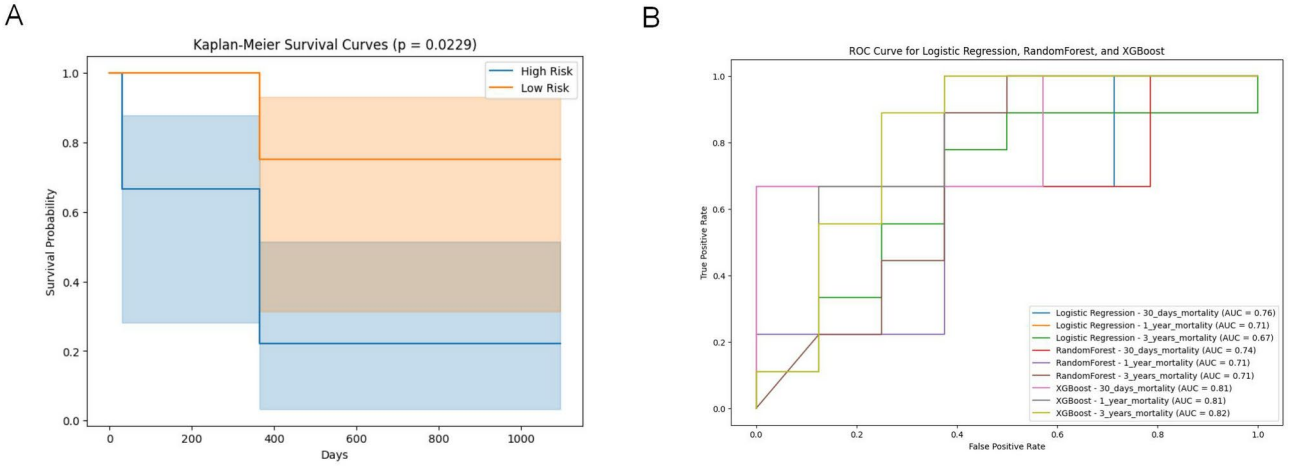

Fig. 1 Kaplan-Meier Survival Curves and ROC Curve for Stroke Patients Receiving Enteral Nutrition. (**A**) Kaplan-Meier survival curves for high-risk and low-risk groups. (**B**) ROC curves for Logistic Regression, RandomForest, and XGBoost models predicting 30-day, 1-year, and 3-year mortality. The Kaplan-Meier curves show a significant difference between the high-risk (blue) and low-risk (orange) groups ($p = 0.0229$). The ROC curves compare model performance, with AUC values indicating prediction accuracy at each time point

