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Prognostic risk factors for pyogenic liver abscess caused by *Klebsiella pneumoniae*

Yunxiao Lyu[1*] and Bin Wang[1]

Abstract

Background Pyogenic liver abscess (PLA) caused by *Klebsiella pneumoniae* can vary in severity, and several risk factors for the development of organ dysfunction in PLA have been implicated. However, few studies to date have explored the most common risk factors for clinical severity.

Methods We conducted a study on patients with PLA caused by *Klebsiella pneumoniae* between February 2013 and December 2022.Using logistic regression analysis, we sought to identify factors associated with positive blood culture, septic shock, and intensive care unit (ICU) admission.

Results After included 200 patients, we found that an elevated procalcitonin (PCT) level ($p=0.03$), higher glucose level ($p=0.03$), and lower total cholesterol (TC) level ($p=0.01$) were associated with a higher likelihood of positive blood bacteriological culture. Additionally, an increased PCT level ($p=0.02$) and lower TC level ($p<0.01$) were associated with an elevated risk of septic shock. Furthermore, a higher PCT level ($p<0.01$) was associated with a higher probability of ICU admission.

Conclusion In patients with PLA caused by *Klebsiella pneumoniae*, the PCT, glucose, and TC levels were found to be associated with positive blood culture, septic shock, and ICU admission.

Keywords Pyogenic liver abscess, *Klebsiella pneumoniae*, Blood bacteriological culture, Septic shock

Background

Pyogenic liver abscess (PLA) is a serious yet relatively uncommon infectious disease with a mortality rate ranging from 2.8 to 10.8% [1, 2]. Common types of bacteria in liver abscesses include *Escherichia coli* and *Klebsiella pneumoniae* [3]. During the past few decades, *K. pneumoniae* has become the most common pathogen in China and throughout the Asia-Pacific region [4, 5]. Patients with diabetes who develop a *K. pneumoniae*-induced liver abscess are more likely to develop invasive *K. pneumoniae* liver abscess syndrome, which is characterized by a PLA with infection in other sites as well (e.g., lung abscess, endophthalmitis, meningitis, necrotizing fasciitis) [6].

Some studies that focused on the risk factors for PLA have shown that advanced age, diabetes mellitus, liver cirrhosis, and malignancy may be associated with the severity of PLA [7, 8]. Additionally, several studies have shown that the C-reactive protein level, neutrophil-to-lymphocyte ratio, and fibrinogen level are associated with a higher risk of poor outcomes in patients with PLA [9, 10]. A recent report showed that the total cholesterol (TC) level on admission is an independent prognostic factor in patients with PLA [11]. Low plasma TC levels are associated with wider changes in cholesterol metabolism and its functional roles, and these appear to play

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a significant role in sepsis pathophysiology [12]. However, studies on these indicators in patients with liver abscesses caused by *K. pneumoniae* infection remain scarce. Therefore, we explored the risk factors for positive blood culture, septic shock, and intensive care unit (ICU) admission in these patients.

Methods

Patients admitted to a tertiary care hospital with an intensive care unit capacity of 20 beds were included in the study from February 2013 to December 2022. PLA caused by *K. pneumoniae* was diagnosed when the following criteria were met. (1) At least one of the following symptoms were present: fever, chills, right upper quadrant or epigastric pain, nausea, vomiting, or diarrhea. (2) Contrast-enhanced computed tomography and/or magnetic resonance imaging findings were compatible with a liver abscess. (3) Pus and/or blood bacteriological culture was positive for *K. pneumoniae* [13]. Patients who met the following criteria were excluded: (1) age of < 18 years; (2) diagnosis of a parasitic, fungal, or amoebic abscess or an abscess caused by a liver tumor; and (3) treatment in another hospital before admission.

The following information was collected from the patients' medical records in the electronic data system of our hospital: demographic characteristics (age and sex), vital signs at admission, clinical symptoms, comorbidities, diagnosis, laboratory data, and current medical condition. The laboratory values were collected on the first day of hospital admission or within 24 h after the clinical diagnosis of PLA. All outcomes were assessed within 24 h of PLA diagnosis.

