Infection and Drug Resistance

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ORIGINAL RESEARCH A Nomogram Based on a Non-Invasive Method to Distinguish Between Gram-Positive and Gram-Negative Bacterial Infections of Liver Abscess

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Purpose: The diagnosis of liver abscess (LA) caused by Gram-positive bacteria (GPB) and Gram-negative bacteria (GNB) depends on ultrasonography, but it is difficult to distinguish the overlapping features. Valuable ultrasonic (US) features were extracted to distinguish GPB-LA and GNB-LA and establish the relevant prediction model.

Materials and Methods: We retrospectively analyzed seven clinical features, three laboratory indicators and 11 US features of consecutive patients with LA from April 2013 to December 2023. Patients with LA were randomly divided into training group (n=262) and validation group (n=174) according to a ratio of 6:4. Univariate logistic regression and LASSO regression were used to establish prediction models. The performance of the model was evaluated using area under the curve(AUC), calibration curves, and decision curve analysis (DCA), and subsequently validated in the validation group.

Results: A total of 436 participants (median age: 55 years; range: 42–68 years; 144 women) were evaluated, including 369 participants with GNB-LA and 67 with GPB-LA, respectively. A total of 11 predictors by LASSO regression analysis, which included gender, age, the liver background, internal gas bubble, echogenic debris, wall thickening, whether the inner wall is worm-eaten, temperature, diabetes mellitus, hepatobiliary surgery and neutrophil(NEUT). The performance of the Nomogram prediction model distinguished between GNB-LA and GPB-LA was 0.80, 95% confidence interval [CI] (0.73-0.87). In the validation group, the AUC of GNB was 0.79, 95% CI (0.69-0.89).

Conclusion: A model for predicting the risk of GPB-LA was established to help diagnose pathogenic organism of LA earlier, which could help select sensitive antibiotics before the results of drug-sensitive culture available, thereby shorten the treatment time of patients.

Keywords: liver abscess, Gram-positive bacteria, Gram-negative bacteria, ultrasonography features, prediction model

Introduction

Globally, liver abscess (LA) ranks as the second most prevalent hepatic infectious diseases and poses a potential threat to life. LA is commonly observed in participants with liver diseases, biliary diseases, and diabetes, and in those who have undergone invasive operations.¹ LA is caused by various organisms, including Klebsiella pneumonia, Escherichia coli, and Streptococcus, among others.²⁻⁴ Although the incidence of Klebsiella pneumoniae LA has significantly increased in the past two decades, with the highest proportion observed in the Asian population, there has been a recent sharp rise in Escherichia coli LA, gradually making it the predominant cause.^{4–6} The prevalence of Escherichia coli LA has notably surged in Western countries, emerging as the predominant form of LA.7 However, Klebsiella pneumonia and Escherichia coli are both Gram-negative bacteria (GNB), which are the most common causative organisms of liver abscesses.⁸

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Moreover, *GNB* and *Gram-positive bacteria* (*GPB*) have different physiological structures, disease causes, and selection of antibiotic treatment. Therefore, it is of great significance to distinguish between *GNB* and *GPB* for the clinical determination of infection and choice of drugs.^{8–12} *GNB*-LA and *GPB*-LA have similar clinical features and laboratory findings, making it challenging to accurately differentiate them.¹³ Blood or pus culture methods are the gold standards for identifying the causative organism. However, it takes several days to produce results, which can delay treatment.

Imaging tests such as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are commonly used to diagnose LA, clarify the possible cause, and exclude other abdominal diseases with similar symptoms.^{14,15} Several reviews have reported the demographic and clinical features of LA.^{4,16,17} However, to the best of our knowledge, the overlap of US features in LA caused by *GPB* and *GNB* is difficult to distinguish, and there is a lack of research reports on this aspect. Therefore, we aim to retrospectively analyze the US and clinical features of *GNB*-LA and *GPB*-LA, and establish the relevant early prediction model.

Materials and Methods

Study Participants

This cross-sectional, single-centered study of retrospectively enrolled participants was conducted at the Fifth Medical Center of the PLA General Hospital. The Ethics Committee of the Fifth Medical Center of the PLA General Hospital approved this retrospective study.

According to the electronic database of the Fifth Medical Center of the PLA General Hospital, 436 consecutive participants (details are provided in the <u>Table S1</u>) diagnosed with LA (International Classification of Diseases, Clinical Modification 572.0)¹⁸ were recruited between April 2013 and December 2023.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: ① positive bacterial culture results of pus with transparent causative organisms; ② negative pus culture results but blood culture results with definite causative organisms; ③ precise US image data on the liver and abscess lesions.

Exclusion criteria: 1) amoebic liver abscess; 2) infected liver cyst; 3) without clear records.

Data Collection

Data were collected and synthesized by reviewing the medical records of each participant. The clinical records included demographic characteristics (age and sex), the time interval between onset and first US examination, the course of the disease, underlying diseases (diabetes mellitus, biliary tract disease), temperature, duration of fever, history of hepatobiliary surgery, microbiological reports, laboratory results (NEUT, c-reaction protein [CRP] and procalcitonin [PCT]) and US imaging features.