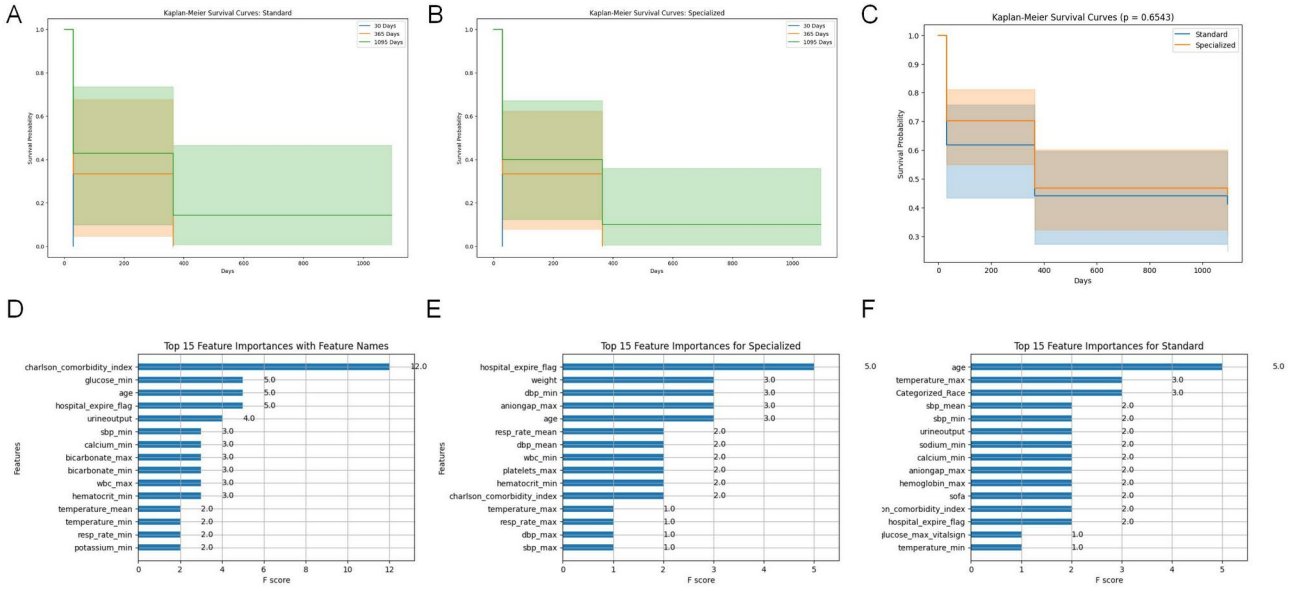

Fig. 2 Kaplan-Meier Survival Curves and Feature Importance Analysis of Stroke Patients Receiving Standard and Specialized Enteral Nutrition. (**A**) Kaplan-Meier survival curve for patients receiving standard enteral nutrition showing survival probabilities over different follow-up times. (**B**) Kaplan-Meier survival curve for patients receiving specialized enteral nutrition. (**C**) Comparative Kaplan-Meier survival curve between standard and specialized nutrition groups. (**D**) Top 15 feature importances from the XGBoost model trained on the full patient cohort. (**E**) Top 15 feature importances from the XGBoost model for the specialized nutrition subgroup. (**F**) Top 15 feature importances from the XGBoost model for the standard nutrition subgroup

at 30, 365, and 1095 days. In the Specialized group, the survival probability was high at 30 days, followed by a gradual decline over time, reaching around 40% at 365 days and approximately 30% at 1095 days. In the Standard group, the trend was similar, with survival probabilities of around 40% and 30% at 365 and 1095 days, respectively. The 95% CIs showed increasing uncertainty in survival rates over time, especially in long-term follow-ups. Although the survival curves were similar, the Specialized group had slightly higher survival rates in the long term compared to the Standard group.

Log-Rank test results showed no statistically significant difference between the survival curves of the two nutrition types ($p = 0.6543$), indicating that both nutrition types had a similar impact on patient survival probabilities. Despite differences observed in Kaplan-Meier curves, the Log-Rank test suggests that these variations might be due to random fluctuations rather than actual effects of nutrition type. This finding provides important insights for clinical nutrition strategies, suggesting that other factors may need to be considered when choosing nutrition types for stroke patients.

Feature importance analysis

XGBoost model feature importance analysis

Using the XGBoost model, we conducted survival analysis on 81 stroke patients who received enteral nutrition from the MIMIC-IV database. Feature importance analysis identified the most influential factors for predicting survival time. The Charlson Comorbidity Index (CCI) was the most important predictor, with an F-score of 12.0, highlighting its critical role in evaluating long-term prognosis. Other significant features included minimum glucose value, age, and in-hospital mortality, each with an F-score of 5.0, indicating their importance in the predictive model. The model's C-index was 0.80 on the test set, further validating its effectiveness in survival time prediction (Fig. 2D).

