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ARTICLE

Development and internal validation of an artificial intelligence-assisted bowel sounds auscultation system to predict early enteral nutrition-associated diarrhoea in acute pancreatitis: a prospective observational study

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Abstract

Aims/Background An artificial intelligence-assisted prediction model for enteral nutrition-associated diarrhoea (ENAD) in acute pancreatitis (AP) was developed utilising data obtained from bowel sounds auscultation. This model underwent validation through a single-centre, prospective observational study. The primary objective of the model was to enhance clinical decision-making by providing a more precise assessment of ENAD risk.

Methods The study enrolled patients with AP who underwent early enteral nutrition (EN). Real-time collection and analysis of bowel sounds were conducted using an artificial intelligence bowel sounds auscultation system. Univariate analysis, multicollinearity analysis, and logistic regression analysis were employed to identify risk factors associated with ENAD. The random forest algorithm was utilised to establish the prediction model, and partial dependence plots were generated to analyse the impact of risk factors on ENAD risk. Validation of the model was performed using the optimal model Bootstrap resampling method. Predictive performance was assessed using accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and an area under the receiver operating characteristic (ROC) curve.

Results Among the 133 patients included in the study, the incidence of ENAD was 44.4%. Six risk factors were identified, and the model's accuracy was validated through Bootstrap iterations. The prediction accuracy of the model was 81.10%, with a sensitivity of 84.30% and a specificity of 77.80%. The positive predictive value was 82.60%, and the negative predictive value was 80.10%. The area under the ROC curve was 0.904 (95% confidence interval: 0.817–0.997).

Conclusion The artificial intelligence bowel sounds auscultation system enhances the assessment of gastrointestinal function in AP patients undergoing EN and facilitates the construction of an ENAD predictive model. The model demonstrates good predictive efficacy, offering an objective basis for precise intervention timing in ENAD management.

Key words: Acute pancreatitis; Artificial intelligence; Auscultation; Bowel sounds; Enteral nutrition-associated diarrhea

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Introduction

Acute pancreatitis (AP) is a severe metabolic disorder triggered by the release of amylase, lipase, toxins, and cytokines, leading to heightened metabolism and negative nitrogen balance. Left untreated, it can precipitate multiple organ system failures (Gomes et al, 2020), prolong hospitalisation, and elevate mortality rates (Ramanathan and Aadam, 2019; Lakananurak and Gramlich, 2020). Enteral nutrition (EN) stands as the preferred primary nutritional route for AP patients, as per the guidelines of the American Society for Parenteral and Enteral Nutrition (ASPEN). However, clinical investigations reveal that approximately 30.5% to 65.7% of AP patients encounter intolerance to enteral nutrition,

with a notably high incidence of diarrhoea ranging from 46% to 77% (Chen et al, 2017). This intolerance can disrupt or suspend enteral nutrition, delay the achievement of target energy intake, compromise overall nutritional status, and escalate the risk of complications and mortality (Gungabissoon et al, 2015; Qiu et al, 2017). Consequently, the exploration of alternative nutritional support strategies is imperative for AP patients.

In the enteral nutrition process for patients with AP, a comprehensive and dynamic assessment of gastrointestinal function holds pivotal importance in averting enteral nutrition-associated diarrhoea (ENAD) and adverse outcomes stemming from energy and protein depletion (Xie et al, 2022). In 2016, ASPEN released updated guidelines for nutrition support in critically ill patients, underscoring the necessity of a comprehensive and stratified evaluation of ENAD complications (Mehta et al, 2017). However, traditional manual auscultation of bowel sounds is subjective, prone to diagnostic oversights, and has even been recommended for discontinuation in clinical practice (Madsen et al, 2005). With the advancement of artificial intelligence (AI) technology, digital bowel sound detection devices offer objective, quantitative, and visualised data presentation for clinical utility. These devices have found application in aiding the diagnosis of irritable bowel syndrome (IBS) (Craine et al, 1999; Du et al, 2019), predicting postoperative intestinal obstruction (Spiegel et al, 2014; Kaneshiro et al, 2016), assessing the effects of anaesthetics and surgical interventions on gastrointestinal motility (Wang et al, 2020), and providing robust evidence for early initiation of water and food intake in enhanced recovery after surgery (ERAS) protocols (Pan et al, 2020; Wang et al, 2022). Nevertheless, this non-invasive real-time monitoring tool for bowel sounds has yet to be applied in early ENAD studies of AP.

The objective of this study is twofold: firstly, to develop a predictive model for ENAD in AP using the random forest algorithm and parameters obtained from a digital bowel sound detection system. Secondly, the study aims to identify early-stage risk factors for ENAD, which can facilitate determining the optimal timing for enteral nutrition intervention in AP patients.

Methods

Study design and definitions

This prospective observational study was conducted at Jiangsu Province Hospital of Chinese Medicine affiliated with Nanjing University of Chinese Medicine from June 2018 to October 2023. The study recruited patients diagnosed with acute pancreatitis (AP) who underwent enteral nutrition. This study has been approved by the Ethics Committee of Jiangsu Province Hospital of Chinese Medicine (2023NL-136-02) and all patients have provided informed consent. Criteria for enteral nutrition-associated diarrhoea (ENAD) were established based on relevant literature (Yuan, 2012; Reintam Blaser et al, 2015) and defined as follows: bowel movement frequency of ≥ 3 times/day, stool volume of ≥ 200 g/day, daily score on The King's of Stool Chart (Whelan et al, 2004) of ≥ 15 points, and exclusion of antibiotic-associated diarrhoea and infectious diarrhoea. Patients were categorised into ENAD and non-ENAD groups based on the occurrence of diarrhoea. The final follow-up was completed on 10 October 2023.

Participants

In this study, patients were included if they met the following criteria: (1) Diagnosis criteria in accordance with the 2012 revised international consensus of Atlanta classification and definition (Banks et al, 2013); (2) Severity grading criteria were developed based on the revised Atlanta classification, including moderate-severe acute pancreatitis (MSAP) and severe acute pancreatitis (SAP); (3) Age ≥ 18 years; (4) Acute onset with typical abdominal symptoms occurring within 72 hours before admission; (5) No nutritional support before admission; (6) Nasoenteric nutrition tube enteral nutrition after admission; (7) Diarrhoea occurred during the enteral nutrition period; (8) Bowel sounds were detected by a digital bowel sound detection system after admission. Patients were excluded if they met any of the following criteria: (1) Diarrhoea present on admission; (2) Enema or use of laxatives during hospitalisation; (3) Other diseases that can cause diarrhoea, such as

inflammatory bowel disease and irritable bowel syndrome; (4) Confirmed antibiotic-related or infectious diarrhoea.

