A systematic evaluation of risk prediction models for feeding intolerance of intensive care unit patients during enteral nutrition

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ABSTRACT

Background and Objectives: It has been found that ICU patients may encounter various complications during enteral nutrition (EN). Of these, feeding intolerance (FI) is a common issue that often necessitates the reduction or cessation of EN. This study aims to evaluate risk prediction models for feeding intolerance (FI) in critically ill patients receiving EN by searching major public databases. **Methods and Study Design:** We searched for relevant studies in Embase, PubMed, Web of Science, Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data, and cqvip.com up until January 2024. Two researchers independently conducted the screening and data extraction processes, and the quality of the literature was assessed using bias risk assessment tools. **Results:** A total of 13 references were included, and the subjects included patients with sepsis, pancreatitis or cerebral apoplexy; the incidence of FI was 35.20%-49.29%. The studies discussed the predictive performance of various models, with 11 studies reporting on their accuracy and calibration. The models demonstrated the area under the curve (AUC) of the receiver operating characteristic (ROC) curve or the concordance index (C-index) between 0.70 and 0.906, sensitivity from 0.814 to 0.933, and specificity from 0.680 to 0.833. **Conclusions:** There is a critical need for risk prediction models for FI in critically ill patients on EN that are both internally and externally validated and exhibit high performance.

Key Words: critically ill patients, enteral nutrition, feeding intolerance, risk prediction model, systematic evaluation

INTRODUCTION

Enteral nutrition (EN) is the preferred method of nutritional support for patients in intensive care units (ICUs) due to its positive effects on intestinal mucosal recovery and stimulation of intestinal peristalsis.[1] However, clinical findings have shown that ICU patients may encounter various complications during EN, with feeding intolerance (FI) being a common issue that often necessitates the reduction or cessation of EN.[2, 3] FI is defined as gastrointestinal dysfunction characterized by abdominal distension, diarrhea, vomiting, constipation, and excessive gastric remnants during EN.[4] Studies have shown that although the factors leading to these findings are not yet clear, the use of high-dose sedatives and prolonged mechanical ventilation may both cause gastrointestinal motility disorders.[5, 6]

The global prevalence of FI in ICU settings ranges from 2% to 75%, while in China, it varies between 30.5% and 65.7%. Severe cases of FI can disrupt or halt nutritional support,

significantly impacting patient outcomes in ICUs.[4, 7] The failure of critically ill patients to achieve the goals of EN has been found to be associated with insufficient energy, prolonged ICU stay, increased incidence of infection complications, and increased mortality rate.[8] Similarly, experience in the nursing of critically ill patients in ICUs has shown that the unprecedented difficulties encountered in providing EN to this population were due to frequent and severe FI.[9] Hence, early identification of FI risk factors is crucial for its prevention and management. The top five risk factors have been found to be the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, patient age, albumin levels, intra-abdominal pressure, and the use of mechanical ventilation.[10] However, existing models are associated with several limitations, such as insufficient sample sizes and inappropriate selection of predictive indicators,[11] which could hinder their effectiveness and reliability in clinical practice.

Risk prediction models, which are statistical tools based on disease etiology, are employed to estimate the likelihood of future adverse events in individuals with specific characteristics.[12] These models are valuable for assessing disease severity, aiding in diagnosis, and forecasting potential complications, thereby informing the development of tailored care plans and therapeutic strategies.

Given the significance of FI in critical care, researchers both domestically and internationally have focused on developing and validating risk prediction models by analyzing factors associated with FI. This study aims to systematically review and evaluate these models to aid clinicians in selecting the most effective ones for preventing FI in critically ill patients.