Feature importance analysis for different nutrition types (Standard vs. Specialized nutrition)

In this study, we compared the impact of Standard and Specialized nutrition types on the survival time of stroke patients. The model's predictive performance was assessed using the C-index, with the Standard nutrition group achieving a perfect C-index of 1.00, demonstrating flawless prediction accuracy. The feature importance analysis of the XGBoost machine learning model showed that age was the most critical predictor in the Standard nutrition group, with an F-score of 5.0. In contrast, the Specialized nutrition group had a C-index of 0.85, indicating good predictive accuracy, and the most important feature in this group was the in-hospital mortality marker, with an F-score of 5.0. These results provide valuable insights for optimizing clinical nutrition interventions, emphasizing the differences in survival time prediction factors between the two nutrition types (Fig. 2E and F).

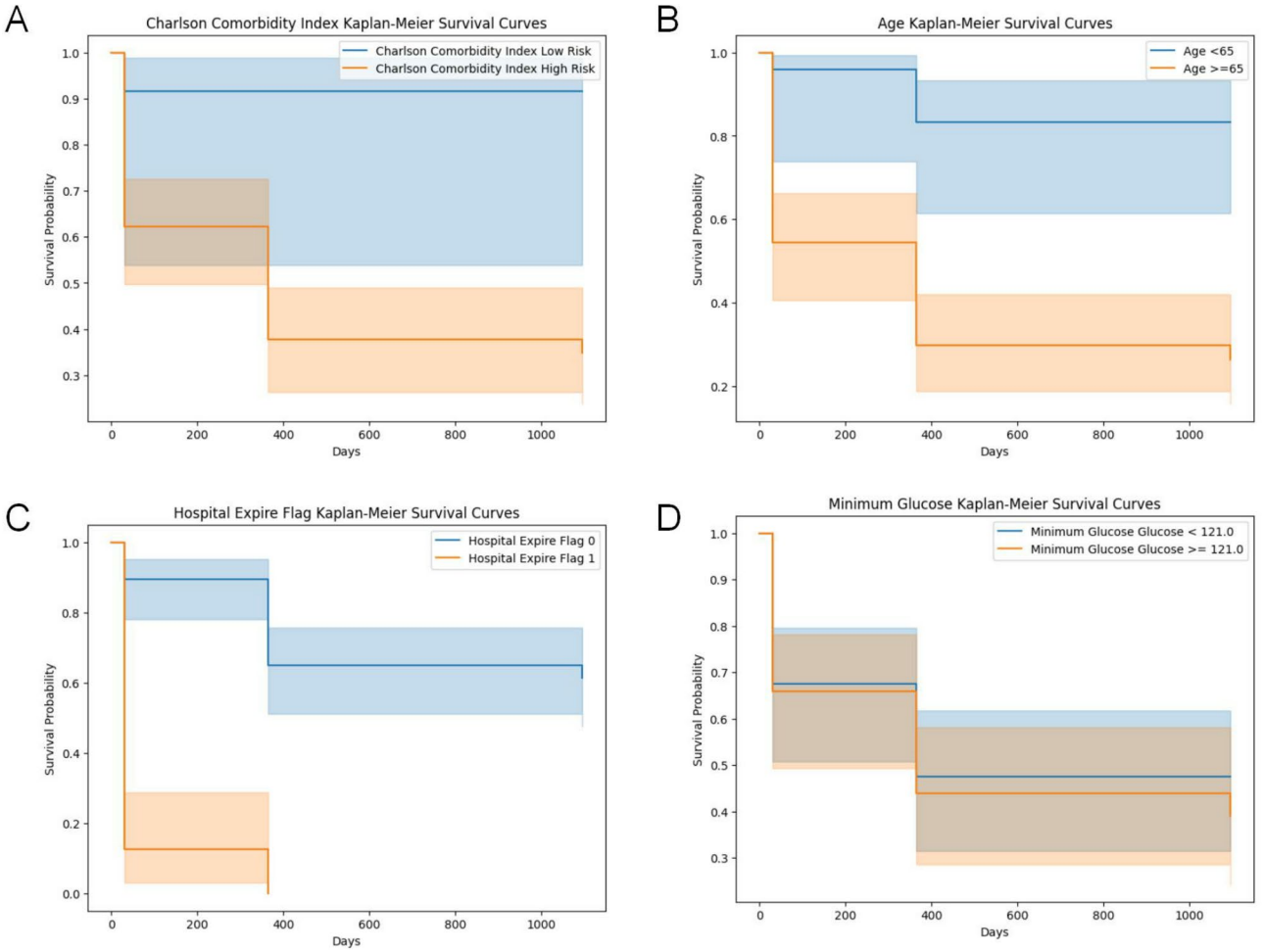

Fig. 3 Kaplan-Meier Survival Curves for Different Risk Factors in Stroke Patients Receiving Enteral Nutrition. (**A**) Kaplan-Meier survival curves for Charlson Comorbidity Index (CCI), stratified by low and high risk. (**B**) Kaplan-Meier survival curves for age, stratified by < 65 years and ≥ 65 years. (**C**) Kaplan-Meier survival curves for hospital expiration flag, comparing patients who expired in the hospital (Flag 1) with those who did not (Flag 0). (**D**) Kaplan-Meier survival curves for minimum glucose levels, comparing patients with glucose < 121.0 mg/dL and those with glucose ≥ 121.0 mg/dL

Stratified analysis of feature importance factors

We performed a stratified analysis of key factors such as Charlson Comorbidity Index (CCI), age, in-hospital mortality marker, and minimum glucose using Kaplan-Meier survival curves and Log-Rank tests to assess their impact on patient survival rates. The results showed that the survival rate in the high-risk CCI group was significantly lower than in the low-risk group (Log-Rank Test $p = 0.0010$), indicating that CCI is an effective predictor of stroke patient survival rates. Age also had a statistically significant effect on survival, with patients aged ≥ 65 having significantly