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Original Article

Nomogram prediction model called “ADPLCP” for predicting linezolid-associated thrombocytopenia in elderly individuals

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ABSTRACT

Background: Linezolid-associated thrombocytopenia (LAT) leads to drug withdrawal associated with a poor prognosis. Some risk factors for LAT have been identified; however, the sample size of previous studies was small, data from elderly individuals are limited, and a simple risk score scale was not established to predict LAT at an early stage, making it difficult to identify and intervene in LAT at an early stage.

Methods: In this single-center retrospective case-control study, we enrolled elderly patients treated with linezolid in the intensive care unit from January 2015 to December 2020. All the data of enrolled patients, including demographic information and laboratory findings at baseline, were collected. We analyzed the incidence and risk factors for LAT and established a nomogram risk prediction model for LAT in the elderly population.

Results: A total of 428 elderly patients were enrolled, and the incidence of LAT was 35.5% (152/428). Age ≥80 years old (OR=1.980; 95% CI: 1.179–3.325; *P*=0.010), duration of linezolid ≥ 10 days (OR=1.100; 95% CI: 1.050–1.152; *P* <0.0001), platelet count at baseline (100–149×10^9/L *vs.* ≥200×10^9/L, OR=8.205, 95% CI: 4.419–15.232, *P* <0.0001; 150–199 ×10^9/L *vs.* ≥200×10^9/L, OR=3.067, 95% CI: 1.676–5.612, *P* <0.001), leukocyte count at baseline ≥16×10^9/L (OR=2.580; 95% CI: 1.523–4.373; *P* <0.0001), creatinine clearance <50 mL/min (OR=2.323; 95% CI: 1.388–3.890; *P*=0.001), and total protein <60 g/L (OR=1.741; 95% CI: 1.039–2.919; *P*=0.035) were associated with LAT. The nomogram prediction model called “ADPLCP” (age, duration, platelet, leukocyte, creatinine clearance, protein) was established based on logistic regression. The area under the curve (AUC) of ADPLCP was 0.802 (95% CI: 0.748–0.856; *P* <0.0001), with 78.9% sensitivity and 69.2% specificity (cut-off was 108). Risk stratification for LAT was performed based on “ADPLCP.” Total points of <100 were defined as low risk, and the possibility of LAT was <32.0%. Total points of 100–150 were defined as medium risk, and the possibility of LAT was 32.0–67.5%. A total point >150 was defined as high risk, and the probability of LAT was >67.5%.

Conclusions: We created the ADPLCP risk score scale to predict the occurrence of LAT in elderly individuals. ADPLCP is simple and feasible and is helpful for the early determination of LAT to guide drug withdrawal or early intervention.

Introduction

Linezolid is a member of the oxazolidinone antibiotics class that selectively inhibits bacterial protein synthesis in a range of gram-positive organisms. Linezolid is widely used to treat gram-positive infections, including methicillin-resistant *Staphylococcus aureus* (MASA), vancomycin-resistant *Staphylococcus aureus* (VRSA), and vancomycin-resistant *Enterococcus* (VRE).[1] One of the most common adverse reactions of linezolid was reversible myelosuppression, including anemia and thrombocytopenia, of which the incidence of linezolid-associated thrombocytopenia (LAT) was 29.9% (95% confidence interval: 18.2-48.3).[2–11] In a systematic review of 24 studies enrolling 6894 patients in ICUs, thrombocytopenia increase the risk of death, after confounding

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factors are adjusted for.[12] Therefore, it is necessary to establish a risk score scale for LAT to help us identify and intervene in LAT at an early stage.

Several risk factors for LAT have been identified, such as kidney dysfunction,[2,5,7,9,13,14] chronic liver disease,[5] duration of linezolid,[5,6,9] and baseline platelet count.[3,4,7–10] However, previous single-center studies with small sample sizes have not established a simple and feasible risk score scale, making it difficult to accurately predict LAT at an early stage. The trough concentration of linezolid in elderly individuals was significantly higher than that in the young,[15] and so the incidence of LAT may be higher, but there are few relevant studies. Therefore, we evaluated the incidence and risk factors for LAT in the elderly population and established a simple risk score scale for the early prediction of LAT.