The treatment procedure for PLA in our hospital was implemented according to the published literature [14]. All patients received broad-spectrum antibiotics until pus or blood culture susceptibility test results were available. If the following symptoms appeared, acute blood bacteriological culture was performed: (1) chills and shivering, (2) body temperature of > 38.5 °C, or (3) manifestations of shock. When ultrasound or CT examination showed that the abscess was liquefied, puncture drainage or puncture aspiration was performed, and bacterial culture of pus was initiated. Our institution employs this comprehensive treatment strategy for patients with PLA. Septic shock was diagnosed in patients with sepsis who developed persistent hypotension requiring vasopressors to maintain the mean arterial pressure at ≥ 65 mmHg and who had a serum lactate level of > 2 mmol/L despite adequate volume resuscitation [15].

Statistical analysis

Continuous variables conforming to a normal distribution are presented as mean ± standard deviation and were compared using a t-test. Non-normally distributed variables are presented as median (interquartile range). Descriptive statistics were used to summarize the demographic and clinical variables, which are presented as mean ± standard error of the mean. We performed multivariate analyses of the statistically significant factors identified in the univariate analyses using a logistic regression model. To identify the predictive factors, variables with a p-value of < 0.1 in the univariate analysis were further examined by logistic regression in the multivariate analysis. All statistical analyses were performed using R software version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was considered at a p-value of < 0.05.

Results

Baseline characteristics

In total, 200 patients were enrolled in this study. The flow diagram of the study was showed in Fig. 1. The patients' baseline characteristics are shown in Table 1. Their age ranged from 18 to 94 years (mean: 61.7 years), and they comprised 135 male and 65 female patients. Their temperature on admission was 38.8 ℃ and mean body mass index was 21.6 kg/m^2. A total of 68 patients did not undergo percutaneous drainage or puncture, 72 patients underwent drainage, and 60 patients underwent puncture. Ninety patients had diabetes mellitus, and 20 patients had a malignant tumor. A total of 132 patients underwent a pus bacteriological culture, among whom 119 patients obtained positive results and 13 obtained negative results; 63 patients did not undergo a pus culture. Finally, 177 patients underwent a blood culture, among whom 42 had positive results and 135 had negative results. Considering the severity of PLA, 18 patients suffered septic shock, and 13 patients required ICU admission that showed in Table 2. Due to the limited ICU beds in our hospital, five shock patients could not be admitted to the ICU for treatment. These patients were treated in the general ward and eventually recovered.The data of microbiological data in this study showed that two bacteriological culture showed ESBL positive. The antibiotic resistance showed ampicillin-resistance in 11 patients (5.50%), ceftriaxone-resistance in three patients (1.50%), cefoperazone and sulbactam-resistance in one patient (0.50%) and levofloxacin-resistance in threepatients (1.50%). The pus and blood bacteriological culture in one patient showed carbapenem-resistance and recovered after the use of cefidine/avibadan (Table 3).

Factors associated with positive blood culture

In univariate analysis, significant predictors of positive blood culture included male, procalcitonin (PCT), glucose, blood urea nitrogen (BUN), TC and low-density lipoprotein (LDL) (Table 4). The multivariate analysis showed that a higher PCT level (OR: 1.019, 95%CI:

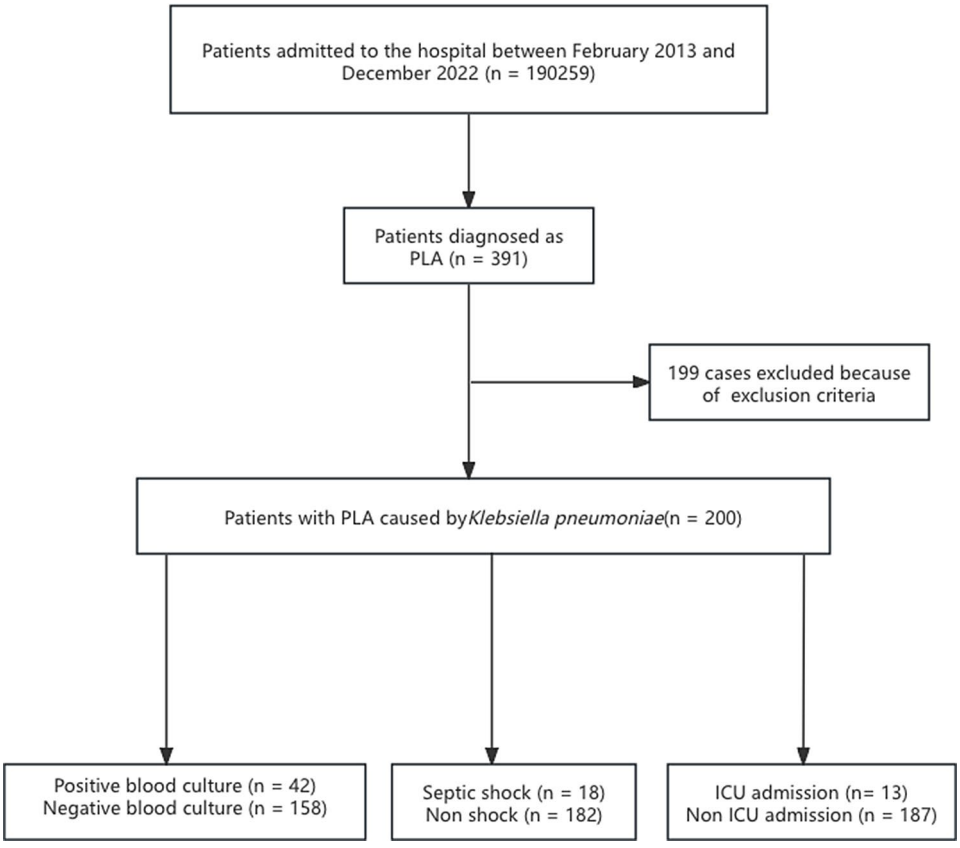

Fig. 1 Flow diagram of the study

1.002–1.038; $p=0.026$), higher glucose level (OR: 1.113, 95%CI: 1.013–1.227; $p=0.027$), and lower TC level (OR: 0.362, 95%CI: 0.152–0.753; $p=0.011$) were associated with a higher incidence of blood culture positivity (Table 4).

Factors associated with septic shock

In the univariate analysis, significant predictors of septic shock included PCT, glucose level, BUN, TC, high-density lipoprotein (HDL), LDL, INR, and D-dimerl (Table 5). In the multivariate analysis, a higher PCT level (OR: 1.031, 95%CI: 1.000-1.052); $p=0.015$) and lower TC level (OR: 0.253, 95%CI: 0.091–0.704; $p=0.008$) were associated with a higher incidence of septic shock (Table 5).

Factors associated with ICU admission

In the univariate analysis, significant predictors of ICU included PCT, aspartate transaminase, glucose, BUN, triglyceride, and INR (Table 6). The multivariate analysis showed that a higher PCT level (OR: 1.018, 95%CI: 0.999–1.036; $p=0.001$) was associated with a greater incidence of ICU admission (Table 6).

Discussion

In this retrospective study, we identified several laboratory indices associated with the severity of PLA caused by *K. pneumoniae.* Our study showed that higher PCT, higher glucose, and lower TC levels were associated with a higher incidence of positive blood bacteriological culture. A higher PCT level, lower TC level, and higher INR were associated with a higher incidence of septic shock. Finally, higher PCT and BUN levels were associated with a higher incidence of ICU admission.

The microbiologic etiology of PLA has recently changed and varies by geographic location [16]. During the past several decades, Escherichia coli is the most frequently isolated bacterium of PLA [7, 8]. Recent studies have shown an increasing prevalence of *K. pneumoniae*, especially in Southeast Asia [17, 18]. In our study, antibiotic resistance was showed in Table 3. Some studies have explored the relationship between certain clinical features and PLA. A recent study conducted by Li et al. [9] showed that a higher C-reactive protein-to-platelet ratio, neutrophil-to-lymphocyte and platelet ratio, and fibrinogen-to-platelet ratio were associated with a higher risk of poor outcomes. Additionally, Zhang et al. [19] found that the serum albumin-to-globulin ratio was associated with worse outcomes. Nonetheless, the bacterial etiology