MATERIALS AND METHODS

Literature retrieval strategy

The literature related to risk prediction models for FI in critically ill patients during EN was searched across databases including Embase, PubMed, Web of Science, Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data, and CQVIP. The search time was from the establishment of the database to January 2024. The Chinese search formula was (‘ICU’ OR ‘critical’ OR ‘critical illness’ OR ‘intensive care’ OR ‘intensive care unit’ OR ‘intensive care unit') AND (‘enteral nutrition’ OR ‘tube feeding’ OR ‘nasal feeding’) AND (‘feeding intolerance’) AND (‘prediction factors’ OR ‘risk factors’ OR ‘prediction model’ OR ‘prediction’ OR ‘risk prediction model’ OR ‘nomogram model’ OR ‘risk score’ OR ‘risk assessment’). The English search formula was (‘ICU’ OR ‘intensive care

unit' OR 'critical care unit' OR 'burn unit' OR 'coronary care unit' OR 'respiratory care unit' OR 'CCU' OR 'SICU' OR 'MICU' OR 'NICU') AND ('Feeding intolerance' OR 'Feeding tolerance' OR 'Enteral nutrition' OR 'tube-feeding'). Additionally, a manual 'snowball' search was conducted by tracing the references included in the initial set of articles to further augment the relevant literature.

Inclusion and exclusion criteria

Inclusion criteria: (1) participants with age ≥ 18 years; (2) studies that developed risk prediction models for FI in critically ill patients during EN; (3) prediction models that were validated internally and/or externally following their establishment; (4) the types of literature included prospective or retrospective cohort studies, case-control studies. Exclusion criteria: (1) studies that identified risk factors or influencing factors without constructing a risk prediction model; (2) studies lacking a clear description of the model-building process or methodology; (3) conference abstracts, grey literature, or studies where the original text is unavailable, or data are incomplete.; (4) reviews, commentaries, animal studies, etc.

Literature screening and data extraction

The researchers independently reviewed the literature using predefined inclusion and exclusion criteria. The literature was searched independently by two investigators, and EndNote literature management software was used to screen and remove duplicate studies. Each study was analyzed to ensure that it met the inclusion and exclusion criteria. If necessary, relevant studies were searched manually using a snowball method to preserve the integrity of the literature search. Subsequently, two investigators evaluated the quality of all the studies included in the analysis. In the event of differences of opinion between the two authors, these were discussed and resolved. If necessary, a third investigator was consulted for resolution. Once the references to be included were determined, they developed a standardized table for data extraction based on the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS) checklist.[13] The extracted data included various study characteristics such as the first author, year of publication, country, research design, study population, sample size, duration of observation, outcomes predicted, incidence of FI, methods used for modeling, techniques for selecting predictive variables, format of model presentation, model performance metrics (including discrimination and calibration), model validation (internal and external), number of predictive factors, and the predictive factors ultimately included in the models. The table also captured each study's applicability and

limitations, assisting a final consensus through careful verification of the contents of the studies.

Quality evaluation of included references

Two researchers employed the Prediction Model Risk of Bias Assessment Tool (PROBAST) to evaluate the risk of bias and applicability of the studies included.[14, 15] The PROBAST tool encompasses evaluations of both bias risk and applicability. Bias risk assessment includes four domains: research subjects, predictive variables, outcomes, and statistical analyses, featuring a total of 20 questions answered using the options 'yes', 'maybe', 'may not be', 'no', and 'no information'. Applicability assessment focuses on three domains: research subjects, predictive variables, and outcome indicators, with each domain rated as 'high applicability', 'low applicability', or 'unclear applicability'. The results of the bias risk and applicability assessments for the included studies are presented in Table 4.

RESULTS

Literature inclusion results

The search yielded 3855 related articles, and 13 were eventually included.16-28 The literature screening process is shown in Figure 1.

Basic characteristics of included references

All references included in the review were published within the last five years and comprised various study designs: three retrospective case-control studies, one prospective observational study, five retrospective cohort studies, one case-control study, one retrospective study, and two prospective cohort studies. The studies involved patients with conditions such as sepsis, pancreatitis, and cerebral apoplexy, with total sample sizes ranging from 118 to 628. The incidence of FI in the studies varied from 35.20% to 49.29% (Table 1).