Method for monitoring bowel sounds

The intestinal sound dynamic recorder (YM-TYJL-01, production batch number: TPD181202, Shandong Yimai Medical Technology Co., Ltd., Liaocheng, China) consists of a YM-TYTP-04 acquisition patch, a YM-TYJS-02 receiver, a YM-TYNFC-02 Near Field Communication (NFC) reader, and bowel sound analysis software V2.0.0. Patient accounts are registered in the bowel sound analysis software, and the acquisition patch is activated using the NFC reader. The patch is then placed on the middle and inner third of the navel to the right anterior superior iliac spine line. The patch transmits the original signal to the receiver via Bluetooth, where it undergoes noise reduction processing. The system utilises a Convolutional Recurrent Neural Network (CRNN) to recognise, analyse, and generate a feature-type intestinal sound spectrum (Figure 1, created using Meitu Version 6.5.7.0, Xiamen Meitu Technology Co., Xiamen, China).

The study measured five parameters of bowel sounds: bowel sound rate (BSR, the average number of bowel sounds per minute), bowel sound duration (BSD, the time required for a single bowel sound), bowel sound amplitude (BSA, the width of the bowel sound waveform oscillation in the frequency domain), bowel sound frequency (BSF, the characteristic frequency of the bowel sound waveform in the frequency domain), and bowel sound interval (BSI, the average time interval between two bowel sounds) (Figure 2). Previous clinical trial data have demonstrated that the specificity and sensitivity of this instrument exceed 90% (Pan et al, 2020).

Nutrition protocol

All patients underwent enteral nutrition therapy. On the first day, normal saline (100 mL) was administered via nasoenteric tube at a rate of 50 mL/h pumped into the intestine. If no adverse symptoms occurred, enteral nutrition suspension Bipei Li 500 mL/bottle (1 kcal/mL) was administered on the same day. The initial infusion rate was set at 20 mL/h and continued for 24 hours, with the rate gradually increasing daily based on the patient's tolerance. The target energy for the first day was 250 mL and 250 kcal. By 24–48 hours (the second day), the rate increased to 31–50 mL/h, aiming for a target energy of 500–750 mL and 500–750 kcal. By 48–72 hours (the third day), the rate was adjusted to 51–79 mL/h, targeting an energy intake of 751–1500 mL and 751–1500 kcal. The objective was to achieve a caloric intake of 25 kcal/(kg·d) within 72 hours, with a benchmark calorie intake range of 80–120 mL/h. The enteral nutrition plan was documented accordingly (**Supplementary Table 1**). Patient demographic information was collected within 24 hours of admission.

Data collection

The survey tools were established based on a literature review (Craine et al, 1999; Dimoulas et al, 2011; Kim et al, 2011; Ching and Tan, 2012; Chen et al, 2019; Kurisu et al, 2019; Xie et al, 2022) and consultations with a chief physician specialising in pancreatitis, a deputy

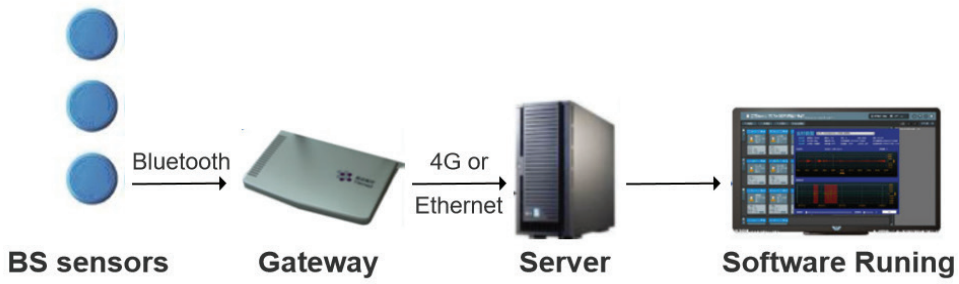

Figure 1. General perspective on recording intestinal sounds using artificial intelligence. BS, bowel sound.

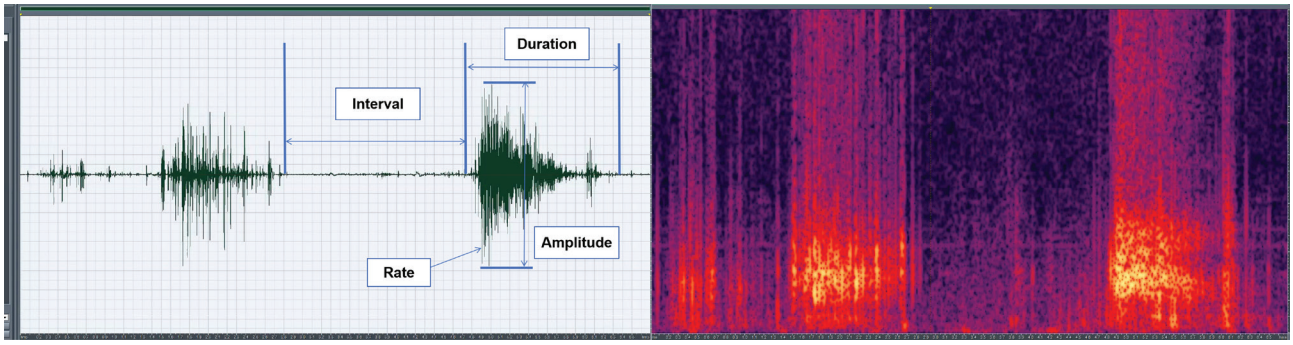

Figure 2. Parameter chart for an artificial intelligence intestinal sound auscultation system.

head nurse, and a nutrition specialist nurse. The tools comprised three parts: (1) Baseline data, including age, gender, weight, height, and body mass index (BMI); (2) Clinical data, such as the gastroparesis cardinal symptom index revised (GCSI-R) scale measured at admission and on EN days 1–4 and 7, the bedside index of severity in acute pancreatitis (BISAP), and bowel sound parameters before and after EN. Additionally, recorded were actual enteral nutrition intake, target amount, duration of EN, frequency, weight, viscosity, number, and time of flatulence and defaecation; (3) Laboratory indicators, including serum C-reactive protein, serum albumin (ALB), and serum pre-albumin (PAB) concentrations measured at admission and on EN days 1–4 and 7.

Sample size

According to the requirements of multivariate analysis, the sample size should be estimated as 5–10 times the number of independent variables in the regression model (Ni et al, 2010). Initially, this study included 12 independent variables. Considering a 10% data loss rate, a minimum sample size of 66 cases was required. Ultimately, the study included 133 cases.

Statistical analysis

Data entry and statistical analyses were conducted using Excel 2010 and R 4.2.1 software (R Foundation for Statistical Computing, Vienna, Austria). To ensure data consistency, two individuals independently entered the data into Excel 2010, and any discrepancies were resolved through cross-checking. Descriptive statistics, such as mean and standard deviation (SD), were used for normally distributed continuous variables, and between-group differences were assessed using two-sample independent *t*-tests. Median and quartiles were employed for non-normally distributed continuous variables, with between-group differences assessed using Mann-Whitney U tests. Categorical variables were described using frequency, percentage, or ratio, and between-group differences were assessed using chi-square tests. Univariate analysis, multicollinearity analysis, and two-way stepwise logistic regression analysis were utilised to identify risk factors. Variables showing statistical significance in univariate analysis were assessed for multicollinearity, with a variance inflation factor (VIF) ≥5 indicating serious multicollinearity (Wang, 2015). In such cases, variable deletion was necessary before logistic regression analysis.