Pus cultures were obtained within 6 to 8 hours post pus aspiration, while blood cultures were collected within 1 week following pus aspiration. In case of a positive result in the pus culture, this method was employed, however, if the pus culture yielded a negative outcome, the blood culture was utilized. LA was classified as *GNB* or *GPB* based on culture results.

Retrospective Classification of US Pattern for Liver Abscesses

The *GNB*-LA (n = 369) and *GPB*-LA (n = 67) groups were divided according to the type of causative organism. Two ultrasonographers with >5 years of experience reviewed the US images in a double-blind manner. In case of disagreement, an imaging specialist with 20 years of experience in liver abscesses was consulted and made the final decision. The abscess size, location, number, septations within the abscess, structure, echo characteristics of lesions, and blood supply status were observed and analyzed. The specific analysis indicators of US images included the following: (a) abscess size; (b) location (left lobe, right lobe, and both); (c) number (single, two or three or more); (d) septations within the abscess (none, unilocular and multilocular); (e) structure (cystic; cystic dominance: abscesses with >60% of the cystic component; solid, solid dominance: abscesses with >60% of the solid component; miscibility); (f) presence of internal

gas bubbles; (g) presence of echogenic debris (poor sound transmission in the liquid part, with floating dotted echoes); (h) whether the inner wall is worm eaten; (i) presence of blood flow signals; (j) presence of variable calcification; (k) margin of the lesion (irregular or indistinct and smooth); and (l) abscess wall thickening (immural, thin wall [<2 mm] and thick wall [\geq 2 mm]); (m) liver background (normal, fatty liver, fibrosis).

Statistical Analysis

All statistical analyses were performed using SPSS 26.0 and R software, version 4.2.2, along with MSTATA software (<u>www.mstata.com</u>).

K-values were used to measure the inter-observer agreement of the US characteristics. Laboratory index and clinical characteristics were standardized on an individual basis with the use of a uniform unit, and extreme values were considered to be missing data if they were found, and entire cases were excluded. Patients with LA were randomly divided into training group and validation group according to a ratio of 6:4. Pathogen type was used as outcome variable. Non-normal data were presented as median (interquartile ranges). In the univariate analysis, chi-square test or Fisher's exact test was used to analyze the categorical variables, while the Student's *t*-test or rank-sum test was used to examine the continuous variables. In the training cohort, the least absolute shrinkage and selection operator (LASSO) analysis to screen the independent risk factors and based a ultrasound features nomogram prediction model were constructed. The ROC curve is used to evaluate the prediction effect of the model. The ROC curve is a function of comparing the real results with the predicted results of the model to define the true positive rate and false positive rate. The Hosmer-Lemeshow calibration curve was used to check the goodness of fit. DCA is used to evaluate clinical effectiveness and can integrate the preferences of patients and decision makers into the analysis process, which is more in line with the actual needs of clinical decision-making.

AUC values range from 0.5 to 1.0, the closer to 1.0, the higher the authenticity of the model. The *k-value* were interpreted as follows: a *k-value* of >0.81 indicated very good agreement; a *k-value* of 0.80-0.61 indicated good agreement; a *k-value* of 0.60-0.41 indicated moderate agreement; and a *k-value* of <0.41 indicated poor agreement.

Results

Participant Characteristics

During the study period, 513 participants were clinically diagnosed with LA, among whom, 77 were excluded from the study for the following reasons: amoebic liver abscess (n=19), infected liver cyst (n=9), incomplete medical record information (n=17), and negative bacterial cultures of pus and blood (n=32). A total of 436 participants (median age: 55 years; interquartile age range [IQR]: 42–68 years; 144 women) were included (Figure 1). The demographic characteristics and clinical findings are summarized in Table 1.

Liver Abscess Etiology

Pus culture yielded positive results in 316 participants. The most common organism in pus cultures was *Klebsiella pneumonia* (n = 257), followed by *Escherichia coli* (n=39). Other cultured organisms included *Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Morganella, Clostridium perfringens, Staphylococcus, Streptococcus, Enterococcus,* and *Enterococcus faecalis.* Blood cultures were positive in 120 pus culture-negative participants, with *Klebsiella pneumonia* being the most prevalent pathogen. The detailed pathogenic organism of the two groups are listed in Table 2.

US Characteristics of Liver Abscesses

The mean size of the abscesses was 6.9 (range: 3.9-9.8) cm. Single and multiple abscesses were present in 335 and 101 patients, respectively. A total of 141 participants had unilobar involvement, with right lobe involvement being the most common (n = 276, 63.3%), which was an insignificant finding. The US radiological features are summarized in Table 3. The inter-observer agreement for US imaging interpretations was excellent (median K value =0.83; range =0.80–1.00, Table 4).

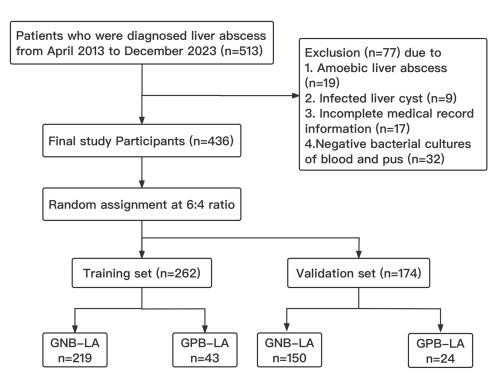


Figure I Flowchart showing the patient enrollment process.