Modeling methods, model presentation, prediction performance and validation in included references

The primary modeling method used was logistic regression, and the models were primarily presented in the forms of nomograms, regression equations, and rating scales. All 13 models documented their prediction performance, with 11 of these also reporting on both prediction accuracy and calibration. In terms of model accuracy, the area under the curve (AUC) of the receiver operating characteristic (ROC) curve or the concordance index (C-index) ranged

from 0.70 to 0.906, sensitivity varied from 0.814 to 0.933, and specificity was between 0.680 and 0.833 (Table 2). Additionally, six studies detailed specific techniques for internal or external validation of the prediction models, predominantly using Bootstrap resampling or sample splitting (Table 2).

Predictive factors included in the models

In the 13 studies analyzed, the prediction models incorporated between 3 to 15 predictive factors, with risk and protective factors being the most common predictors of FI in critically ill patients during EN (Table 3). Specifically, the risk factors identified were acute gastrointestinal injury (AGI) grade, the initiation timing of EN, average infusion rate, C-reactive protein levels, hypertension, mechanical ventilation, use of analgesic and sedative drugs, hyperglycemia, hyperkalemia, the use of two or more antibiotics, and abnormal serum sodium levels. Protective factors included albumin levels, early enema, addition of glutamine, use of probiotics, and early initiation of feeding. The most significant predictive factors were age ≥ 60 years, APACHE II score, AGI grade, and mechanical ventilation. Additionally, it has also been reported that the use of probiotics, early enema and the addition of glutamine are protective factors.[17]

Evaluation of the quality of studies included in the analysis

In this study, the PROBAST tool was employed to assess the quality of the 13 included papers. Initially, regarding research subjects, 10 studies were identified with a high bias risk, primarily due to their retrospective cohort or case-control design; the other 3 studies demonstrated low bias risk. In terms of predictive factors, 2 studies presented an unclear bias risk because it was not specified whether the assessors were blinded to the outcome information when evaluating predictive factors. Regarding the results, 3 studies had unclear bias risks due to the lack of reported timing between the assessment of predictive factors and outcome determination; the other 10 studies were considered to have low bias. Lastly, in statistical analysis, 11 studies were categorized as high risk and 2 as low risk, mainly because of inadequate reporting on how missing values were handled during the modeling process, as shown in Table 4.

DISCUSSION

Higher clinical interest in risk prediction models for FI of critically ill patients during EN

Currently, scholars are primarily focusing on the development and implementation of risk prediction models in clinical settings, including several models for FI of critically ill patients during EN. This study included 13 such models, all of which focused on ICU patients. Logistic regression was predominantly used to construct these models, and all models reported area under the receiver operating characteristic curves (AUROCs) above 0.7, demonstrating good predictive accuracy. Nonetheless, the broad applicability and stability of these models require further investigation, which suggests that healthcare professionals should exercise caution when selecting these models for clinical use. Additionally, seven studies used Bootstrapping for internal validation after modeling,[16, 17, 19, 21, 25, 27, 28] and the Hosmer-Lemeshow test was used to verify the consistency between model prediction rate and actual incidence in studies.[17, 19, 22-24, 26, 27] However, some studies,[17, 19, 27] lacked external validation of their models. Therefore, both internal and external validations are crucial for the future clinical evaluation of these tools.

Limitations of risk prediction model construction method

Currently, the methodologies used to construct and validate risk prediction models for FI in critically ill patients during EN have several limitations. Many of the included studies are based on retrospective case-control data, which is susceptible to recall bias and may introduce selection bias in the control groups. Additionally, most studies do not specify operational definitions for predictive factors, making it difficult to determine if the methods, procedures, and timing of measurements are consistent. The absence of reported blinding methods could lead to information bias. Furthermore, there is a need for these studies to provide details on handling missing data and to further elaborate on data censoring, control sampling, and competing risks.

Predictive factors in risk prediction models for FI of critically ill patients during EN

In this study, the predictive factors included in the model were identified as patient age, APACHE II score, AGI grade, mechanical ventilation, intra-abdominal pressure, hyperglycemia, the use of two or more antibiotics, pre-existing gastrointestinal diseases, and early initiation of feeding.