In R 4.2.1 software, the mtry and ntree values were tuned using tenfold cross-validation for the 133 patients, and the lowest error rate determined the optimal predictive performance of the random forest model. The importance of risk factors was ranked by calculating the average drop in prediction accuracy before and after variable permutation. Partial dependence plots were utilised to visualise the effect of a risk factor on model prediction results while holding other variables constant. The area under the receiver operating characteristic curve (AUC) was calculated. The random forest model underwent internal validation using Bootstrap resampling, 1000 times. Evaluation metrics included accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and AUC. Statistical significance was set at $p < 0.05$, with appropriate citations provided for references.

Results

General information of patients before enteral nutrition

Out of 138 patients deemed eligible based on the inclusion criteria, 133 were included in the final analysis (Figure 3). The characteristics of the recruited patients are summarised in Table 1. While 138 patients were initially considered eligible, 133 were ultimately included in the analysis (Figure 3). The general characteristics of both patient groups were comparable, except for the $BISAP_0$ index, which showed statistically significant differences ($p < 0.05$). There were no significant differences observed in the other indicators ($p > 0.05$, Table 1).

Risk factors for enteral nutrition-associated diarrhoea in acute pancreatitis: analysis of single and multiple factors

The single-factor analysis outcomes demonstrated statistically significant differences ($p < 0.05$) in GCSI-R_1, GCSI-R_3, PAB_2, PAB_3, enteral nutrition volume of the second day (V_2), V_3, BSR_2, BSR_5, BSD_2, BSD_5, BSA_1, and BSF_1 between the ENAD and non-ENAD groups (Table 2). Following multiple collinearity analysis of the 12 variables displaying statistical significance in the single-factor analysis, it was found that the VIF for each variable ranged from 1.235 to 2.606, indicating the absence of multicollinearity. Subsequently, a bidirectional stepwise regression was employed to select the 12 variables as independent variables, with the incidence of ENAD as the dependent variable for logistic regression analysis. The results of the logistic regression analysis identified V_2, BSA_1, BSF_1, BSR_2, PAB_3, and $BISAP_0$ as risk factors for ENAD in patients with AP ($p < 0.05$) (Table 3).

Development of a risk prediction model for enteral nutrition-associated diarrhoea in acute pancreatitis patients

The tenfold cross-validation results indicated that the early prediction model for ENAD in AP achieved optimal predictive capability when ntree=325 and mtry=1, resulting in the lowest error rate. The model demonstrated an accuracy of 82.71% (95% CI: 0.752–0.887),

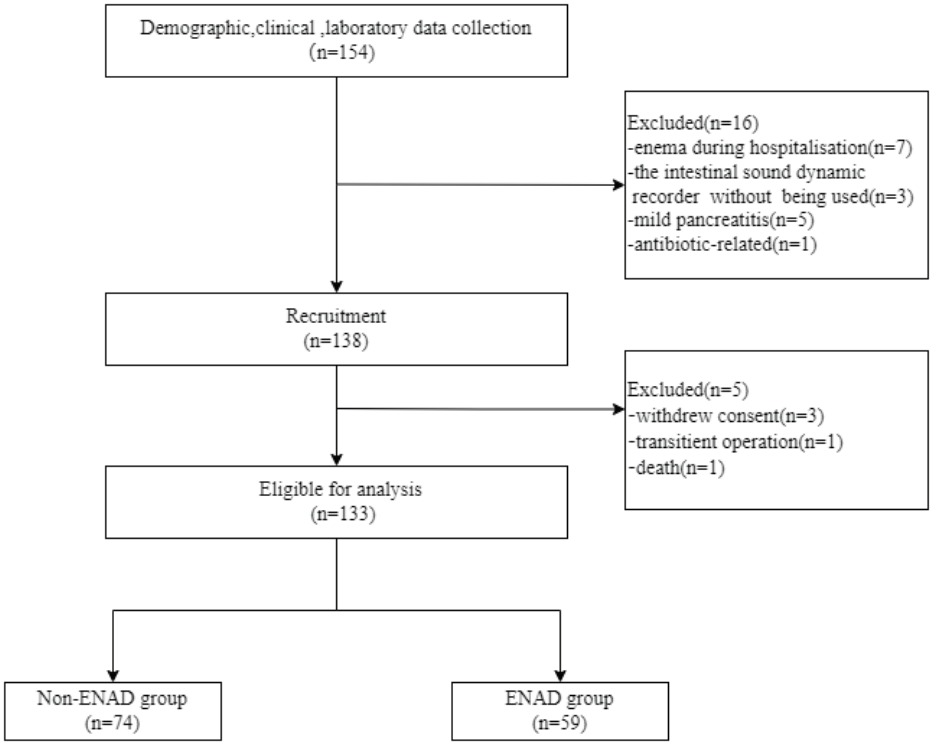

Figure 3. Flowchart for enrolment. ENAD, enteral nutrition-associated diarrhoea.

Table 1. Characteristics of non-enteral nutrition-associated diarrhoea and enteral nutrition-associated diarrhoea patients

Variable	Overall (n=133)	Non-ENAD (n=74)	ENAD (n=59)	$t/\chi^2/Z$	*p* value
Age (Y)[b]	51 (41,61)	48.5 (39,60.5)	55 (44.5,65.5)	–1.815[3]	0.070
Male[a]	65 (48.9%)	36 (48.6%)	29 (49.2%)	0.003[2]	0.954
Female[a]	68 (51.1%)	38 (51.4%)	30 (50.8%)		
BMI at baseline (kg/m^2)[a]	24.79 ± 3.11	24.60 ± 3.30	25.03 ± 2.88	–0.800[1]	0.425
$BISAP_0$ Score[b]	1 (1,2)	1 (1,1)	2 (1,3)	–4.885[3]	< 0.001
GCSI-R_0 Score[b]	4 (3,6)	4 (3,5.75)	4 (3.5,6)	–0.044[3]	0.965
BSR_0 (Times/min)[b]	3.45 (2.42, 4.57)	3.78 (2.31, 5.45)	3.23 (2.45, 4.34)	–1.477[3]	0.140
BSD_0 (s/min)[a]	0.16 ± 0.08	0.16 ± 0.09	0.16 ± 0.08	–0.243[1]	0.808
BSA_0 (db)[a]	29.20 ± 10.03	29.94 ± 10.05	28.17 ± 9.99	0.982[1]	0.328
BSF_0 (Hz)[a]	723.58 ± 283.36	702.68 ± 295.17	749.81 ± 267.98	–0.953[1]	0.337
BSI_0 (s)[b]	9.54 (8.17, 11.36)	10.12 (8.36, 11.69)	9.40 (7.48, 11.01)	–1.635[3]	0.102
ALB_0 (g/L)[a]	39.57 ± 5.70	39.51 ± 5.99	39.64 ± 5.36	–0.1316[1]	0.893
PAB_0 (mg/L)[a]	155.63 ± 51.00	158.96 ± 53.00	151.46 ± 48.49	0.850[1]	0.397

[a] Data are presented as the means ± standard deviation (SD) for continuous variables or absolute n (%) for categorical variables.

[b] Data are presented as the medians (interquartile range). Patients were included in summary tables via the intention-to-treat principle.