lower survival rates than those aged < 65 (Log-Rank Test $p = 0.0000$). The in-hospital mortality marker was strongly associated with survival, as patients who did not die in the hospital had significantly higher survival rates compared to those who died in the hospital (Log-Rank Test $p = 0.0000$). However, the minimum glucose level did not show a statistically significant impact on survival (Log-Rank Test $p = 0.5109$), suggesting that it was not a crucial predictor of survival in this study (Fig. 3). These findings highlight the importance of CCI, age, and in-hospital mortality markers in predicting stroke patient outcomes.

Discussion

In this study, we explored the impact of enteral nutrition types (exposure variable) on the 30-day, 1-year, and 3-year survival rates (outcome variables) of stroke patients. A highlight of this study is its use of the MIMIC-IV database, allowing us to analyze a relatively large sample size and long-term follow-up data. The results showed that the 30-day survival rate of stroke patients was 66.67%, gradually declining to 45.68% at 1 year and 43.21% at 3 years. In the survival analysis, the Kaplan-Meier curve indicated that patients in the low-risk group had significantly higher survival rates than those in the high-risk group ($p = 0.0229$). Further machine learning model analysis revealed that the Charlson Comorbidity

Index was the most predictive factor (F score = 12.0) and was significantly correlated with survival. These findings highlight the critical role of early intervention and multifactorial prediction in improving stroke patient outcomes.

Our findings share similarities with some studies in the literature, while also differing in certain aspects. Our study found a 30-day survival rate of 66.67% for stroke patients receiving enteral nutrition, which aligns with the results of Zheng et al. [13]. Their prospective randomized controlled trial (sample size of 146) demonstrated that early enteral nutrition support could improve the short-term prognosis of acute stroke patients. However, our study, based on the MIMIC-IV database with a retrospective analysis approach and a sample size of 81 patients, allowed us to conduct longer follow-up assessments, evaluating the 1-year and 3-year survival rates.