Patient age

In this review, patient age was a factor in the prediction models of five studies,[16, 21, 24, 27, 28] with three indicating that patients over 60 may have diminished tolerance to nutritional solutions due to declining gastrointestinal function, thereby increasing the risk of FI. In

contrast, one study reported that being 60 years or older may act as a protective factor against FI in critically ill patients during EN.28 This conflicting result might be explained by considering that older patients often receive less energy due to impaired gastrointestinal function and are frequently supplemented with probiotics to support gut health. The variations in findings across studies could stem from differences in study populations. It is important to note that in clinical practice, the primary goal of initiating EN in critically ill patients is to preserve the structural and functional integrity of the gastrointestinal tract, rather than merely meeting energy requirements.[29] Therefore, the disparities in the results may be attributed to variations in sample selection, such as patient age and disease.

APACHE II score

The present study shows that the higher the APACHE II score, the higher the risk of FI of critically ill patients during EN. After suffering severe injuries, the body prioritizes the protection of vital organs such as the heart, brain, and kidneys, often at the expense of gastrointestinal blood flow. This reduction in blood flow can slow gastrointestinal peristalsis, resulting in reduced tolerance to EN.30 Moreover, a stress-induced state can lead to abnormal hormone levels and excessive tissue protein consumption, further damaging the gastrointestinal mucosa. This damage decreases gastrointestinal tolerance,[31] which ultimately leads to the occurrence of FI. It has been reported that critically ill patients in the ICU who receive EN while on mechanical ventilation and have APACHE II score $\geq$ 20 are at a significantly greater risk of developing FI.[32] This indicates that as the APACHE score increases, the likelihood of EN intolerance in patients also rises.

AGI grading

The European Society of Intensive Care Medicine recognizes AGI grading as a method for evaluating the severity of gastrointestinal dysfunction in critically ill patients. Damage to the gastrointestinal barrier may facilitate the invasion of toxins, resulting in intestinal immune disorders and dysbiosis. These complications can significantly increase the likelihood of FI during EN.[33] In addition, other clinical monitoring methods, such as bedside intestinal ultrasound, have demonstrated the predictive value of indicators such as intestinal wall thickness, intensity of peristalsis, and intestinal diameter in assessing enteral FI among critically ill patients.[34]

Mechanical ventilation

Previous studies have demonstrated that mechanical ventilation is associated with an increased risk of FI in critically ill patients during EN.[20, 27, 28] This is likely due to the release of inflammatory factors in the lungs from the use of positive pressure ventilation, particularly at high expiration levels.[35] The increased risk of FI in mechanically ventilated patients may be attributed to the positive end-expiratory pressure (PEEP) applied by the ventilator. The PEEP is used during mechanical ventilation to maintain a specific level of positive pressure in the airways at the end of expiration. This may lead to an elevation in intrathoracic pressure, resulting in reduced cardiac output and subsequent hypoperfusion.36 The positive correlation between PEEP and the incidence of enteral FI was also reported in another study. [37] These findings indicate the importance of meticulous monitoring of mechanically ventilated patients, paying particular attention to the PEEP levels, as this is crucial for reducing the risk of enteral FI in critically ill patients.

Benefits of the use of antibiotics and antibiotics

The risk factors of FI increased with the simultaneous administration of two antibiotics, as the extensive and inappropriate use of broad-spectrum antibiotics can eliminate beneficial gut bacteria, disturb the host's microbial equilibrium, and lead to intestinal dysbiosis.[17, 27, 38] Meanwhile, It has been discovered that intake of probiotics, albumin, and adding glutamine to support the gastrointestinal environment could mitigate FI occurrences.[17, 27] The use of intact protein formulas was also recommended to decrease the consumption of short peptide EN,[18] effectively lowering the risk of gastrointestinal side effects such as diarrhea. Moreover, hyperglycemia is recognized as a risk factor because elevated blood glucose levels can reduce the smooth muscle tone in the gastric sinus, impair sinus dynamics, cause duodenal dyscontractions, and delay gastric emptying.[31]