[1] Independent samples t-test.

[2] Pearson's chi-square test.

[3] Mann-Whitney U test.

BMI at baseline: body mass index on the first day of admission; $BISAP_0$ Score: beside index of severity in acute pancreatitis on the first day of admission; GCSI-R_0 Score: gastroparesis cardinal symptom index revised on the first day of admission; BSR_0: bowel sound rate on the first day of admission; BSD_0: bowel sound duration on the first day of admission; BSA_0: bowel sound amplitude on the first day of admission; BSF_0: bowel sound frequency on the first day of admission; BSI_0: bowel sound interval on the first day of admission; ALB_0: serum albumin on the first day of admission; PAB_0: serum pre-albumin on the first day of admission; SD: standard deviation; ENAD: enteral nutrition-associated diarrhoea.

a Kappa value of 0.71, sensitivity of 83.78%, specificity of 81.36%, positive predictive value of 84.93%, and negative predictive value of 80.00% (Table 4).

Importance analysis of enteral nutrition-associated diarrhoea risk factors in acute pancreatitis patients

The random forest algorithm was utilised to rank the importance of risk factors, demonstrating that V_2, BSA_1, BSF_1, BSR_2, PAB_3, and $BISAP_0$ significantly contributed to the accuracy of the model (Table 5).

Risk factors analysis for enteral nutrition-associated diarrhoea in acute pancreatitis patients: partial dependence results

When mtry=1, the error rate is at its lowest. Subsequently, we generated partial dependence plots for the top six significant risk factors. On the second day of enteral nutrition, the risk of ENAD is at its highest, reaching approximately 80%, when the average total intake of enteral nutrition is below 800 mL, and intake is between 200–400 mL. As enteral nutrition intake increases, the risk of ENAD decreases, and when the intake is above 400 mL, the risk of ENAD rapidly drops. At 600–800 mL, the occurrence rate of ENAD gradually decreases to 40% and stays consistent (Figure 4A). On the first day of enteral nutrition, when the average BSA_1 is below 50 db, the risk of ENAD slowly rises with an increase in sound level, reaching over 60% when the sound level is between 30–40 db (Figure 4B). On the first day of enteral nutrition, when the average BSF_1 fluctuates below 2500 HZ, the risk of ENAD is almost 70% within the range of large bowel sounds of approximately 0–100 HZ. As the audio value increases, the risk slowly decreases from almost 70% to 40% (Figure 4C). On the second day of enteral nutrition, when BSG_2 fluctuates between 0–35 times/min, the risk of ENAD gradually increases with an increase in BSG_2, from around

Table 2. Single-factor analysis results of enteral nutrition-associated diarrhoea in patients with acute pancreatitis

Variable	Non-ENAD group (n=74)	ENAD group (n=59)	*t*/Z	*p* value
GCSI-R_1 Score[b]	4.00 (3.00, 6.00)	5.00 (2.00, 11.00)	–2.091[3]	0.037
GCSI-R_3Score[b]	8.00 (7.00, 12.00)	15.00 (14.00, 16.00)	–8.831[3]	< 0.001
PAB_2 (mg/L)[b]	142 (100.00, 170.50)	113.00 (91.00, 142.00)	2.663[3]	0.008
PAB_3 (mg/L)[a]	144.88 ± 48.97	120.23 ± 48.22	2.908[1]	0.004
V_2 (mL)[a]	612.28 ± 97.96	499.20 ± 142.17	5.203[1]	< 0.001
V_3 (mL)[b]	1067.00 (1004.25, 1143.50)	708.00 (541.50, 886.00)	8.553[3]	< 0.001
BSR_2 (Times/min)[b]	3.14 (2.12, 5.14)	4.31 (2.44, 9.21)	–2.079[3]	0.038
BSR_5 (Times/min)[b]	3.97 (2.65, 5.75)	3.35 (2.15, 4.15)	2.702[3]	0.007
BSD_2 (s/min)[b]	0.15 (0.11, 0.20)	0.20 (0.15, 0.25)	–3.001[3]	0.003
BSD_5 (s/min)[b]	0.20 (0.16, 0.24)	0.17 (0.12, 0.22)	2.402[3]	0.016
BSA_1 (db)[b]	15.40 (10.25, 22.38)	27.55 (16.95, 34.83)	–4.334[3]	< 0.001
BSF_1 (Hz)[b]	736.49 (602.11, 1001.08)	718.35 (391.77, 983.26)	2.4[3]	0.019

GCSI-R_1 Score, GCSI-R_3 Score: gastroparesis cardinal symptom index revised scores of the first day and the third day of enteral nutrition, respectively; PAB_2, PAB_3: serum pre-albumin of the second day and the third day of enteral nutrition, respectively; V_2, V_3: enteral nutrition volume of the second day and the third day, respectively; BSR_2, BSR_5: bowel sound rates of the second day and the fifth day of enteral nutrition, respectively; BSD_2, BSD_5: bowel sound durations of the second day and the fifth day of enteral nutrition, respectively; BSA_1: bowel sound amplitude of the first day of enteral nutrition; BSF_1: bowel sound frequency of the first day of enteral nutrition. SD: standard deviation.

[a] Data are presented as the means ± standard deviation (SD) for continuous variables or absolute n (%) for categorical variables.

[b] Data are presented as the medians (interquartile range). Patients were included in summary tables via the intention-to-treat principle.

[1] Independent samples t-test.

[3] Mann-Whitney U test.

Table 3. Results of multivariate logistic regression analysis for enteral nutrition-associated diarrhoea in patients with acute pancreatitis

	B value	Standard error	Wald value	*p* value	*OR* value	95% CI
Constant	4.963	1.954	6.448	0.011	142.985	3.792–8934.490
GCSI-R_1 Score	–0.014	0.078	0.033	0.855	0.986	0.846–1.153
PAB_3	–0.015	0.006	6.085	0.014	0.985	0.972–0.996
V_2	–0.008	0.003	8.545	0.003	0.992	0.987–0.997
$BISAP_0$ Score	0.838	0.308	7.382	0.007	2.311	1.297–4.405
BSR_2	0.169	0.063	7.149	0.008	1.184	1.050–1.360
BSA_1	0.139	0.037	14.203	< 0.001	1.150	1.078–1.248
BSF_1	–0.004	0.001	10.849	< 0.001	0.996	0.993–0.998
BSD_5	–6.083	3.659	2.764	0.096	0.002	0.000–1.550

GCSI-R_1 Score: gastroparesis cardinal symptom index revised score of the first day of enteral nutrition; PAB_3: serum pre-albumin of the third day of enteral nutrition; V_2: enteral nutrition volume of the second day; $BISAP_0$ Score: beside index of severity in acute pancreatitis score on the first day of admission; BSR_2: bowel sound rate of the second day of enteral nutrition; BSA_1: bowel sound amplitude of the first day of enteral nutrition; BSF_1: bowel sound frequency of the first day of enteral nutrition; BSD_5: bowel sound duration of the fifth day of enteral nutrition; CI: confidence interval.