The elevated 30-day mortality rate observed in our study may be attributed to several factors. First, the characteristics of the study population could play a significant role. Many patients may have been in a severe health condition upon admission, accompanied by multiple comorbidities, which can substantially increase the risk of short-term mortality. For instance, common comorbidities such as cardiovascular disease, diabetes, and chronic kidney disease are particularly prevalent among elderly patients, and their presence can impair recovery capacity post-surgery or treatment, thereby elevating mortality rates. Second, the selection and implementation of treatment protocols may also influence mortality rates. Certain therapeutic approaches may be less effective for specific patient populations, especially in cases where the underlying health conditions are complex [14]. However, over time, patients typically demonstrate improved recovery and adaptability following treatment, with many experiencing significant health improvements and stabilization after initial interventions. Long-term medical management and monitoring play a crucial role in reducing mortality, as regular follow-ups can facilitate the timely identification and management of potential health issues, thereby mitigating death risk. Furthermore, advancements in medical technology and treatment strategies have enabled a growing number of patients to receive more effective therapies, which have contributed to lower recurrence rates of chronic diseases and reduced incidence of complications, ultimately enhancing long-term survival rates [15]. Lastly, selective survival bias may also impact mortality statistics over extended periods; many high-risk patients may succumb within the initial 30 days, while those who survive typically possess better health status or more resilient coping mechanisms, resulting in lower mortality rates in subsequent one- and three-year follow-ups.

The Charlson Comorbidity Index is a scoring system used to assess the impact of comorbidities on patient prognosis. This score includes various common diseases, such as heart disease, diabetes, kidney disease, and tumors, with each disease assigned different points based on its severity. The total score is the sum of the points for each condition; a higher score indicates more severe comorbidities and a higher risk of poor prognosis. This scoring system is commonly used in clinical research and practice to help physicians evaluate patients' prognostic risks and develop treatment plans [16, 17]. Our study emphasized the importance of the Charlson Comorbidity Index as a predictor of survival, consistent with the findings of Goldstein et al. [18]. Their large-scale cohort study ($n = 26{,}676$) confirmed the predictive value of the Charlson Index for long-term survival in stroke patients. Additionally, we observed that the baseline blood glucose level was a significant predictor, which aligns with the findings of Capes et al. [19]. Their systematic review and meta-analysis of 32 studies, encompassing 26,151 patients with ischemic stroke, demonstrated that admission hyperglycemia was associated with increased risk of in-hospital mortality and poor functional recovery in non-diabetic stroke patients.

However, our findings differ from those of some other studies. For example, the FOOD trial [4, 7] found that early enteral nutrition did not significantly improve survival or functional outcomes in stroke patients compared to usual care. This large multicenter randomized controlled trial ($n = 859$) yielded results different from ours, likely due to differences in study design, population characteristics, and follow-up duration. This discrepancy may be attributed to differences in study design, sample characteristics, and follow-up duration. Firstly, the patient population in the FOOD trial primarily focused on acute stroke patients, whereas our study included all stroke patients receiving enteral nutrition, which could lead to variations in disease severity and comorbidities between the two studies. Secondly, the follow-up period in the FOOD trial was relatively short, concentrating mainly on short-term outcomes, while our research provided survival data at 30 days, 1 year, and 3 years, allowing for a more comprehensive assessment of the long-term effects of enteral nutrition [20]. Moreover, the nutritional intervention strategies in the FOOD trial differed from those in our study. The FOOD trial employed a standard enteral nutrition protocol, whereas our research considered various types of enteral nutrition, which may influence patient survival and prognosis. Therefore, while the FOOD trial did not demonstrate the benefits of early enteral nutrition, our findings suggest that personalized nutritional management and early intervention may play a crucial role in improving the long-term survival rates of stroke patients. Although the results of the FOOD trial

did not support the efficacy of early enteral nutrition, our study offers a new perspective by analyzing different types of enteral nutrition and their impact on long-term survival, emphasizing the importance of personalized nutritional management [21].

Zhu et al. found that early initiation of enteral nutrition in critically ill stroke patients may be associated with a higher 28-day mortality risk [22]. This multicenter retrospective cohort study ($n = 1009$) differs from our findings, possibly due to differences in study populations (we included all stroke patients receiving enteral nutrition, not just critically ill patients).