FI of critically ill patients during EN can be prevented, and accurate risk prediction assessment tools are particularly important. Based on the results of this review, the previously developed models demonstrate high accuracy and have undergone both internal and external validations, integrating their predictive factors into routine clinical assessments.[18, 19, 21] It is advisable to incorporate these predictive indicators into clinical information systems for real-time monitoring to help identify patients at high risk. However, the number of available risk prediction models for FI during EN is currently limited, and the quality of the foundational studies requires enhancement. Thus, future research could focus on improving study quality by refining data sources, selecting and measuring prediction factors, processing missing data,

and evaluating models. Overall, employing the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) reporting guidelines can enhance the accuracy and thoroughness of reports by providing detailed and objective descriptions in six sections, namely, title, abstract introduction, methods, results, discussion and other information, with a total of 22 aspects.

Limitations of this study: This review was restricted to English and Chinese articles published by institutions in China, which might introduce publication bias. It is suggested that the research scope of future investigations be expanded to include studies from other parts of the world to reduce the risk of publication bias and enhance the diversity of the data. The focus of related prediction model studies was primarily on patients in ICU and NICU settings, with less attention given to critically ill patients in other care units. Despite these limitations, the risk prediction models for FI in critically ill patients during EN demonstrated good predictive efficacy. However, improvements are needed in the selection and measurement of predictive factors, handling of missing data, and external validation of models. Furthermore, future investigation of more sophisticated predictive models, together with their improved integration into clinical monitoring systems, is of significant importance in the early detection of potential FI during EN issues in critically ill patients. This is crucial for establishing a robust foundation for high-quality clinical decision-making in practice.

Conclusion

In conclusion, 13 published articles were selected for systematic evaluation, with the results indicating that the models used for predicting the risk of enteral FI in critically ill patients demonstrate relatively good predictive performance. However, a high risk of bias remains. Future researchers may consider incorporating more sensitive and reproducible evaluation indicators for the evaluation of gastrointestinal dysfunction and conducting large-sample multicenter studies with external validation. This would provide a more scientifically reliable reference for the early identification and prevention of FI risk in critically ill patients in clinical practice.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare that there are no conflicts of interest regarding the publication of this article.

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Table 1. Essential characteristics of the included references

Research design	Research type	Research object	Publication year	Modeling sample size (example)	Observation time	Prediction results	Incidence of FI (%)
Retrospective case-control study	Development and validation	Pancreatitis patients in ICU	2019[16]	118	N.A.	FI	41.50%
Prospective observational study	Development and validation	Sepsis patients in ICU	2021[17]	271	Evaluate every 6 h for a total of 7 d	FI	41.20%
Retrospective case-control study	Development	Sepsis patients in ICU	2021[18]	124	N.A.	FI	44.10%
Case-control study	Development	Critical patients	2022[19]	230	Every day at 7:00, 13:00, 19:00	FI	35.20%
Prospective cohort study	Development	Neurological patient in ICU	2022[20]	127	No follow-up	FI	36.20%
Retrospective study	Development and validation	Patients with severe stroke	2022[27]	282	No follow-up	FI	37.94%
Prospective cohort study	Development and validation	Patients in ICU	2022[28]	203	No follow-up	FI	37.93%
Retrospective case-control study	Development and validation	Patients with severe stroke	2023[21]	118	No follow-up	FI	43.27%
Prospective cohort study	Development and validation	Patients in ICU	2023[22]	628	No follow-up	FI	49.00%
Retrospective study	Development and validation	Neurosurgical patients in critical condition	2023[23]	144	No follow-up	FI	47.2%
Retrospective study	Development and validation	Patients in ICU	2024[24]	160	No follow-up	FI	26.25%
Retrospective study	Development and validation	Patients in ICU	2023[25]	140	No follow-up	FI	49.29%
Retrospective study	Development and validation	Patients with severe acute pancreatitis	2023[26]	246	No follow-up	FI	41.87%

N.A. means not not applicable.