Methods

Study design and participants

For this retrospective case-control study, we screened patients aged >65 years in the intensive care units in the First Medical Center of the PLA General Hospital who were administered linezolid between January 2015 and December 2020. Exclusion criteria were the following: (1) treated with drugs that affect platelet, such as chemotherapy drugs and tigecycline; (2) blood routine and other indicators were not monitored every 2 days; (3) platelet count at baseline $<100\times10^9$/L; (4) linezolid was used for <3 days; (5) hematological system diseases; (6) patients with trauma, bleeding, or surgery; (7) disseminated intravascular coagulation (DIC) or prone to DIC[16]; (8) died within 7 days of initiation of linezolid; (9) pregnancy or lactation; and (10) linezolid allergy.

Linezolid is from Pfizer (New York, USA). Specification: linezolid injection (0.6 g: 300 mL); linezolid tablet (0.6 g). Dosage regimen: linezolid injection or linezolid tablet (0.6 g, twice daily).

The primary endpoint or event of interest in this study was the development of LAT. Thrombocytopenia was defined as a decrease in platelet count of $<100\times10^9$/L or a 30% reduction.[5,6] The WHO-UMC method was used to evaluate LAT, and the causal relationship was certain or probable/likely to be classified as LAT.

Data collection

All the data of enrolled patients, including demographic information and laboratory findings at baseline, were extracted from electronic medical records. Demographic information consisted of sex, age, duration of linezolid therapy, infection site, and comorbid diseases. Laboratory findings consisted of routine blood tests and total protein (TP), albumin, liver and kidney function, and lactate dehydrogenase (LDH) levels. Laboratory results within 3 days of starting medication were used as baseline data. When baseline laboratory indicators were tested multiple times, the results of the first test closest to the initiation of medication were used for the study. The platelets count of the patients enrolled in this study was reviewed at least once every 48 h during treatment. We averaged the platelets count data of the patients who were reviewed multiple times on the same day.

Statistical analysis

IBM SPSS Statistics 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) and R 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.) were used for statistical analyses. A Kolmogorov–Smirnov test was used to test the normality of the continuous variables. Quantitative data with normal distributions were expressed as the means±standard deviations and were analyzed by *t*-tests. Quantitative data with non-normal distributions are presented as the medians and interquartile ranges (IQRs) and were assessed with the Mann–Whitney *U* test. The chi-squared test or Fisher's exact probability test was used to compare count data. The cut-off value for each selected factor and combined index was determined by the Youden index and receiver operating characteristic (ROC) curve. To obtain the OR of each factor and calculate the point of each factor in the scoring scale, continuous variables were converted into categorical variables by cut-off, and the duration of linezolid therapy was classified as per day. Factors with significant differences (P <0.2) in univariate analysis were entered into a multivariate binary logistic regression model (forward: LR) to determine their independent effects. The nomogram prediction model was established using R 3.6.2 based on logistic regression, and an ROC curve was used to evaluate the validity of the nomogram prediction model. Decision curve analysis was used to evaluate the model's benefits.[17] All tests were two-tailed, and a P <0.05 was considered statistically significant.

Results

Demographic profiles and laboratory findings

A total of 428 patients were enrolled in our study (Figure 1). The incidence of LAT was 35.5% (152/428), and it appeared after 12.0 ± 5.6 days of linezolid administration. The clinical characteristics and laboratory findings are shown in Table 1.

Univariate and multivariate logistic regression analyses of categorical variables

In univariate analysis, age, duration of linezolid, platelet count at baseline, leukocyte count at baseline, serum creatinine, creatinine clearance (Ccr), and LDH were associated with LAT (P <0.05, Table 1).

Factors with P <0.2 in the univariate analysis were entered into a multivariate binary logistic regression model (forward: LR). Before the multivariate analysis, we made a collinearity diagnosis of all the factors, and no collinearity problems were found.