40% to over 60% (Figure 4D). On the third day of enteral nutrition, when the average PAB_3 concentration fluctuates between 30–280 mg/L, the risk of ENAD is at its highest, reaching around 70% when the average PAB_3 concentration is 50 mg/L. As the average PAB_3 concentration rises, the risk slowly decreases to approximately 40% (Figure 4E).

Table 4. The parameters table of risk prediction model for enteral nutrition-associated diarrhoea in patients with acute pancreatitis

Parameters	Value
Accuracy	82.71% (95% CI: 0.752–0.887)
Kappa value	0.71
Sensitivity	83.78%
Specificity	81.36%
Positive predictive value	84.93%
Negative predictive value	80.00%

Table 5. Results of importance analysis for risk factors associated with enteral nutrition-associated diarrhoea in patients with acute pancreatitis

Independent variable	Importance ranking	Average decline in prediction accuracy (%)
V_2	1	8.29
BSA_1	2	6.15
BSF_1	3	3.71
BSR_2	4	2.06
PAB_3	5	1.80
$BISAP_0$	6	4.26

V_2: enteral nutrition volume of the second day; BSA_1: bowel sound amplitude of the first day of enteral nutrition; BSF_1: bowel sound frequency of the first day of enteral nutrition; BSR_2: bowel sound rate of the second day of enteral nutrition; PAB_3: serum pre-albumin of the third day of enteral nutrition; BISAP0 Score: beside index of severity in acute pancreatitis score on the first day of admission; BSR_2: bowel sound rate of the second day of enteral nutrition.

The relationship between pre-enteral nutrition $BISAP_0$ and the risk of ENAD follows a "slow mountain slope" pattern. When BISAP is between 0–3, the occurrence rate of ENAD gradually increases from almost 30% to 60% with an increase in BISAP. When BISAP is between 3–4 points, the occurrence rate of diarrhoea drops to 50% (Figure 4F).

Internal validating a risk model for enteral nutrition-associated diarrhoea in acute pancreatitis patients

The model underwent internal validation through, 1000 rounds of Bootstrap resampling, yielding an accuracy of 81.10%, sensitivity of 84.30%, specificity of 77.80%, positive predictive value of 82.60%, and negative predictive value of 80.10%. Furthermore, the area under the ROC curve was 0.904 (95% CI: 0.817–0.997) with a cut-off value of 0.737 (95% CI: 0.750–0.882) (Figure 5).

Discussion

In the present study, we have devised a predictive model for early-onset ENAD among patients suffering from AP through the use of the random forest algorithm and an AI-based bowel sound auscultation system. By quantifying the association between gut-associated risk factors for ENAD and the corresponding risk, we have facilitated quick and accurate identification of the risk of diarrhoea, thereby enhancing awareness and prevention of the same. Our model offers precise and proactive medical care.

The existing conventional method for auscultating bowel sounds mainly relies on manual auscultation, which is susceptible to individual differences in hearing and experience of the auscultator, leading to doubts about its accuracy. Gade et al (1998) found that the

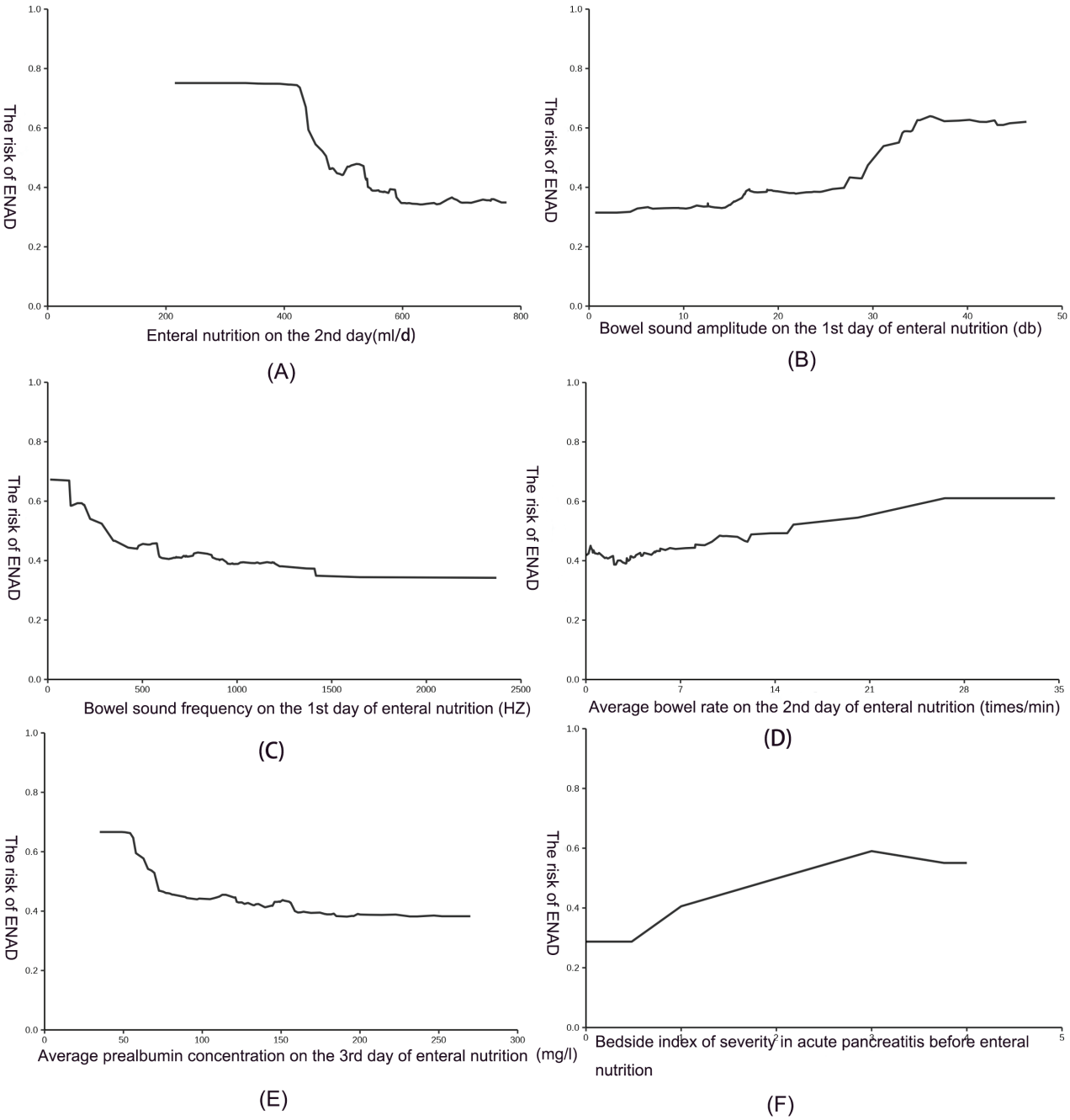

Figure 4. Partial dependence plots depicting the relationship between enteral nutrition and the risk of diarrhoea in patients with acute pancreatitis. (A) Enteral nutrition on the second day. (B) Bowel sound amplitude on the first day of enteral nutrition. (C) Bowel sound frequency on the first day of enteral nutrition. (D) Average bowel rate on the second day of enteral nutrition. (E) Average prealbumin concentration on the third day of enteral nutrition. (F) Bedside index of severity in acute pancreatitis before enteral nutrition.