Table 2. Performance of the models used for assessing feeding intolerance (FI) in critically ill patients during enteral nutrition

Modeling methods	Publication year	Predictive variables screening method	Model presentation	Prediction performance		Validation	
				Discrimination	Calibration	Internal	External
Logistic regression	2019[16]	χ^2 test	nomogram	AUC=0.857 (95%CI: 0.779~0.931)	/	Bootstrapping	no
Logistic regression	2021[17]	*t*-test, nonparametric test, χ^2 test	nomogram	AUC=0.885 (95%CI: 0.845~0.921) sensitivity = 0.814, specificity = 0.832	H-L goodness-of-fit test: χ^2 = 5.400, p = 0.714	Bootstrapping	no
Logistic regression	2021[18]	The mean with standard deviation for continuous variables, The frequency with percentage for categorical variables.	multilayer artificial neural network model	AUC=0.82 (95%CI: 0.74-0.90)	The calibration curve showed good consistency between predictions and observations	Five-fold cross-validation	yes
Logistic regression	2022[19]	*t*-test, Mann-Whitney U test, χ^2 test	regression equation	AUC=0.879 (95%CI: 0.811~0.947) sensitivity = 0.933 specificity = 0.743	H-L goodness-of-fit test: χ^2 = 5.683, p = 0.683	Bootstrapping	yes
Logistic regression	2022[20]	*t*-test, Mann -Whitney U test, χ^2 test	nomogram	AUC=0.889 (95%CI: 0.821~0.938) Sensitivity = 89.13% specificity = 74.07%	Calibration slope = 0.8092 calibration intercept = − 0.0811	/	no
Logistic regression	2022[27]	χ^2 test or Fisher's exact probability method	regression equation	AUC=0.746 (95%CI: 0.690~0.839)	H-L goodness-of-fit test: χ^2 = 5.889, p = 0.659	Bootstrapping	no
Logistic regression	2022[28]	*t*-test, χ^2 test, Z test	nomogram	AUC=0.70 (95%CI: 0.6~0.77)	Calibration curve	Bootstrapping	no
Logistic regression	2023[21]	*t*-test, Mann-Whitney U test, χ^2 test	nomogram	C-Index=0.879	Calibration curve slope = 1	Bootstrapping	yes
Logistic regression	2023[22]	*t*-test, Mann-Whitney U test, χ^2 test	nomogram	AUC=0.850 (95%CI:0.821~0.879)	H-L goodness-of-fit test, the fitting degree between the calibration curve and the diagonal dashed line was approximately 1	/	yes

AUC: area under the curve of the receiver operating characteristic curve; C-index: concordance index..

Table 2. Performance of the models used for assessing feeding intolerance (FI) in critically ill patients during enteral nutrition

Modeling methods	Publication year	Predictive variables screening method	Model presentation	Prediction performance		Validation	
				Discrimination	Calibration	Internal	External
Logistic regression	2023[23]	Two sample *t*-test, Mann-Whitney U test, χ^2 test or Fisher's exact test	nomogram	AUC=0.860 (95%CI:0.810~0.928) specificity = 0.803 sensitivity = 0.838	H-L goodness-of-fit test: χ^2 = 5.601, p = 0.692	/	no
Logistic regression	2024[24]	χ^2 test	Regression analysis	AUC=0.904 (95%CI:0.864~0.944) sensitivity = 0.889 specificity = 0.766	H-L goodness-of-fit test: χ^2 = 1.507, p = 0.158	/	yes
Logistic regression	2023[25]	*t*-test, nonparametric test, χ^2 test	nomogram	AUC= 0.906 (95%CI:0.783~1.000) Maximum constraint index 0.192, specificity = 0.833, sensitivity = 0.875	/	Bootstrapping	no
Logistic regression	2023[26]	χ^2 test	nomogram	AUC=0.793 (95%CI:0.735~0.851) The maximum value of the Youden's index was 0.498, sensitivity = 81.8%, specificity = 68%	H-L goodness-of-fit test: χ^2 = 3.481, p = 0.901	/	no

AUC: area under the curve of the receiver operating characteristic curve; C-index: concordance index..