Age ≥80 years old, duration of linezolid ≥ 10 days, platelet count at baseline, leukocyte count at baseline $\geq16\times10^9$/L, Ccr <50 mL/min, and TP <60 g/L were associated with LAT (Table 2).

Nomogram prediction model for LAT

The nomogram prediction model "ADPLCP" based on logistic regression analysis was established to quantitatively predict LAT. ADPLCP represents "age, duration, platelet, leukocyte, creatinine clearance, protein" (Figure 2). The calibration curve

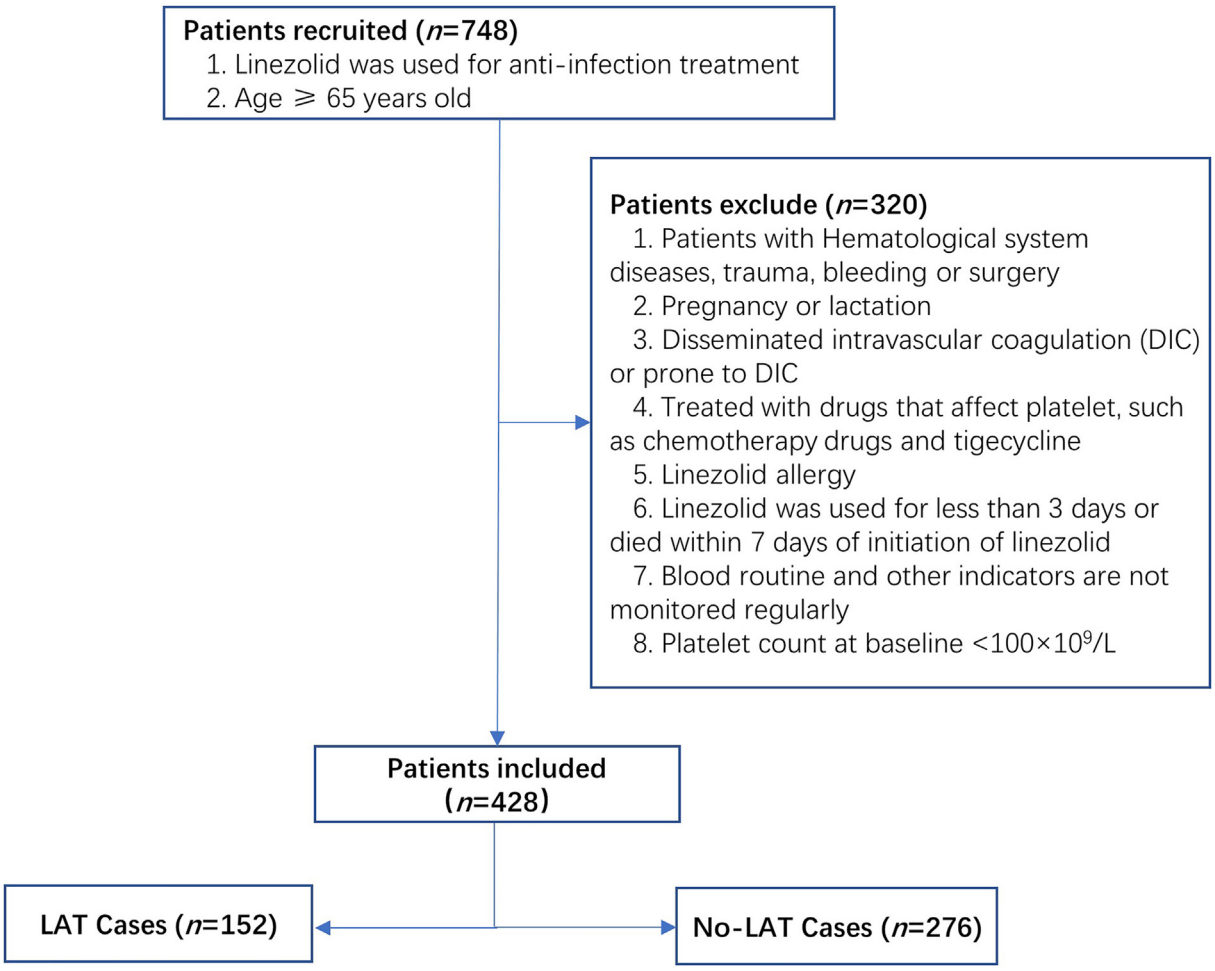

Figure 1. Screening of patient selection and enrollment.
LAT: Linezolid-associated thrombocytopenia.