accuracy rate of medical personnel in auscultating normal bowel sounds was 72%, and the misdiagnosis rate for abnormal bowel sounds was as high as 36%. Gu et al (2010) reported that the accuracy rates of auscultating bowel sounds for normal individuals, mechanical intestinal obstruction patients, and paralytic intestinal obstruction patients by doctors were 84.5%, 78.1%, and 72.7%, respectively. Meanwhile, when nursing students were instructed to auscultate bowel sounds on the abdomen, they were required to auscultate each quadrant for 3–5 minutes (Evans et al, 2009), a total of 20 minutes, which can lead to auscultation fatigue and waste of time, thus only collecting immediate data on bowel sounds. A clinical survey (Madsen et al, 2005) showed that 80% of nurses actually auscultated bowel sounds

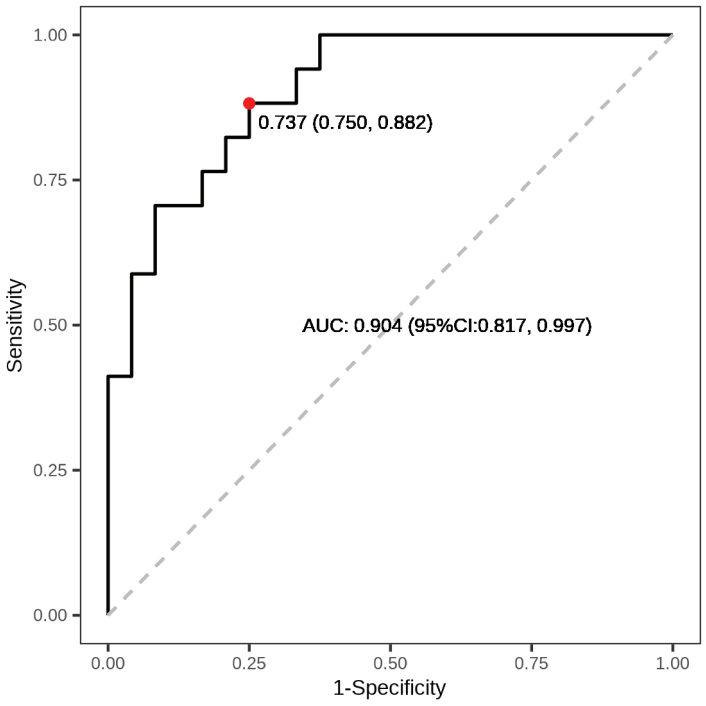

Figure 5. Receiver operating characteristic curve of the risk prediction model for enteral nutrition-associated diarrhoea in patients with acute pancreatitis. AUC, the area under the receiver operating characteristic curve.

for less than 1 minute per quadrant, which can result in missed diagnosis of abnormal bowel sounds. In contrast, the non-invasive, wearable AI bowel sound auscultation device used in this study has the ability to monitor and record bowel sound data in real time for a long time. Through AI methods such as CRNN recognition and analysis, it can assist in ENAD's decision-making process, reduce medical errors, save medical time, and predict risks (He et al, 2019; Sakamoto et al, 2022). This device has undergone preliminary volunteer testing, and its specificity and sensitivity have both reached 90%.

In the current study, the selection of an AI bowel sound system for detection is based on the principle that bowel sounds are generated by the activity and mechanical characteristics of the intestine (Felder et al, 2014). Therefore, the variability of bowel sound auscultation is associated with the condition of the intestine (Mansy and Sandler, 2000). Meanwhile, the baseline selection is based on the principle of GCSI-R, which uses the GCSI-R scale to assess gastrointestinal function. This self-assessment scale was initially developed by Revicki et al (2003) with three dimensions and nine items and later revised by Ma et al (2016) to include three dimensions and eight items, for self-evaluation of symptoms in patients with gastroparesis, including those with mild to SAP who require nasogastric feeding. The Chinese version of the GCSI-R was translated by Wang et al (2019), with a Cronbach's α coefficient of 0.765 and a test-retest reliability of 0.805. It is used to evaluate early gastrointestinal symptoms in patients with acute pancreatitis. Before EN initiation, we evaluated gastrointestinal function and found that gastrointestinal dysfunction is common in patients with acute pancreatitis. In our univariate analysis, there was a significant difference in GCSI-R1 Score and GCSI-R3 Score between groups, indicating that the severity of gastrointestinal dysfunction is associated with the occurrence of ENAD. Therefore, it is important to evaluate gastrointestinal function before EN initiation, and ASPEN guidelines recommend a comprehensive and dynamic assessment of gastrointestinal function in patients during EN, while early enteral nutrition can also help restore gastrointestinal function (Petrov and Windsor, 2013). The principle behind the baseline bowel sound parameters is that the various parameters of bowel sounds before EN initiation serve as acoustic records. Ching and Tan (2012) used an electronic stethoscope to record bowel

sounds in patients with intestinal obstruction and found that the characteristics of bowel sounds may help determine the location of obstruction based on BSD, BSI, BSF, and peak frequency; Craine et al (1999) used BSI to distinguish between normal individuals and those with irritable bowel syndrome, while Emoto et al (2013) believed that BSD reflects intestinal peristalsis. Spiegel et al (2014) successfully predicted postoperative intestinal obstruction using the BSR index.

The present study aimed to develop a predictive model for early ENAD in patients with AP, utilising the random forest algorithm and an AI-based bowel sound auscultation system. Internal validation was conducted by Bootstrap resampling for, 1000 iterations, with AUC used to evaluate the model's predictive efficacy. The validation results demonstrated an accuracy of 81.10%, sensitivity of 84.30%, specificity of 77.80%, positive predictive value of 82.60%, and negative predictive value of 80.10%, with AUC of 0.904 (95% CI: 0.817–0.997), indicating the model's good predictive performance and clinical utility.

Chen et al (2023) constructed an ENAD prediction model for 114 ICU patients receiving enteral nutrition experiencing days of EN, high urea nitrogen levels, probiotics, respiratory system disease, and daily doses of nutrient solution as predictive factors. The model had predictive energy of 0.736 (95% CI, 0.634–0.837) in the validation cohort. Xie et al (2022) constructed an ENAD prediction model for ICU patients according to nine risk factors, including the number of days of oral potassium preparations, Acute Physiology and Chronic Health Evaluation II score, average daily enteral nutrition intake, fasting days, and albumin concentration ≤ 35 g/L. The model had an accuracy of 76.27%, sensitivity of 70.73%, specificity of 79.70%, and AUC of 0.810 (95% CI, 0.638–0.827).

Compared with these two models, the predictive performance of our model seems to be better. This may be because our model incorporates gastrointestinal function parameters that directly affect EN digestion and absorption. Moreover, our study focused on patients with AP, while the predictive factors in Chen and Xie's models (Chen et al, 2023; Xie et al, 2022) are indirectly related to gastrointestinal function, and the study population is ICU patients with more complex diseases, which may result in a lower predictive performance compared to our study. Furthermore, our study has a smaller sample size than the previous two studies, which may increase the false positive rate.