Abbreviations: GNB-LA, Gram-negative bacteria pyogenic liver abscess; GPB-LA, Gram-positive bacteria pyogenic liver abscess.

Model Construction and Visualization

The model was built using the training set and 23 variables were screened for non-zero coefficient predictors using LASSO regression (Figure 2). Vertical lines are drawn at λ minimum (λ =0.005) and 1 SE of the minimum (λ =0.035), and finally the minimum 10 times cross-validation error 1 SE is selected as the optimal value, and 11 predictors with non-zero

Characteristics	All Patients	Training	Internal Test	P-value
	(n=436)	Cohort (n=262)	Cohort (n=174)	
Clinical findings				
Age	55 ± 13	55 ± 13	54 ± 14	0.544
Gender				0.463
Male	292 (67.0%)	179 (68.3%)	113 (64.9%)	
Female	144 (33.0%)	83 (31.7%)	61 (35.1%)	
Temperature (°C)	39.42 ± 0.79	39.43 ± 0.81	39.40 ± 0.75	0.654
Duration of fever(d)	25 ± 76	19.27 ± 36.30	30.14 ± 67.70	0.892
Underlying disease				
Diabetes mellitus	153 (35.1%)	88 (33.6%)	65 (37.4%)	0.419
Biliary tract disease	53 (12.2%)	26 (9.9%)	27 (15.5%)	0.080
Medical histories				
Hepatobiliary surgery	38 (8.7%)	24 (9.2%)	14 (8.0%)	0.686
Laboratory index				
NEUT (10^9/L)	7.4 ± 4.4	7.6 ± 4.5	7.2 ± 4.1	0.368
CRP (mg/L)	218 ± 579	215 ± 556	223 ± 614	0.901
PCT (ng/mL)	4.0 ± 10.9	4.3 ± 10.7	3.7 ± 11.2	0.605
			1	1

 Table I Clinical Findings of All Study Patients with Liver Abscesses

Notes: Value are presented as number (%), mean±standard deviation. Normally distributed data were tested using independent samples *t*-tests, and nonparametric tests were used for nonnormal data.

Abbreviations: IQR, interquartile range; GNB-LA, Gram negative bacteria liver abscess; GPB-LA, Gram positive bacteria liver abscess; NEUT, neutrophil; CRP, c-reaction protein; PCT, procalcitonin.

Pathogenic Bacteria	Total	Constituent Ratio
Gram negative bacteria	369	84.63%
Klebsiella pneumonia	273	62.61%
Escherichia coli	56	12.84%
Pseudomonas aeruginosa	12	2.75%
Stenotrophomonas maltophilia	11	2.52%
Burkholderia cepacia	9	2.06%
Morganella morganii	4	0.92%
Enterobacter cloacae	4	0.92%
Gram positive bacteria	67	15.37%
Staphylococcus	28	6.42%
Streptococcus	20	4.59%
Enterococcus	13	2.98%
Propionibacterium bullosum	6	1.38%

 Table 2 Microbiologic Characteristics

Table 3 Ultrasounic Features

Characteristics	All Patients	Training	Internal Test	P-value
	(n=436)	Cohort (n=262)	Cohort (n=174)	
Liver background				0.648
Normal	135 (31.0%)	79 (30.2%)	56 (32.2%)	
Fatty liver	172 (39.4%)	108 (41.2%)	64 (36.8%)	
Fibrosis	129 (29.6%)	75 (28.6%)	54 (31.0%)	
Abscess size(cm)	6.87 ± 2.96	6.92 ± 2.99	6.79 ± 2.92	0.649
Number				0.077
Single	335 (76.8%)	211 (80.5%)	124 (71.3%)	
Тwo	23 (5.3%)	(4.2%)	12 (6.9%)	
Three or more	78 (17.9%)	40 (15.3%)	38 (21.8%)	
Location				0.555
Left	67 (15.4%)	39 (14.9%)	28 (16.1%)	
Right	276 (63.3%)	171 (65.3%)	105 (60.3%)	
Both	93 (21.3%)	52 (19.8%)	41 (23.6%)	
Septations within the abscess				0.850
None	49 (11.2%)	28 (10.7%)	21 (12.1%)	
Multilocular	135 (31.0%)	80 (30.5%)	55 (31.6%)	
Unilocular	252 (57.8%)	154 (58.8%)	98 (56.3%)	
Structure of the abscess				0.112
Cystic	47 (10.8%)	22 (8.4%)	25 (14.4%)	
Cystic dominance	139 (31.9%)	93 (35.5%)	46 (26.4%)	
Solid dominance	78 (17.9%)	38 (14.5%)	40 (23.0%)	
Solid	55 (12.6%)	31 (11.8%)	24 (13.8%)	
Miscibility	117 (26.8%)	78 (29.8%)	39 (22.4%)	
Echogenic debris	87 (20.0%)	51 (19.5%)	36 (20.7%)	0.754
Internal gas bubble	34 (7.8%)	19 (7.3%)	15 (8.6%)	0.602
Variable calcification	127 (29.1%)	72 (27.5%)	55 (31.6%)	0.353
Blood flow signals	226 (51.8%)	130 (49.6%)	96 (55.2%)	0.256
Margin of lesion				0.279
Irregular or indistinct	162 (37.2%)	92 (35.1%)	70 (40.2%)	
Smooth	274 (62.8%)	170 (64.9%)	104 (59.8%)	