Table 3. Risk factors identified in models used for the prediction of feeding intolerance in critically ill patients receiving enteral nutrition

Predictive factors number	The final included predictive factors	Model presentation format	Publication year	Applicability and limitations
7	Age, APACHE II score, fasting blood glucose, starting time of EN, addition of dietary fiber, intra-abdominal pressure, central venous pressure	nomogram	2019[16]	Good applicability, but limitations not mentioned
7	AGI grade, starting time of EN, average infusion speed, C-reactive protein, albumin, early enema, addition of glutamine	nomogram	2021[17]	Good applicability, but the sample size was small, single-center, and not externally validated
15	Infection site, nutritional type, shock, continuous feeding, coronary artery disease, antibiotics category, chronic obstructive pulmonary disease, mechanical ventilation, hypertension, stroke, intra-abdominal pressure, and analgesia	Online prediction Tool chart	2021[18]	A dual-center retrospective observational study with a small sample size
4	APACHEE II score, NRS2002 score, intra-abdominal pressure and albumin	regression equation	2022[19]	There was no further validation of the model, and the sample lacked multicenter evidence to support it.
7	hypertension, mechanical ventilation, analgesic and sedative drugs, hyperkalemia, hyperglycemia, ICU stay days	nomogram	2022[20]	Good applicability, however, the study was limited by a small, single-center sample size.
4	age ≥ 60 years old, application of more than 2 antibacterial agents, implementation of mechanical ventilation, use of probiotics	regression equation	2022[27]	Good applicability, but the sample size was small and single-center
5	Age, gastrointestinal diseases, early feeding, initiation of mechanical ventilation before EN, abnormal serum sodium levels	rating scale	2022[28]	Good applicability, but the study was constrained by a small, single-center sample size and had limited representations.
6	Age, APACHEE II score, time in bed, albumin, vasoactive drugs, bedside angle	nomogram	2023[21]	Good applicability, but the sample size was small
3	primary diagnosis, AGI grading, APACHE II score	nomogram	2023[22]	The study was conducted with a small, single-center sample size, which could introduce some selection bias. Additionally, there were variations in baseline conditions between patients with primary and secondary acute gastrointestinal injury (AGI), and the data was not reanalyzed for subgroups.
4	Mean arterial pressure, Glasgow Coma Score, combination of more than 2 antibiotics, intake and output	nomogram	2023[23]	Good applicability, but the sample size was small and the study was retrospective
7	age >70 years old, bowel sounds <2 per minute, blood glucose ≥12mmol/L, EEN initiation time >48 h, no bed head elevation of 30°, APACHII score >20, no dietary fiber added	Regression analysis	2024[24]	The sample size was small
5	APACHE II score, mNutric score, CRRT, intra-abdominal pressure, low calorific energy	nomogram	2023[25]	Good applicability, but the sample size was small, and the study was retrospective in nature
6	hypertriglyceridemia, hypoproteinemia, intra-abdominal pressure ≥12 mm Hg, APACHE Ⅱ score ≥ 20, starting time of EN ≥72 h, addition of micro-ecological agents	nomogram	2023[26]	Good applicability, but the sample size was small, and the study was retrospective in nature

APACHE II (Acute Physiology and Chronic Health Evaluation, Acute Physiology and Chronic Health Status Score), Acute gastrointestinal injury (AGI) grade, the modified Nutrition Risk in the Critically ill (mNutric), and Continuous Renal Replacement Therapy (CRRT).

Table 4. Quality evaluation of the included studies

Reference publication year	Research objects	Predictive factors	Result	Statistical analysis	Total bias risk
2019[16]	High bias	Low bias	Not sure	High bias	High bias
2021[17]	High bias	Not sure	Not sure	High bias	High bias
2021[18]	Low bias	Not sure	Not sure	High bias	High bias
2022[19]	High bias	Low bias	Low bias	High bias	High bias
2022[20]	High bias	Low bias	Low bias	High bias	High bias
2022[27]	Low bias	Low bias	Low bias	High bias	High bias
2022[28]	High bias	Low bias	Low bias	High bias	High bias
2023[21]	Low bias	Low bias	Low bias	Low bias	Low bias
2023[22]	High bias	Low bias	Low bias	Low bias	High bias
2023[23]	High bias	Low bias	Low bias	High bias	High bias
2024[24]	High bias	Low bias	Low bias	High bias	High bias
2023[25]	High bias	Low bias	Low bias	High bias	High bias
2023[26]	High bias	Low bias	Low bias	High bias	High bias