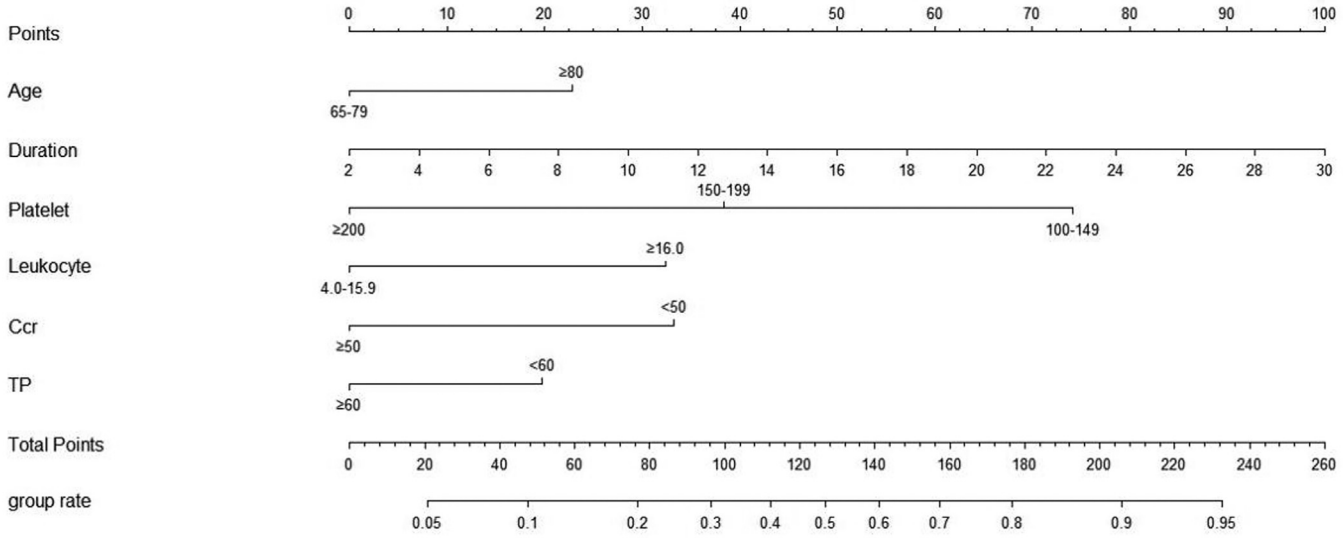

Figure 2. ADPLCP created by nomogram prediction model was to predict the probability of LAT. To estimate the probability of LAT, mark patient values at each axis, draw a straight line perpendicular to the point axis, and sum the points for all variables. Next, mark the sum on the total point axis and draw a straight line perpendicular to the probability axis. For example, "A" patient was aged 85 years, and his Ccr was 45 mL/min, platelet was 180×10^9/L, leukocyte was 17.0×10^9/L, total albumin was 65 g/L, and planned duration of linezolid was 14 days; accordingly, the total point of the patient would be 164, which indicates a probability of 0.73 for developing LAT.
ADPLCP: Age, duration, platelet, leukocyte, creatinine clearance, protein; Ccr: Creatinine clearance; LAT: Linezolid-associated thrombocytopenia; TP: Total protein.

Table 1
Clinical characteristics and laboratory tests of 428 enrolled patients.