(Continued)

Table 3 (Continued).	Table	3	(Continued).
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Characteristics	All Patients (n=436)	Training Cohort (n=262)	Internal Test Cohort (n=174)	P-value
Abscess wall thickening				0.510
Immural	68 (15.6%)	38 (14.5%)	30 (17.2%)	
Thin wall (< 2 mm)	71 (16.3%)	40 (15.3%)	31 (17.8%)	
Thick wall (≥ 2 mm)	297 (68.1%)	184 (70.2%)	113 (64.9%)	
Inner wall is worm-eaten	170 (39.0%)	104 (39.7%)	66 (37.9%)	0.712

Table 4 Inter-Observer Agreement for Ultrasound Characteristics

Imaging Finding	k Value
Liver background	0.97
Abscess size	0.86
Number	0.92
Location	1.00
Septations within the abscess	0.90
Structure	0.82
Necrotic debris	0.85
Internal gas bubble	0.83
Variable calcification	0.82
Inner wall is worm-eaten	0.80
Blood flow signals	0.81
Margin of lesion	0.80
Abscess wall thickening	0.82

coefficients are screened out, including gender (odds ratio [OR], 0.44; 95% CI, 0.18–0.95), age (OR, 0.98 95% CI: 0.95–1.00), the liver background (OR, 5.08; 95% CI: 1.76–18.47), internal gas bubble (OR, 2.57; 95% CI: 0.86–6.95), echogenic debris (OR, 2.06; 95% CI: 0.96–4.26), wall thickening (OR, 4.38; 95% CI: 1.25–27.72), whether the inner wall is worm-eaten (OR, 1.75; 95% CI: 0.91–3.40), temperature (OR, 1.27; 95% CI: 0.85–1.86), diabetes mellitus (OR, 0.40; 95% CI: 0.16–0.86), hepatobiliary surgery (OR, 6.68; 95% CI: 2.74–16.36) and NEUT (OR, 1.08; 95% CI: 1.01–1.15). Figure 3 shows the US features in the predictors.

The coefficients of Lasso regression analysis in Table 5). The 11 variables selected by LASSO regression analysis were used to build the *GPB*-LA prediction model and draw a column graph (Figure 4). The total score was obtained by

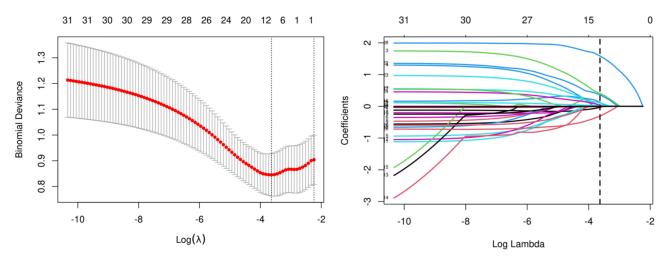


Figure 2 Selection of predictive variables using LASSO regression.

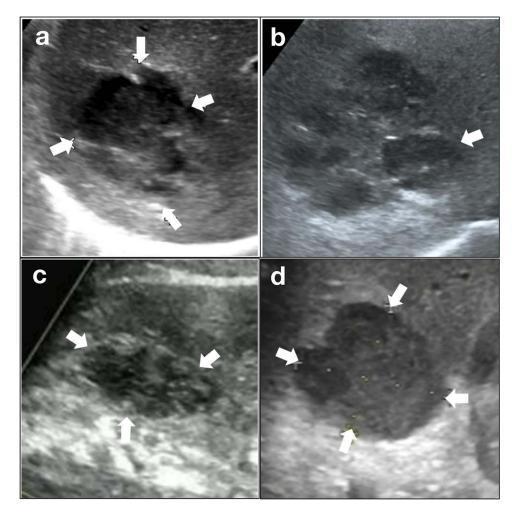


Figure 3 (a) GNB-LA (caused by Klebsiella pneumonia) in a 56-year-old man with diabetes. Two-dimensional-US shows an abscess containing echogenic debris (arrow) in the right lobe of the liver. (b) GNB-LA (caused by Escherichia coli) in a 68-year-old woman with diabetes and fatty liver. Two-dimensional-US shows a multiloculated abscess in the right lobe of the liver. (c) GPB-LA (caused by Staphylococcus aureus) in a 32-year-old man with liver fibrosis. Two-dimensional-US shows a solitary abscess containing echogenic debris in the right lobe of the liver. (d) GPB-LA (caused by Staphylococcus cloacae) in a 33-year-old man without diabetes and fatty liver. Two-dimensional-US shows a solitary abscess containing echogenic debris in the right lobe of the liver.