Table 1 The characteristics of included patients

Characteristics	Values
Age, y	61.7 (13.4)
Male, n (%)	135 (67.5)
Temperature on admission, ℃	38.8 (1.1)
MAP, mmHg	92.6 (14.9)
BMI, Kg/m^2	21.6 (3.6)
Procalcitonin (< 0.1) ng/L	13.9 (24.7)
C-reactive protein (< 10) mg/L	160.5 (55.8)
WBC, (3.95–9.5)×10^9/L	12.9 (5.8)
Neutrophil, (1.8–6.3)×10^9/L	10.9 (5.5)
Platelet, (125–350)×10^9/L	196.5 (101.9)
Total bilirubin, (< 21) μmol/L	20.8(17.9)
Direct bilirubin, (< 7)μ mol/L	12.4 (14.6)
Aspartate aminotransferase, (7–40) U/L	74.1 (135.2)
Alanine aminotransferase, (13–35) U/L	72.6 (84.9)
γ-GT, (7–45) U/L	164.3 (145.2)
Albumin, (40–55) g/L	31.2 (5.6)
Glucose, (9.9–6.1) mmol/L	8.9 (4.2)
Creatinine, (41–81) umol/L	77.8 (81.3)
BUN, (3.1–8.8) mmol/L	6.1 (3.8)
Total cholesterol, (< 5.18) mmol/L	3.3 (0.9)
Triglycerides, (< 1.7) mmol/L	1.5 (0.9)
HDL, (1.29–1.55) mmol/L	0.7 (0.3)
LDL, (< 3.4) mmol/L	1.9 (0.8)
INR (0.8–1.25)	1.2 (0.2)
D-dimmer, (< 0.5) ug/ml	3.8 (3.9)
Length, mm	45 (4.6)
Comorbidities	
Diabetes mellitus, n (%)	90.0(45)
Malignant tumor, n (%)	20.0(10)
Length of hospital stay, days	15.1 (8.9)
Duration of use of antibiotics, days	10.3 (7.6)

Note Values are presented as mean (±standard deviation) or number (percentage). BMI: body mass index, WBC: white blood cell count, γ-GT: gamma-glutamyl transferase, BUN: blood urea nitrogen, HDL: high-density lipoprotein, LDL: low-density lipoprotein, INR: international normalized ratio

Table 3 The microbiological and antimicrobial susceptibility characteristics of the included patients

Characteristics	Values
ESBL	
Positive, n (%)	2 (1.0)
Negative, n (%)	198 (99.0)
Antibiotic resistance	
Ampicillin	11 (5.5)
Ceftriaxone	3 (1.5)
Cefoperazone and Sulbactam	1 (0.5)
Levofloxacin	3 (1.5)
Carbapenem	1 (0.5)

Note ESBL, extended-spectrum beta-lactamases

Table 2 The characteristics of severity in PLA

Characteristics	Values
Procedure of drainage	
None, n (%)	68(34.0)
Percutaneous drainage, n (%)	72 (36.0)
Percutaneous puncture, n (%)	60 (30.0)
Blood bacteriological culture	
Positive, n (%)	42 (21.0)
Negative, n (%)	135(67.5)
Pus bacteriological culture	
Positive, n (%)	119 (59.5)
Negative, n (%)	13 (6.5)
Septic shock	
Yes	18 (9.0)
No	182 (91.0)
ICU admission	
Yes	13 (6.5)
No	187 (93.5)

Note ICU, intensive care unit

of liver abscesses in these studies varied and included *E. coli*, *K. pneumoniae*, and other microorganisms. Studies have shown that PLA caused by *K. pneumoniae* infection may be more severe, and some patients may even have multiple organ infections (e.g., intracranial infection or endophthalmitis) [20, 21]. However, few studies to date have focused on the factors related to the severity of PLA caused by *K. pneumoniae* infection.

Positive blood cultures are often considered an aspect of the severity of infectious disease, and they often increase patient mortality [22]. The serum PCT level has been shown to be positively correlated with the severity of several diseases [23, 24]. In our study, a higher PCT level was associated with a higher incidence of positive blood culture, septic shock, and ICU admission. These findings are consistent with those of previous studies showing that the PCT level can be used to predict bloodstream infection [25]. Our study also demonstrated that a higher glucose level was a risk factor for positive blood culture. Patients with diabetes are at greater risk of liver abscesses caused by *K. pneumoniae* infection than patients without diabetes [26]. Our study showed that the fasting blood glucose level is a risk factor for positive blood culture, suggesting that poorly controlled blood glucose may be more likely to cause *K. pneumoniae*-positive bloodstream infections. However, diabetes mellitus was not a risk factor for blood culture positivity in our study.