Factors	All patients (*n*=428)	Linezolid associated thrombocytopenia		*P*-value
		Event (*n*=152)	Free of event (*n*=276)	
Sex				0.855*
Female	130 (30.4)	47 (30.9)	83 (30.1)	
Male	298 (69.6)	105 (69.6)	193 (69.9)	
Age (years)				0.013*
65–74	126 (29.4)	34 (22.4)	92 (33.3)	
75–84	187 (43.7)	66 (43.4)	121 (43.8)	
≥85	115 (26.9)	52 (34.2)	63 (22.8)	
BMI (kg/m^2)				0.369*
< 18.5	81 (18.9)	25 (16.4)	56 (20.3)	
18.5–<24.0	187 (43.7)	73 (48.0)	114 (41.3)	
≥24.0	160 (37.4)	54 (35.5)	106 (38.4)	
Duration of linezolid (days)	10.6 ± 5.5	12.0 ± 5.6	9.8 ± 5.2	<0.001†
Duration of linezolid (days)				<0.001*
<7	105 (24.5)	20 (13.2)	85 (30.8)	
7–13	224 (52.3)	90 (59.2)	134 (48.6)	
≥14	99 (23.1)	42 (27.6)	57 (20.7)	
Infection site				0.353*
Pulmonary	398 (93.0)	139 (91.4)	259 (93.8)	
Non-pulmonary	30 (7.0)	13 (8.6)	17 (6.2)	
Mechanical ventilation	177 (41.3)	66 (43.4)	111 (40.2)	0.421*
Basic disease				
COPD	278 (65.0)	96 (63.2)	182 (65.9)	0.563*
Pulmonary fibrosis	37 (8.6)	13 (8.6)	24 (8.7)	0.960*
Coronary heart disease	205 (47.9)	68 (44.7)	137 (49.6)	0.331*
Hypertension	250 (58.4)	93 (61.2)	157 (56.9)	0.388*
Diabetes mellitus	177 (41.4)	68 (44.7)	109 (39.5)	0.292*
Chronic kidney disease	124 (29.0)	52 (34.2)	72 (26.1)	0.076*
Neurological disease	46 (10.7)	14 (9.2)	32 (11.6)	0.446*
Cardiac dysfunction	69 (16.1)	22 (14.5)	47 (17.0)	0.491*
Laboratory tests				
Platelet count (×10^9/L)	205 (152, 267)	166 (127, 225)	223 (175, 283)	<0.001†
Platelet count groups				<0.001*
100–149	99 (23.1)	63 (41.4)	36 (13.0)	
150–199	101 (23.6)	41 (27.0)	60 (21.7)	
≥200	228 (53.3)	48 (31.6)	180 (65.2)	
Leukocyte (×10^9/L)	12.3 (8.9, 17.3)	13.1 (9.9, 18.8)	11.9 (8.6, 16.6)	0.013‡
Erythrocyte (×10^{12}/L)	3.4 (2.9, 3.8)	3.2 (2.9,3.8)	3.5 (2.9,3.9)	0.190‡
TP (g/L)	63.1 (58.5, 68.6)	62.9 (57.1, 68.1)	63.4 (59.4, 68.7)	0.197‡
Albumin (g/L)	32.2 (28.6, 35.4)	31.9 (28.4, 35.8)	32.2 (28.9, 35.2)	0.969‡
Creatinine (μmol/L)	80 (56, 122)	95 (63, 164)	73 (54, 105)	<0.001‡
Ccr (mL/min)	52 (31, 80)	42 (26, 73)	60 (37, 84)	<0.001‡
Total bilirubin (μmol/L)	10.3 (6.9, 16.0)	10.8 (6.7, 16.6)	9.9 (7.1, 15.4)	0.488‡
Direct bilirubin (μmol/L)	4.7 (2.9, 7.0)	5.1 (3.3,7.8)	4.3 (2.8,6.7)	0.086‡
ALT (U/L)	18.9 (11.2, 34.4)	19.4 (12.3, 36.6)	18.7 (11.1, 32.9)	0.777‡
LDH (U/L)	251 (189, 341)	259 (203, 363)	242 (183, 327)	0.049‡
CRP (mg/L)	7.9 (3.5, 13.5)	8.6 (4.1, 14.2)	7.6 (3.1, 13.3)	0.122‡

Data were expressed as *n* (%), mean±standard deviation or median (range).
ALT: Alanine dehydrogenase; BMI: Body mass index; Ccr: Creatinine clearance; COPD: Chronic obstructive pulmonary disease; LDH: Lactate dehydrogenase; TP: Total protein.
* Chi-squared test.
† *t*-test.
‡ Mann–Whitney *U* test.

shows that the nomogram performed well when compared to the actual results (Figure 3). Decision curve analysis showed that the created nomogram added more net benefit than either the all-positive or no-positive situation in a large threshold range (0.1–1.0, Figure 4).