Abbreviations: GPB-LA, Gram positive bacteria liver abscess; US, Ultrasonography.

adding the scores of each variable. The risk of *GPB*-LA can be marked by plotting a vertical line downward through the total score.

Model Evaluation

The model was applied to internal validation data and receiver operating characteristic curve (ROC curve) validation, and the results showed that the AUC of the training group was $0.80 (95\% \text{ CI}=0.73\sim0.87)$ and that of the validation group was $0.79 (95\% \text{ CI}=0.69\sim0.89)$ (Figure 5).

The calibration plots of the nomogram in the different cohorts are plotted in Figure 6, which demonstrate a good correlation between the observed and predicted Pathogenic bacteria. The results showed that the original nomogram was still valid for use in the validation sets, and the calibration curve of this model was relatively close to the ideal curve, which indicates that the predicted results were consistent with the actual findings.

Figure 7 displays the DCA curves related to the nomogram. A high-risk threshold probability indicates the chance of significant discrepancies in the model's prediction when clinicians encounter major flaws while utilizing the nomogram for diagnostic and decision-making purposes. This research shows that the nomogram offers substantial net benefits for clinical application through its DCA curve.

Coefficient	Variable
-3.44	(Intercept)
-0.03	Gender (female)
-0.01	Age
0.41	Liver background (fatty liver)
0.12	Internal gas bubble
0.10	Echogenic debris
0.36	Abscess wall thickening [Thick wall (≥ 2 mm)]
0.03	Inner wall is worm eaten
0.04	Temperature
-0.3 I	Diabetes
1.59	Hepatobiliary surgery
0.02	NEUT

Table 5 The Coefficients of Lasso Regression Analysis

Discussion

GPB and *GNB* have different antibiotic options. Currently, the imaging features of LA caused by *GPB* and *GNB* are unclear. In the current study, we developed and validated a nomogram for predicting pathogenic organism (*GPB* or *GNB*), based on a cohort of 436 patients. The main predictors incorporated into the nomogram included gender, age, liver background, internal gas bubble, echogenic debris, abscess wall thickening, whether the inner wall is worm-eaten, temperature, diabetes mellitus, hepatobiliary surgery, and NEUT.

Previous studies on the imaging characteristics of LA were mainly single-center retrospective studies, mostly comparative studies of Klebsiella pneumonia LA vs non-Klebsiella pneumonia LA.^{19,20} Some studies have reported that typical findings of Klebsiella pneumonia LA on abdominal contrast-enhanced CT/MRI include single, thin-walled, multiseptate, solid mass with necrotic centers.^{15,21} Klebsiella pneumonia LA is related to solid, single, multilocular, and indistinct edges on US.^{19,20,22} Moreover, 74% of the GNB-LA cases in our study were pathogenic Klebsiella pneumonia; therefore, the result of GNB-LA is non-thick wall mostly in the US, which is consistent with the findings of previous studies. This characteristic may be related to the complexity of the cell wall of GNB.²³⁻²⁵ In contrast to the feature reported by Joyce Y that Klebsiella pneumonia LA is primarily solid, we did not observe this feature in GNB-LA with predominantly Klebsiella pneumonia. This may be due to the long interval between the onset and the first US in our participants, and the fact that most of them already had liquefied necrotic lesions at the time of examination. In addition, the absence of echogenic debris as a typical feature, which has not been interpreted but is present in 82% of GNB-LA, representing a simple, easy-to-determine, and sensitive US imaging indicator. In terms of clinical characteristics, GNB-LA was used in the majority of our study, which is consistent with the actual clinical distribution.^{4–6} Interestingly, we found that the polytendency of the internal gas bubble and inner wall is worm-eaten is called GPB-LA, which has not been mentioned before. We found significant differences between GNB-LA and GPB-LA patients in that the former tended to be older women with diabetes, without fatty liver disease, liver cancer surgery, and higher body temperature and NEUT. The finding that GPB-LA patients had higher NEUT compared to GNB-LA patients was consistent with the findings of Nasser et al.²⁶

Ample antibiotic coverage and abscess drainage are the therapeutic regulatory strategies for LA. In contrast, broadspectrum antibiotics capable of covering a wider range of pathogens or multiple antibiotic combinations are generally used while waiting for culture results.²⁷ The use of multiple antibiotics increases the risk of resistance, with some studies reporting an increased risk of resistance ranging from 13–17% due to the misuse of antibiotics, especially broad-spectrum antibiotics.^{28–32} Broad-spectrum antibiotics are also associated with a higher incidence of adverse reactions, such as diarrhea and liver and kidney injury, than narrow-spectrum antibiotics and are more expensive, which can increase the financial burden.^{31,32} As the choice of antibiotics used to treat *GNB*-LA and *GPB*-LA is different,^{8–12,33} studying the differences in comorbidities and US features between the two groups can assist with selecting the best antibiotic to reduce these risks. Furthermore, patients with *GNB*-LA have much longer courses and relatively poorer prognoses,^{34,35}