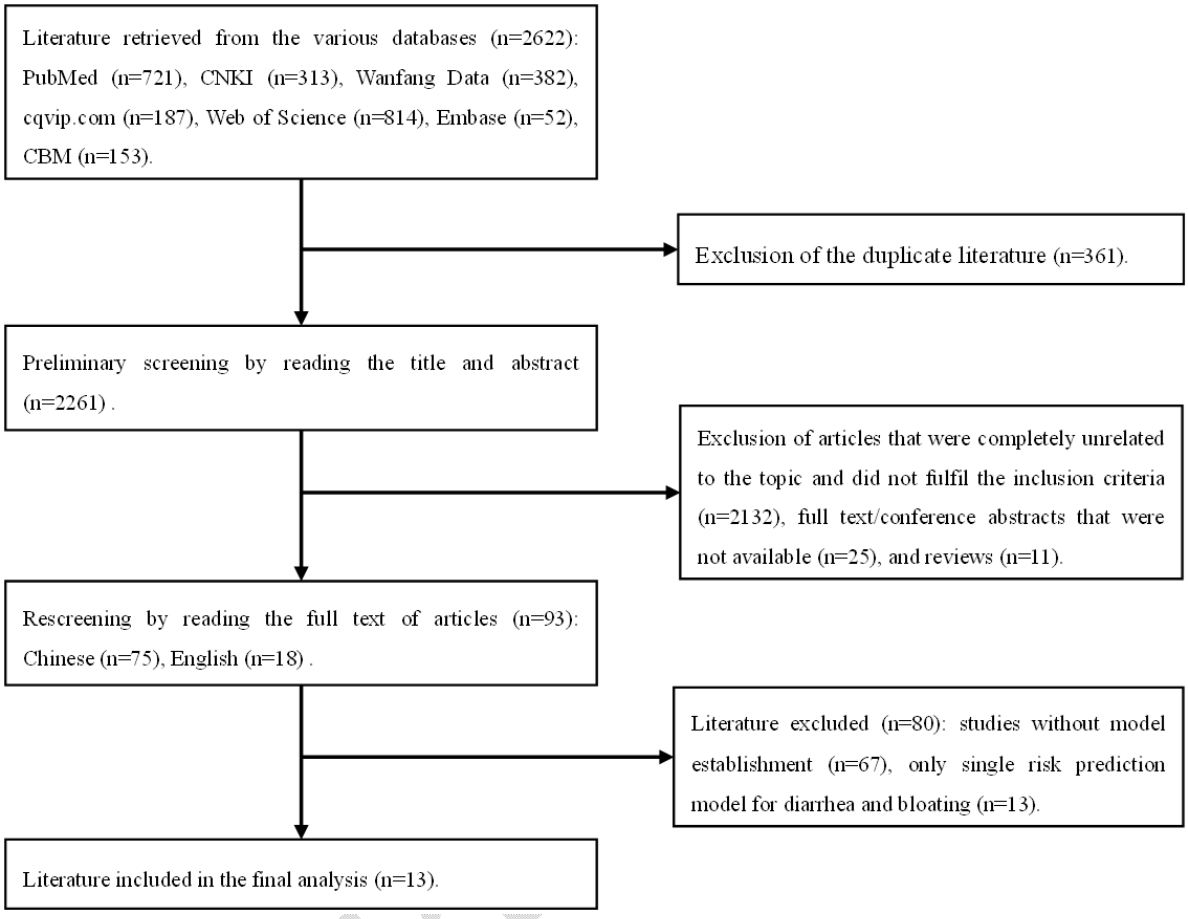

Figure 1. Flowchart of the literature screening process.