Our study also identified age as an important factor influencing survival, consistent with the findings of Saposnik et al. [23]. Their large cohort study ($n = 12,262$) demonstrated that age is an independent predictor of stroke outcomes. Furthermore, our study highlighted the importance of in-hospital mortality markers, aligning with the findings of Fonarow et al. [24]. Their national registry study ($n = 26,676$) found that complications during hospitalization significantly impact the long-term prognosis of stroke patients.

In terms of nutritional strategies, Albrecht et al. suggested that early low-calorie enteral nutrition in severe stroke may be associated with higher mortality compared to modified full-volume enteral nutrition [25]. This multicenter, randomized, open-label clinical trial ($n = 120$) emphasized the critical impact of nutritional strategies on patient outcomes, although our study did not specifically differentiate between caloric levels of enteral nutrition.

From a mechanistic perspective, our findings may reflect the multifaceted effects of early enteral nutrition on stroke patients. Ojo et al.'s systematic review [6] pointed out that early nutritional support may improve patient outcomes by maintaining gut barrier function, reducing inflammatory responses, and improving immune function. Meanwhile, Teramoto et al.'s research [26] emphasized the importance of appropriate nutritional support in preventing aspiration pneumonia, which is a key factor affecting long-term survival in stroke patients.

Overall, our findings offer new insights into the nutritional management of stroke patients, underscoring the importance of early intervention, individualized management, and close monitoring of comorbidities and metabolic parameters. However, given the limitations of study design and sample size, further large-scale prospective studies are needed to validate these findings.

The clinical value of this study lies in providing a new perspective for assessing and optimizing enteral nutrition management in stroke patients. By combining machine learning techniques with traditional survival analysis methods, we not only identified key factors affecting long-term survival rates but also developed a predictive model that can assist clinicians in formulating individualized nutrition plans. This innovative approach addresses the gap in existing studies that lack a focus on long-term prognosis while offering more precise quantitative evidence for clinical decision-making. Furthermore, the study results indicate that nutritional plans should be adjusted based on patients' age, comorbidities, and nutritional status, providing a foundation for developing more accurate clinical guidelines. Based on these findings, we recommend that healthcare institutions establish standardized nutritional assessment processes and incorporate the predictive model into clinical decision support systems. This would not only help improve patient outcomes but also potentially reduce healthcare costs and optimize resource allocation. Future research could explore the impact of nutritional interventions on cognitive function recovery and quality of life, as well as develop more comprehensive tools for prognosis evaluation.

This study has several notable strengths. First, we employed a prospective cohort study design, which allows for the establishment of a temporal sequence between exposure and outcome and minimizes recall bias. Second, our sample size was sufficient and representative, covering patients of various age groups and disease severities, enhancing the external validity of the findings. In terms of data collection, we used standardized assessment tools and implemented strict quality control measures to ensure the accuracy and reliability of the data. Our data analysis strategy is another key highlight of this study. We not only applied traditional survival analysis methods but also innovatively incorporated machine learning algorithms, offering a new perspective for more accurately predicting patient outcomes. Additionally, we considered various potential confounding factors and adjusted for them through multivariable analysis, which strengthened the internal validity of the study results. Finally, we focused not only on statistical significance but also on clinical relevance, providing a solid foundation for the practical application of our findings. These strengths collectively form the unique value of this study, offering important scientific evidence for the nutritional management of stroke patients.