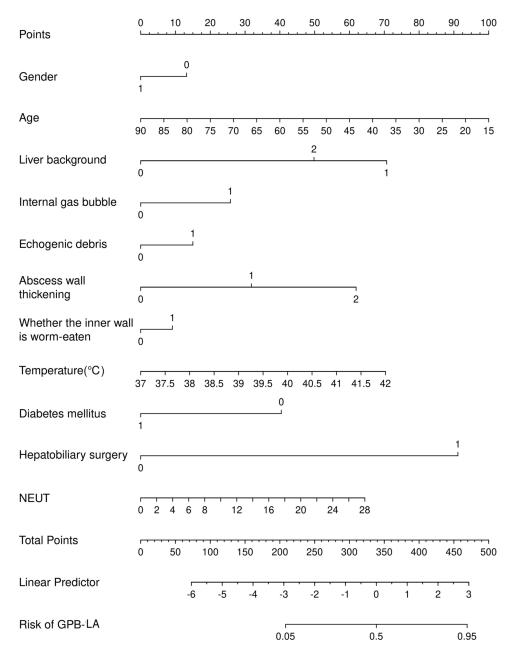


Figure 4 Nomogram prediction model to distinguish between GPB-LA and GNB-LA.

which also increases the risk of drug resistance, side effects, and medical costs; therefore, it is necessary to clarify *GNB*-LA. The based US features nomogram offers several clinical implications. Firstly, it provides a quantitative tool for clinicians to distinguish between *GNB*-LA and *GPB*-LA more accurately than traditional methods, aiding in better risk stratification. Moreover, early identification of high-risk individuals through this nomogram can lead to earlier selection of sensitive antibiotics, thereby shortening treatment time and improving patient prognosis.

Our study has several limitations that should be acknowledged. First, selection bias may have occurred when individuals with liver abscesses showed no development of pus or blood cultures given that the pathogen could not be identified in this case. Second, the cohort was a single-center retrospective study with data bias, however, the large sample size can compensate for some deficiencies. Finally, because most of the sample population was in the abscess formation stage when they visited the hospital, we did not perform a specific analysis of the abscesses before they were liquefied. Hence, the therapeutic options for this stage remain unclear. Furthermore, demographics and underlying

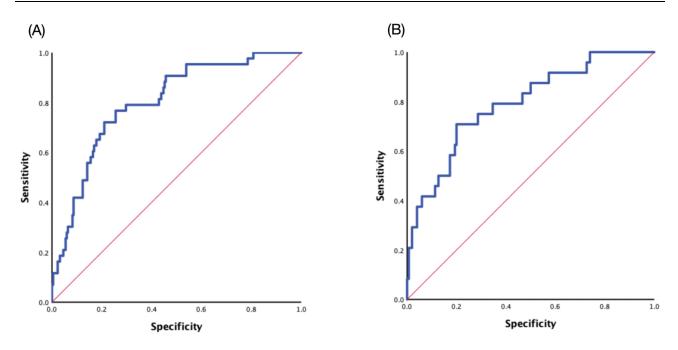


Figure 5 ROC curves of the model for predicting GPB-LA. (A) Training cohort (B) Validation cohort.

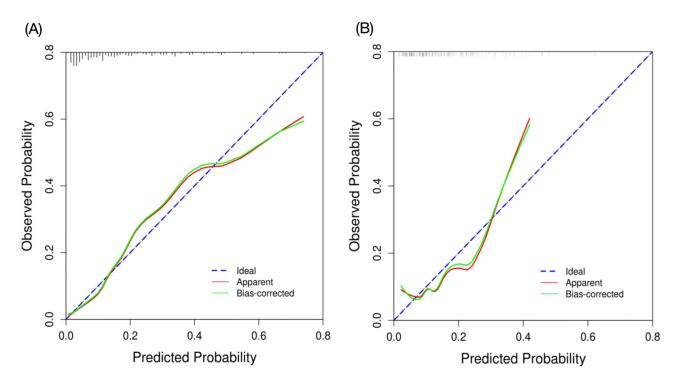


Figure 6 Calibration plots for predicting GPB-LA probabilities in the training cohort (A) and validation cohort (B).

disorders were collected as potential confounders in this study. Lifestyle and environmental factors that may have affected the outcomes are not stated. Therefore, additional confounding data should be collected and analyzed to improve confounding control in future studies. Future research should aim to externally validate the accuracy and effectiveness of our nomogram in different populations and settings. Additionally, integrating novel US predictors could enhance the predictive accuracy of the nomogram, warranting further investigation.