Clinical implications and recommendations for future research

The bowel sound auscultation system provides the advantage of real-time acquisition and analysis of bowel sound data, reducing the misdiagnosis and missed diagnosis of abnormal bowel sounds. The use of acoustic characteristics of bowel sounds can objectively reflect the recovery of gastrointestinal function, providing early warning information for the precise intervention of ENAD. The study ranked the importance of ENAD risk factors, guiding clinical nurses to dynamically adjust nursing strategies and reduce the risk of ENAD.

An EN intake of 200–400 mL is an important observational point for EN administration. Nurses need to closely monitor the recovery of the patient's gastrointestinal motility and tolerance to the nutritional fluid at this time, adjust the feeding rate and plan in real-time according to tolerance. At the same time, the initial EN intake speed on the second day should not be too fast, starting from 31 mL/h or even lower, and gradually increasing to the target speed every 2–4 hours. If there are prodromal symptoms of diarrhoea, such as abdominal pain and bloating, they should be promptly addressed. Achieving the patient's target energy intake of 500–750 mL on the second day should be done slowly and gradually.

In terms of the importance of ENAD incidence, BSA in the bowel sound monitoring parameters is ranked higher than BSF1 and BSR2. This suggests that nurses may experience lag and deviation when predicting diarrhoea occurrence solely by auscultating bowel sound rate during EN administration. Therefore, it may be more accurate to combine the sound intensity with audio value in the sound index, even though it is an unquantifiable parameter in manual auscultation. However, with the use of AI-powered bowel sound instruments, this issue can be addressed, allowing for more objective and accurate quantification of parameter values, thereby achieving better warning effects.

In addition, for patients with low PAB, it is recommended to administer enteral nutrition while correcting the low PAB and to dynamically monitor the PAB concentration to reduce the incidence of ENAD.

For future research, to the best of our knowledge, this study is the first to use an AI bowel sound auscultation system to predict ENAD in AP patients. Due to factors such as time, funding, and sample size, external validation of the model was not performed. In future research, acoustic experts and AI algorithm experts will be invited to conduct multi-centre, multi-time-point external validation to make the model more robust and have better generalizability. Insufficient EN feeding can hinder the expected recovery of gastrointestinal function and indirectly lead to the occurrence of malnutrition-related symptoms such as ENAD (Chen et al, 2023). These two are interrelated, so in the future, under the premise of external validation, various ENAD intervention measures should be standardised to reduce the occurrence of adverse events caused by inadequate nutrient intake. At the same time, nomograms or evaluation scales can be constructed in the future to make this study more quantitative and provide clearer predictive effects for clinical use.

Limitations

The study, however, did not encompass variables associated with the implementation process of enteral nutrition, and the model lacked external validation. Additionally, the sample size was small, warranting further multi-centre, large-sample, prospective studies to corroborate the findings.

Conclusion

The utilisation of an AI-based bowel sound auscultation system proves to be an effective tool for predicting ENAD in AP patients and mitigating the misdiagnosis and missed diagnosis of abnormal bowel sounds. This assists in the management of clinical feeding practices. Nevertheless, given the limited sample size and absence of external validation, further research is necessary to validate these findings.

Key points

- Traditional manual bowel sound auscultation is highly subjective with low accuracy, and prone to diagnostic negligence.
- With the advancement of artificial intelligence (AI) technology, digital bowel sound detection devices offer objective, quantitative, and visualised data presentation for clinical utility.
- This study developed an artificial intelligence-assisted prediction model for acute pancreatitis (AP) associated enteral nutrition-associated diarrhoea (ENAD) using data obtained from bowel sound auscultation.
- The model was internally validated through a single-centre prospective observational study.
- The primary objective of the model was to enhance clinical decision-making by providing a more precise assessment of ENAD risk.

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Availability of data and materials

All data included in this study are available upon request by contact with the corresponding author.

Author contributions

CCL and LW drafted the manuscript. NS and QHJ collected the clinical data. ZXD, XPX, CCL and RX conducted statistical analysis. CCL, RX, and ZWJ summarised all collected data. LW and CCL designed the study. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

This study is part of a project and serves as observational research in the early stage of the project. The project was conducted following the Helsinki Declaration (revised in 2013). This study has been approved by the Ethics Committee of Jiangsu Province Hospital of Chinese Medicine (2023NL-136-02) and all patients have provided informed consent.

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Conflict of interest

The authors declare that they have no competing interests.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0120.

References

Banks PA, Bollen TL, Dervenis C et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102–111. https://doi.org/10.1136/gutjnl-2012-302779

Chen Q, Chen Y, Wang H et al. Development and validation of a predictive model for diarrhea in ICU patients with enteral nutrition. J Parenter Enteral Nutr. 2023;47(4):563–571. https://doi.org/10.1002/jpen.2501

Chen T, Wang T, Li Q et al. Current status and influencing factors of enteral feeding intolerance in patients with severe acute pancreatitis. Chin J Nurs. 2017;52(6):716–719. http://zh.zhhlzzs.com/CN/Y2017/V52/I6/716

Chen W, Wang H, Chen Y, Yuan D, Chen R. The independent risk factors of early diarrhoea in enteral nutrition for ICU patients. J Int Med Res. 2019;47(10):4929–4939. https://doi.org/10.1177/0300060519868340

Ching SS, Tan YK. Spectral analysis of bowel sounds in intestinal obstruction using an electronic stethoscope. World J Gastroenterol. 2012;18(33):4585–4592. https://doi.org/10.3748/wjg.v18.i33.4585

Craine BL, Silpa M, O'Toole CJ. Computerized auscultation applied to irritable bowel syndrome. Dig Dis Sci. 1999;44(9):1887–1892. https://doi.org/10.1023/A:1018859110022

Dimoulas CA, Papanikolaou GV, Petridis V. Pattern classification and audiovisual content management techniques using hybrid expert systems: a video-assisted bioacoustics application in Abdominal

Sounds pattern analysis. Expert Syst. Appl. 2011;38(10):13082–13093. https://doi.org/10.1016/j.eswa.2011.04.115

Du X, Allwood G, Webberley KM et al. Noninvasive diagnosis of irritable bowel syndrome via bowel sound features: proof of concept. Clin Transl Gastroenterol. 2019;10(3):e00017. https://doi.org/10.14309/ctg.0000000000000017

Emoto T, Shono K, Abeyratne UR et al. ARMA-based spectral bandwidth for evaluation of bowel motility by the analysis of bowel sounds. Physiol Meas. 2013;34(8):925–936. https://doi.org/10.1088/0967-3334/34/8/925

Evans MM, Evans M, Lashinski K, Franklin A. Assessing the abdomen. Nursing. 2009;39(11):12. https://doi.org/10.1097/01.NURSE.0000363366.10288.cd

Felder S, Margel D, Murrell Z, Fleshner P. Usefulness of bowel sound auscultation: a prospective evaluation. J Surg Educ. 2014;71(5):768–773. https://doi.org/10.1016/j.jsurg.2014.02.003