Our study showed that a lower TC level was associated with a higher incidence of positive blood culture and septic shock, similar to the findings reported by Feng et al. [11]. They showed that a low TC level on admission was an independent risk factor for PLA. Multiple studies have showed that a lower TC level is associated with higher mortality in patients with sepsis [27, 28]. The specific biological mechanism underlying this association is not fully understood. The reduction in the TC level caused by severe infection may be related to reduced

Table 4 Univariate and multivariate analysis for PLA patients with positive blood bacteriological culture

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	0.999 (0.974–1.025)	0.939		
Gender (male)	2.391 (1.082–5.881)	0.042	2.241 (0.853–6.531)	0.116
DM	1.644 (0.831–3.289)	0.155		
Malignant tumor	1.714 (0.574–4.602)	0.302		
Procalcitonin	1.025 (1.013–1.038)	< 0.001	1.019 (1.002–1.038)	0.026
C-reactive protein	1.002 (0.996–1.009)	0.428		
Total bilirubin	1.009 (0.991–1.026)	0.311		
Direct bilirubin	1.011 (0.989–1.033)	0.275		
Aspartate aminotransferase	1.001 (0.999–1.003)	0.311		
Alanine aminotransferase	1.002 (0.999–1.005)	0.294		
WBC	1.028 (0.97–1.087)	0.34		
PLT	0.997 (0.993-1.000)	0.086	0.999 (0.995–1.004)	0.873
Albumin	0.942 (0.885–1.001)	0.0572	1.001 (0.916–1.091)	0.989
Glucose	1.172 (1.083–1.274)	< 0.001	1.113 (1.013–1.227)	0.027
Creatinine	1.000 (0.994–1.004)	0.839		
BUN	1.121 (1.029–1.236)	0.015	1.051 (0.9-1.164)	0.419
Total cholesterol	0.463 (0.303–0.685)	< 0.001	0.362 (0.152–0.753)	0.011
Triglycerides	1.394 (0.974–2.058)	0.071	1.374 (0.819–2.452)	0.247
HDL	0.552 (0.181–1.566)	0.278		
LDL	0.731(0.259–0.851)	0.002	1.803 (0.65–5.494)	0.272
INR	5.549 (0.989–45.342)	0.073	5.551 (0.097–11.39)	0.919
D-Dimer	1.071 (0.99–1.155)	0.077	0.962 (0.857–1.068)	0.484

Note OR, Odds Ratio, WBC: white blood cell count, γ-GT: gamma-glutamyl transferase, BUN: blood urea nitrogen, HDL: high-density lipoprotein, LDL: low-density lipoprotein, INR: international normalized ratio. P-values less than 0.05 were considered statistically significant

Table 5 Univariate and multivariate analysis for PLA patients with shock

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.011 (0.974–1.05)	0.568		
Gender (male)	1.764 (0.603–6.428)	0.334		
DM	1.247 (0.466–3.334)	0.655		
Malignant tumor	1.139(0.171–4.456)	0.869		
Procalcitonin	1.04 (1.03–1.06)	< 0.001	1.031 (1.000-1.052)	0.015
C-reactive protein	1.007 (0.997–1.016)	0.179		
Total bilirubin	1.002 (0.971–1.025)	0.879		
Direct bilirubin	1.008 (0.974–1.035)	0.552		
Aspartate aminotransferase	1.001 (0.997–1.003)	0.488		
Alanine aminotransferase	0.998 (0.989–1.004)	0.758		
WBC	0.968 (0.879–1.052)	0.471		
PLT	0.995 (0.989-1.000)	0.113		
Albumin	0.891(0.813–0.972)	0.011	1.00 (0.991–1.013)	0.821
Glucose	1.148 (1.034–1.275)	0.009	1.03 (0.891–1.291)	0.368
Creatinine	0.992 (0.983–1.004)	0.858		
BUN	1.123 (1.018–1.253)	0.022	0.99 (0.792–1.231)	0.871
Total cholesterol	0.206 (0.099–0.384)	< 0.001	0.253 (0.091–0.704)	0.008
Triglycerides	1.432 (0.919–2.167)	0.079	1.37 (0.411–4.594)	0.628
HDL	0.113 (0.016–0.633)	0.023	0.77 (0.021–37.472)	0.911
LDL	0.195 (0.073–0.447)	< 0.001	1.38 (0.261–3.374)	0.630
INR	1.415 (1.271–1.642)	< 0.001	1.09 (0.781–2.323)	0.122
D-Dimer	1.161 (1.06–1.273)	0.001	1.09 (1.282–3.429)	0.291