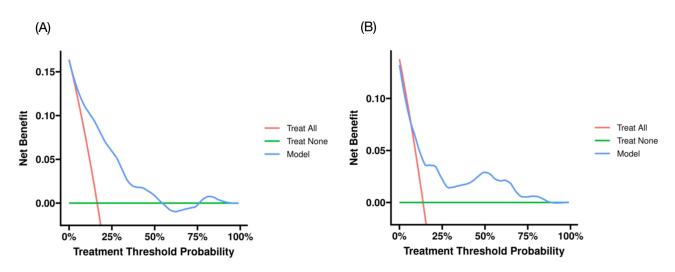


Figure 7 Decision curves for the training cohort (\boldsymbol{A}) and validation cohort $(\boldsymbol{B}).$

Conclusions

Gender, age, the liver background, internal gas bubble, echogenic debris, wall thickening, whether the inner wall is worm-eaten, temperature, diabetes mellitus, hepatobiliary surgery and NEUT are the predictors that distinguish *GPB*-LA from *GNB*-LA. A risk prediction model was established using the above 11 factors and a nomogram was developed to help early diagnosis of LA pathogenic organism and select sensitive antibiotics before the results of drug-sensitive culture were available, thereby improving patient prognosis.

Abbreviations

GPB, Gram-positive bacteria; GNB, Gram-negative bacteria; LA, liver abscess; LASSO, least absolute shrinkage and selection operator; AUC, area under the curve; NEUT, neutrophil; US, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; CRP, c-reaction protein; PCT, procalcitonin; ROC, receiver operating characteristic curve.

Ethics Approval and Consent to Participate

This retrospective study was carried out using the opt-out method for the case series of our hospital. The study was approved by the Ethics Committee of the Fifth Medical Center of Chinese PLA General Hospital and was conducted in accordance with the 1964 helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was waived by our Institutional Review Board because of the retrospective nature of our study.