Gade J, Kruse P, Andersen OT, Pedersen SB, Boesby S. Physicians' abdominal auscultation: a multi-rater agreement study. Scand J Gastroenterol. 1998;33(7):773–777. https://doi.org/10.1080/00365529850171756

Gomes CA, Di Saverio S, Sartelli M et al. Severe acute pancreatitis: eight fundamental steps revised according to the 'PANCREAS' acronym. Ann R Coll Surg Engl. 2020;102(8):555–559. https://doi.org/10.1308/rcsann.2020.0029

Gu Y, Lim HJ, Moser MA. How useful are bowel sounds in assessing the abdomen? Dig Surg. 2010;27(5):422–426. https://doi.org/10.1159/000319372

Gungabissoon U, Hacquoil K, Bains C et al. Prevalence, risk factors, clinical consequences, and treatment of enteral feed intolerance during critical illness. JPEN J Parenter Enteral Nutr. 2015;39(4):441–448. https://doi.org/10.1177/0148607114526450

He J, Baxter SL, Xu J et al. The practical implementation of artificial intelligence technologies in medicine. Nat Med. 2019;25(1):30–36. https://doi.org/10.1038/s41591-018-0307-0

Kaneshiro M, Kaiser W, Pourmorady J et al. Postoperative gastrointestinal telemetry with an acoustic biosensor predicts ileus vs. uneventful GI recovery. J Gastrointest Surg. 2016;20(1):132–139. https://doi.org/10.1007/s11605-015-2956-3

Kim KS, Seo JH, Song CG. Non-invasive algorithm for bowel motility estimation using a back-propagation neural network model of bowel sounds. Biomed Eng Online. 2011;10(1):69. https://doi.org/10.1186/1475-925X-10-69

Kurisu K, Yoshiuchi K, Ogino K, Oda T. Machine learning analysis to identify the association between risk factors and onset of nosocomial diarrhea: a retrospective cohort study. PeerJ. 2019;7:e7969. https://doi.org/10.7717/peerj.7969

Lakananurak N, Gramlich L. Nutrition management in acute pancreatitis: clinical practice consideration. World J Clin Cases. 2020;8(9):1561–1573. https://doi.org/10.12998/wjcc.v8.i9.1561

Ma J, Pendharkar SA, O'Grady G, Windsor JA, Petrov MS. Effect of nasogastric tube feeding vs Nil per Os on dysmotility in acute pancreatitis: results of a randomized controlled trial. Nutr Clin Pract. 2016;31(1):99–104. https://doi.org/10.1177/0884533615603967

Madsen D, Sebolt T, Cullen L et al. Listening to bowel sounds: an evidence-based practice project: nurses find that a traditional practice isn't the best indicator of returning gastrointestinal motility in patients who've undergone abdominal surgery. Am J Nurs. 2005;105(12):40–50. https://doi.org/10.1097/00000446-200512000-00029

Mansy HA, Sandler RH. Detection and analysis of gastrointestinal sounds in normal and small bowel obstructed rats. Med Biol Eng Comput. 2000;38(1):42–48. https://doi.org/10.1007/BF02344687

Mehta NM, Skillman HE, Irving SY et al. Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient: society of critical care medicine and American Society for parenteral and enteral nutrition. Pediatr Crit Care Med. 2017;18(7):675–715. https://doi.org/10.1097/PCC.0000000000001134

Ni P, Chen J, Liu N. The sample size estimation in quantitative nursing research. Chin J Nurs. 2010;45(04):378–380. http://www.irtree.cn/3233/articles/33431599/article_detail.aspx

Pan HF, Gong GW, Liu XX et al. Clinical research of a continuous auscultation recorder based on artificial intelligence. Zhonghua Yi Xue Za Zhi. 2020;100:3157–3160. https://rs.yiigle.com/CN115399202004/1256253.htm

Petrov MS, Windsor JA. Nutritional management of acute pancreatitis: the concept of 'gut rousing'. Curr Opin Clin Nutr Metab Care. 2013;16(5):557–563. https://doi.org/10.1097/mco.0b013e3283638ed1

Qiu C, Chen C, Zhang W et al. Fat-modified enteral formula improves feeding tolerance in critically ill patients: a multicenter, single-blind, randomized controlled trial. JPEN J Parenter Enteral Nutr. 2017;41(5):785–795. https://doi.org/10.1177/0148607115601858

Ramanathan M, Aadam AA. Nutrition management in acute pancreatitis. Nutr Clin Pract. 2019;34 Suppl 1:S7–S12. https://doi.org/10.1002/ncp.10386

Reintam Blaser A, Deane AM, Fruhwald S. Diarrhoea in the critically ill. Curr Opin Crit Care. 2015;21(2):142–153. https://doi.org/10.1097/MCC.0000000000000188

Revicki DA, Rentz AM, Dubois D et al. Development and validation of a patient-assessed gastroparesis symptom severity measure: the Gastroparesis Cardinal Symptom Index. Aliment Pharmacol Ther. 2003;18(1):141–150. https://doi.org/10.1046/j.1365-2036.2003.01612.x

Sakamoto T, Nakashima H, Nakamura K, Nagahama R, Saito Y. Performance of computer-aided detection and diagnosis of colorectal polyps compares to that of experienced endoscopists. Dig Dis Sci. 2022;67(8):3976–3983. https://doi.org/10.1007/s10620-021-07217-6

Spiegel BMR, Kaneshiro M, Russell MM et al. Validation of an acoustic gastrointestinal surveillance biosensor for postoperative ileus. J Gastrointest Surg. 2014;18(10):1795–1803. https://doi.org/10.1007/s11605-014-2597-y

Wang B. Econometric models and the application of R language. Jinan University Press: Guangzhou. 2015.

Wang G, Wang M, Liu H et al. Changes in bowel sounds of inpatients undergoing general anesthesia. Biomed Eng Online. 2020;19(1):60. https://doi.org/10.1186/s12938-020-00805-z

Wang G, Yang Y, Chen S et al. Flexible dual-channel digital auscultation patch with active noise reduction for bowel sound monitoring and application. IEEE J Biomed Health Inform. 2022;26(7):2951–2962. https://doi.org/10.1109/JBHI.2022.3151927

Wang M, Zhang X, Chen M. Reliability and validity of the Chinese version of Gastroparesis Cardinal Symptom Index revised. Chin J Mod Nurs. 2019;25:2664–2667. https://rs.yiigle.com/cmaid/1161875

Whelan K, Judd PA, Taylor MA. Assessment of fecal output in patients receiving enteral tube feeding: validation of a novel chart. Eur J Clin Nutr. 2004;58(7):1030–1037. https://doi.org/10.1038/sj.ejcn.1601927

Xie W, Wang S, Li X, Zhang Q. Establishment and validation of a risk prediction model for enteral nutrition-associated diarrhea in ICU patients. Chin J Nurs. 2022;57(1):2324–2332. http://zh.zhhlzzs.com/CN/10.3761/j.issn.0254-1769.2022.19.003

Yuan G. Diarrhea related factors analysis and TCM syndrome retrospective study in general ICU patients. China Academy of Chinese Medical Sciences. 2012. https://www.doc88.com/p-7969838665785.html