Note OR, Odds Ratio, WBC: white blood cell count, γ-GT: gamma-glutamyl transferase, BUN: blood urea nitrogen, HDL: high-density lipoprotein, LDL: low-density lipoprotein, INR: international normalized ratio. P-values less than 0.05 were considered statistically significant

Table 6 Univariate and multivariate analysis for PLA patients with ICU admission

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.006 (0.965–1.052)	0.772		
Gender (male)	1.653 (0.485–7.568)	0.457		
DM	1.461 (0.468–4.699)	0.509		
Malignant tumor	1.707 (0.252–7.027)	0.508		
Procalcitonin	1.024(1.009–1.039)	0.021	1.018 (0.999–1.036)	0.001
C-reactive protein	1.001 (0.991–1.012)	0.749		
Total bilirubin	0.994 (0.95–1.023)	0.744		
Direct bilirubin	1.002 (0.954–1.033)	0.934		
Aspartate aminotransferase	1.003 (1.000-1.005)	0.026	1.011 (1.001–1.023)	0.047
Alanine aminotransferase	1.004 (0.998–1.007)	0.091	0.986 (0.965–1.27)	0.174
WBC	0.986 (0.886–1.083)	0.794		
PLT	0.996 (0.989–1.002)	0.306		
Albumin	0.923 (0.834–1.02)	0.118		
Glucose	1.149 (1.02–1.295)	0.019	1.103 (0.958–1.27)	0.164
Creatinine	1.001 (0.994–1.005)	0.487		
BUN	1.153 (1.039–1.303)	0.017	1.119 (0.988–1.252)	0.232
Total cholesterol	0.983 (0.547–1.744)	0.954		
Triglycerides	1.83 (1.192–3.026)	0.007	1.478 (0.881–2.669)	0.137
HDL	0.469 (0.067–2.622)	0.416		
LDL	0.649 (0.283–1.395)	0.284		
INR	1.883 (1.143–2.174)	0.044	1.909 (0.126–2.913)	0.641
D-Dimer	1.027 (0.882–1.15)	0.679		

Note OR, Odds Ratio, WBC: white blood cell count, γ-GT: gamma-glutamyl transferase, BUN: blood urea nitrogen, HDL: high-density lipoprotein, LDL: low-density lipoprotein, INR: international normalized ratio. P-values less than 0.05 were considered statistically significant

intake; impaired intestinal absorption; or disrupted cholesterol transport, increased metabolism, and cholesterol consumption due to toxin removal [12, 28]. Although a previous study showed that the HDL and LDL levels are reduced in patients with sepsis [28], the HDL and LDL levels were not significantly correlated with PLA severity in the present study. Further research is needed to elucidate the specific mechanism for this.

Our study had several limitations. First, it was a retrospective study, which may have resulted in bias. Larger-sample studies are required in the future. Second, we only collected data within the first 24 h; however, some indices may change significantly in the early stage of the disease.

Conclusion

The PCT level, glucose level, TC level, INR, and BUN level were associated with a higher incidence of blood culture positivity, septic shock, and ICU admission in patients with PLA caused by *K. pneumoniae*.

Abbreviations

PLA Pyogenic liver abscess
ICU Intensive care unit
PCT Procalcitonin
OR Odds ratio
TC Total cholesterol

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YX.L. and B.W. wrote the main manuscript text and YX.L. prepared tables and figure. All authors reviewed the manuscript.

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Data availability

The datasets generated and/or analyzed during the current study are not publicly available because of hospital policy but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Dongyang People's Hospital and followed the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients before data collection.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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