Author Contributions

Haoran Li was the first author. Ping Liang was corresponding author and Jie Yu was the co-corresponding author. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- 1. Lederman ER, Crum NF. Pyogenic liver abscess with a focus on Klebsiella pneumoniae as a primary pathogen: an emerging disease with unique clinical characteristics. *Am J Gastroenterol*. 2005;100(2):322–331. doi:10.1111/j.1572-0241.2005.40310.x
- Chan DS, Archuleta S, Llorin RM, Lye DC, Fisher D. Standardized outpatient management of Klebsiella pneumoniae liver abscesses. Int J Infect Dis. 2013;17:e185–e188. doi:10.1016/j.ijid.2012.10.002
- 3. Tsai FC, Huang YT, Chang LY, Wang JT. Pyogenic liver abscess as endemic disease, Taiwan. *Emerg Infect Dis.* 2008;14(10):1592–1600. doi:10.3201/eid1410.071254
- 4. Wang JH, Liu YC, Lee SSJ, et al. Primary liver abscess due to Klebsiella pneumoniae in Taiwan. Clin Infect Dis. 1998;26(6):1434-1438. doi:10.1086/516369
- 5. Chung DR, Lee SS, Lee HR, et al. Emerging invasive liver abscess caused by K1 serotype Klebsiella pneumoniae in Korea. J Infect. 2007;54 (6):578–583. doi:10.1016/j.jinf.2006.11.008
- Wang J, Yan Y, Xue XY, Wang KF, Shen DX. Comparison of pyogenic liver abscesses caused by hypermucoviscous Klebsiella pneumoniae and non-Klebsiella pneumoniae pathogens in Beijing: a retrospective analysis. J Int Med Res. 2013;41(4):1088–1097. doi:10.1177/0300060513487645
- 7. Braiteh F, Golden MP. Cryptogenic invasive Klebsiella pneumoniae liver abscess syndrome. Int J Infect Dis. 2007;11(1):16-22. doi:10.1016/j. ijid.2005.10.006
- 8. Sharma S, Ahuja V. Liver abscess: complications and treatment. Clin Liver Dis. 2021;18(3):122-126. doi:10.1002/cld.1128
- 9. Karki BR, Costanzo L, Jha SK, Nainan S, McFarlane SI. Multiple hepatic abscesses secondary to Streptococcus anginosus infection: a case report and review of the literature. *Cureus*. 2022;14(8):e28415. doi:10.7759/cureus.28415
- Myeong JH, Kyoung DS, Park MA, et al. Anaerobe coverage is important for the prognosis of pyogenic liver abscess: a population-based study in Korea. J Infect Public Health. 2022;15(4):425–432. doi:10.1016/j.jiph.2022.03.003
- Kumar SK, Perween N, Omar BJ, et al. Pyogenic liver abscess: clinical features and microbiological profiles in tertiary care center. J Family Med Prim Care. 2020;9(8):4337–4342. doi:10.4103/jfmpc.jfmpc_927_20
- 12. Giangiuli SE, Mueller SW, Jeffres MN. Transition to oral versus continued intravenous antibiotics for patients with pyogenic liver abscesses: a retrospective analysis. *Pharmacotherapy*. 2019;39(7):734–740. doi:10.1002/phar.2296
- 13. Rahimian J, Wilson T, Oram V, Holzman RS. Pyogenic liver abscess: recent trends in etiology and mortality. *Clin Infect Dis.* 2004;39 (11):1654–1659. doi:10.1086/425616
- 14. Mortelé KJ, Segatto E, Ros PR. The infected liver: radiologic-pathologic correlation. *RadioGraphics*. 2004;24(4):937–955. doi:10.1148/ rg.244035719
- 15. Alsaif HS, Venkatesh SK, Chan DSG, Archuleta S. CT appearance of pyogenic liver abscesses caused by Klebsiella pneumoniae. *Radiology*. 2011;260(1):129–138. doi:10.1148/radiol.11101876
- 16. Siu LK, Yeh KM, Lin JC, Fung CP, Chang FY. Klebsiella pneumoniae liver abscess: a new invasive syndrome. *Lancet Infect Dis.* 2012;12 (11):881-887. doi:10.1016/S1473-3099(12)70205-0
- 17. Qian Y, Wong CC, Lai S, et al. A retrospective study of pyogenic liver abscess focusing on Klebsiella pneumoniae as a primary pathogen in China from 1994 to 2015. *Sci Rep.* 2016;6:38587. doi:10.1038/srep38587
- 18. World Health Organization. International classification of diseases (ICD). 2016:21.
- Chan KS, Chia CTW, Shelat VG. Demographics, radiological findings, and clinical outcomes of Klebsiella pneumonia vs. non-Klebsiella pneumoniae pyogenic liver abscess: a systematic review and meta-analysis with trial sequential analysis. *Pathogens*. 2022;11(9). doi:10.3390/ pathogens11090976
- 20. Liu Y, Wang JY, Jiang W. An increasing prominent disease of Klebsiella pneumoniae Liver abscess: etiology, diagnosis, and treatment. Gastroenterol Res Pract. 2013;2013:258514. doi:10.1155/2013/258514
- Lee JH, Jang YR, Ahn SJ, Choi SJ, Kim HS. A retrospective study of pyogenic liver abscess caused primarily by Klebsiella pneumoniae vs. non-Klebsiella pneumoniae: CT and clinical differentiation. *Abdom Radiol (NY)*. 2020;45(9):2669–2679. doi:10.1007/s00261-019-02389-2
- 22. Hui JY, Yang MK, Cho DH, et al. Pyogenic liver abscesses caused by Klebsiella pneumoniae: US appearance and aspiration findings. *Radiology*. 2007;242(3):769–776. doi:10.1148/radiol.2423051344
- 23. Shi SH, Zhai ZL, Zheng SS. Pyogenic liver abscess of biliary origin: the existing problems and their strategies. *Semin Liver Dis.* 2018;38 (3):270–283. doi:10.1055/s-0038-1661363
- 24. Oliveira J, Reygaert WC. Gram Negative Bacteria. Treasure Island (FL): StatPearls Publishing; 2022:5.
- 25. Wang Z, Ji W, Guo HB, Tao YZ, Ding YF. Comparative studies on the composition and antibiotic-resistance of pathogenic bacteria between children with community-acquired and hospital-acquired pneumonia. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2011;45(3):211–216.
- 26. Nasser A, Moradi M, Jazireian P, et al. Staphylococcus aureus versus neutrophil: scrutiny of ancient combat. *MICROB PATHOGENESIS*. 2019;131:259–269. doi:10.1016/j.micpath.2019.04.026
- 27. Webb GJ, Chapman TP, Cadman PJ, Gorard DA. Pyogenic liver abscess. Frontline Gastroenterol. 2014;5(1):60-67. doi:10.1136/flgastro-2013-100371
- 28. Kourtis AP, Sheriff EA, Weiner-Lastinger LM, et al. Antibiotic multidrug resistance of Escherichia coli causing device- and procedure-related infections in the United States reported to the national healthcare safety network, 2013–2017. *Clin Infect Dis.* 2021;73(11):e4552–e4559. doi:10.1093/cid/ciaa1031
- 29. Goldstein E. Rise in the prevalence of resistance to extended-spectrum cephalosporins in the USA, nursing homes and antibiotic prescribing in outpatient and inpatient settings. J Antimicrob Chemother. 2021;76(11):2745–2747. doi:10.1093/jac/dkab251
- 30. Hagiya H, Kokado R, Ueda A, et al. Association of adverse drug events with broad-spectrum antibiotic use in hospitalized patients: a single-center study. *Intern Med.* 2019;58(18):2621–2625. doi:10.2169/internalmedicine.2603-18
- Shehab N, Lovegrove MC, Geller AI, et al. US Emergency Department visits for outpatient adverse drug events, 2013–2014. JAMA. 2016;316 (20):2115–2125. doi:10.1001/jama.2016.16201
- 32. Gerber JS, Ross RK, Bryan M, et al. Association of broad- vs narrow-spectrum antibiotics with treatment failure, adverse events, and quality of life in children with acute respiratory tract infections. *JAMA*. 2017;318(23):2325–2336. doi:10.1001/jama.2017.18715
- 33. François P, Schrenzel J, Götz F. Biology and regulation of staphylococcal biofilm. Int J Mol Sci. 2023;24(6):5218. doi:10.3390/ijms24065218

- 34. Zibari GB, Maguire S, Aultman DF, McMillan RW, McDonald JC. Pyogenic liver abscess. Surg Infect. 2000;1(1):15-21. doi:10.1089/109629600321254
- 35. Mischnik A, Kern WV, Thimme R. Pyogenic liver abscess: changes of organisms and consequences for diagnosis and therapy. Dtsch Med Wochenschr. 2017;142(14):1067–1074. doi:10.1055/s-0043-100540

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