In this study, we recognize that the representativeness of the sample is an important factor influencing the results. Although we utilized the MIMIC-IV database with a sample size of 81 stroke patients, the selection of the sample may be biased, particularly regarding the criteria for patient selection and inclusion, which may limit the generalizability of the results [27]. Furthermore, selection bias may arise from including only patients who received enteral nutrition, which could be related to the severity of the patients' conditions, comorbidities, and

other clinical characteristics. Therefore, future studies should consider a broader patient population to enhance the generalizability of the findings. Regarding methodological bias, we discussed the potential for classification bias. Since this study relies on records from the database, there may be instances of data entry errors or omissions, which could affect our accurate assessment of patients' clinical characteristics and outcomes. We made efforts to control for known confounding factors in our analysis, but it is still important to note that unmeasured confounders may influence the results [20]. Therefore, while our study provides valuable insights, caution should be exercised in interpreting the results, and we recommend that future larger-scale prospective studies be conducted to validate our findings.

This study acknowledges certain limitations. One notable aspect is the relatively small sample size, which may influence the statistical power and generalizability of our conclusions. Although the sample size is modest ($n = 81$), the rigorous implementation of inclusion and exclusion criteria ensured the homogeneity of the data. This methodological rigor enhances the validity of the analyses while reducing clinical variability. Furthermore, the use of a robust database, such as MIMIC-IV, provides detailed and reliable information, mitigating the impact of this limitation. Despite the limited sample size, this study provides significant exploratory findings in the field, which offer direction for future research. However, caution is warranted when applying and generalizing these results, particularly regarding their applicability to diverse populations. Therefore, subsequent research should aim to validate these results in larger and more representative independent cohorts to ensure their reliability and generalizability. Regarding the predictive model for the "standard diet" group, the observed C-index of 1.00 indicates a high degree of accuracy. However, in the context of a limited sample size, this raises concerns about potential overfitting. Thus, although the model performs well within the current dataset, careful interpretation of these results is necessary. Future studies should focus on obtaining larger datasets to validate the model's applicability in broader clinical settings. Moreover, enhancing the interpretability of machine learning models is crucial. While the current variable importance analysis provides some insights into factors relevant to patient outcomes, its application and understanding in clinical practice may still be limited. Future research should consider incorporating methods such as SHAP (Shapley Additive Explanations) and LIME (Local Interpretable Model-agnostic Explanations) to improve the interpretability of the model and enhance clinicians' understanding and trust in the model's outputs. Finally, we utilized the Charlson Comorbidity Index to stratify the risk of mortality in post-stroke patients and established a protocol for the early initiation of enteral nutrition within 48 h of admission, specifically targeting high-risk patients. In this framework, the predictive model will support clinicians in making informed nutritional decisions based on the specific needs and acute risk levels of their patients. Nutritional formulas should be customized according to individual comorbidities and metabolic requirements, particularly emphasizing products enriched with omega-3 fatty acids. Future research could explore prospective multi-center study designs to validate these predictive results in more diverse populations and compare the effects of different types of specialized nutrition (such as high-calorie formulas and fiber-enriched formulas) in ischemic and hemorrhagic stroke patients.

Conclusion

This study employs innovative machine learning techniques to preliminarily investigate the potential significance of personalized enteral nutrition interventions in enhancing the prognosis of stroke patients. While acknowledging certain limitations, our findings offer preliminary guidance for clinical practice and establish a foundation for future research. It is crucial to interpret these results with caution, as further studies are needed to validate our findings and ensure the efficacy of personalized nutritional management in stroke patients, which may ultimately improve survival rates and long-term outcomes.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3: **Supplementary Figure**. A detailed flowchart illustrating the participant recruitment process

Author contributions

X.F. and C.H. contributed equally to this work. X.F. and J.X. designed the study. X.F. extracted, collected, and analyzed the data. J.X. contributed to data analysis and interpretation. R.Y. and J.Z. prepared tables and figures. Y.W. and J.X. reviewed the results, interpreted the data, and assisted in writing the manuscript. All authors made intellectual contributions to the manuscript and approved the final submission.

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Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the guidelines of the Helsinki Declaration. The use of the MIMIC-IV database was approved by the Institutional Review Board of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. Since the data is publicly available through the MIMIC-IV database, ethical approval and informed consent requirements were waived for this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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