Predictive performance of ADPLCP and risk stratification for LAT

ROC curves were used to analyze the predictive performance of ADPLCP and other factors. The optimal cut-offs and corresponding sensitivity and specificity are listed in Table 3. The area under the curve (AUC) of total points in ADPLCP was 0.802 (95% CI: 0.748–0.856; *P* <0.001, Figure 5) with a sensitivity of 78.9% and a specificity of 69.2%; the cut-off was 108, and the corresponding incidence of LAT was 35% (Table 3).

Risk stratification for LAT was performed based on ADPLCP. Total points of <100 were defined as low risk, and the possibility of LAT was <32.0%. Total points of 100–150 were defined as medium risk, and the possibility of LAT was 32.0–67.5%. Total points >150 were defined as high risk, and the probability of LAT was >67.5%. In the study, 227 (53.0%) patients belonged to the low risk group; 146 (34.1%) patients belonged to the moderate risk group; and 55 (12.9%) patients belonged to the high risk group.

Table 2
Univariate and multivariate logistic regression analysis of categorical variables.

Variables		Univariate analysis		Multivariate analysis	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age (years)	≥80	2.147 (1.434–3.215)	<0.0001	1.980 (1.179, 3.325)	0.010
Sex	Male	0.961 (0.625–1.476)	0.855	NA	NA
BMI (kg/m^2)	18.5–<24.0	1.434 (0.823–2.500)	0.203	NA	NA
	≥24.0	1.141 (0.643–2.026)	0.652	NA	NA
Duration of linezolid (days)	≥10 days	1.074 (1.034, 1.115)	<0.0001	1.100 (1.050, 1.152)	<0.001
Platelet count (×10^9/L)	100–149	6.562 (3.907, 11.024)	<0.0001	8.205 (4.419, 15.232)	<0.001
	150–199	2.562 (1.540, 4.263)	<0.0001	3.067 (1.676, 5.612)	<0.001
Leukocyte (×10^9/L)	≥16.0	1.608 (1.054, 2.452)	0.027	2.580 (1.523, 4.373)	<0.001
Erythrocyte (×10^{12}/L)	≥3.5	0.722 (0.483–1.079)	0.112	NA	NA
TP (g/L)	<60	1.556 (1.013–2.389)	0.043	1.741 (1.039, 2.919)	0.035
Albumin (g/L)	≥35	1.135 (0.706–1.825)	0.600	NA	NA
Creatinine (μmol/L)	<90	2.606 (1.735–3.914)	<0.0001	NA	NA
Ccr (mL/min)	<50	2.917 (1.934–4.398)	<0.0001	2.323 (1.388, 3.890)	0.001
Total bilirubin (μmol/L)	≥17	0.896 (0.552–1.455)	0.658	NA	NA
Direct bilirubin (μmol/L)	≥7	0.701 (0.441–1.113)	0.132	NA	NA
ALT (U/L)	≥40	0.775 (0.507–1.187)	0.241	NA	NA
LDH (U/L)	≥250	0.704 (0.466–1.063)	0.095	NA	NA
CRP (mg/L)	≥6	0.723 (0.476–1.097)	0.128	NA	NA

ALT: Alanine dehydrogenase; BMI: Body mass index; Ccr: Creatinine clearance; COPD: Chronic obstructive pulmonary disease; LDH: Lactate dehydrogenase; NA: Not applicable; TP: Total protein.

Table 3
Predictive performance of the nomogram prediction model and other factors.

Variables	Cut-off	AUC (95% CI)	Sensitivity	Specificity	*P*-value
Total points	108	0.802 (0.748, 0.856)	0.789	0.692	<0.001
Age (years)	80	0.621 (0.553, 0.689)	0.767	0.470	0.001
Duration (days)	10	0.619 (0.550, 0.687)	0.589	0.638	0.001
Platelet (×10^9/L)	200	0.703 (0.635, 0.771)	0.656	0.685	<0.001
Ccr (mL/min)	50	0.661 (0.593, 0.729)	0.634	0.644	<0.001
Leukocyte (×10^9/L)	16.0	0.591 (0.520, 0.663)	0.667	0.486	0.014
TP (g/L)	60.0	0.549 (0.490, 0.608)	0.714	0.616	0.102

AUC: Area under the curve; Ccr: Creatinine clearance; TP: Total protein.

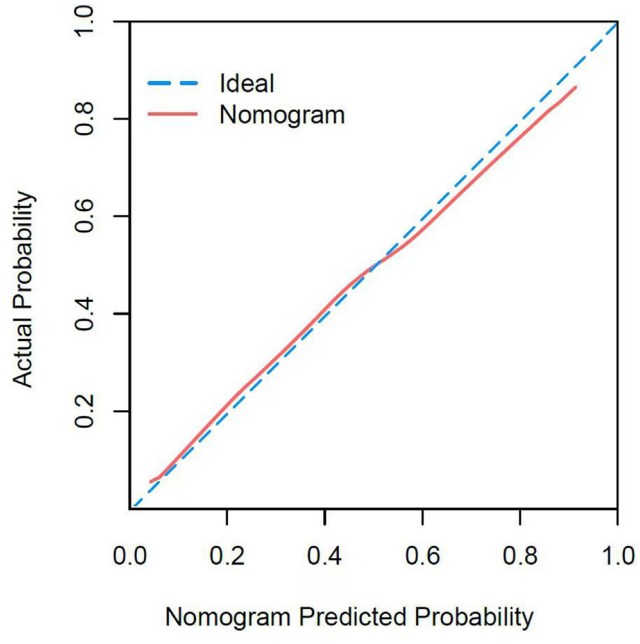

Figure 3. Calibration curves of nomograms in terms of agreement between the predicted risk and actual observed outcomes.

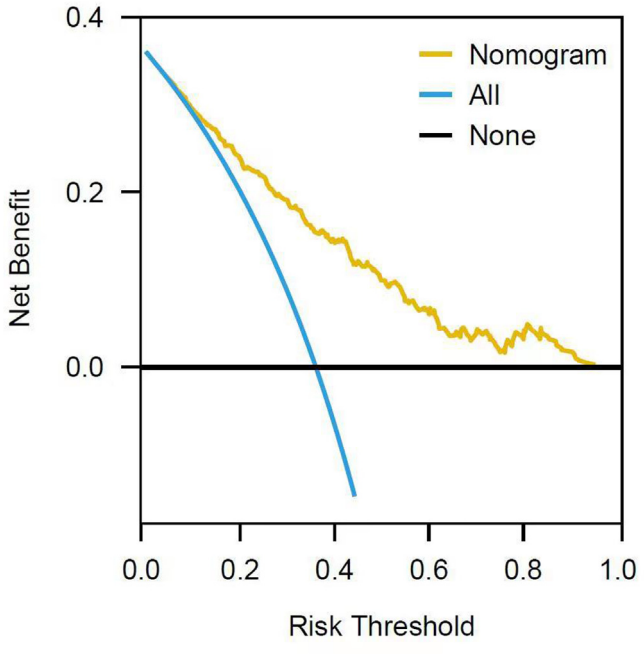

Figure 4. Decision curve analysis of the nomogram for LAT.
LAT: Linezolid-associated thrombocytopenia.

Discussion

We found that age, duration of linezolid, platelet count at baseline, leukocyte count at baseline, Ccr, and TP were risk factors for LAT in elderly individuals. We also established a nomogram prediction model called the ADPLCP risk score scale for LAT. With ADPLCP, we were able to assess patients' risk of daily

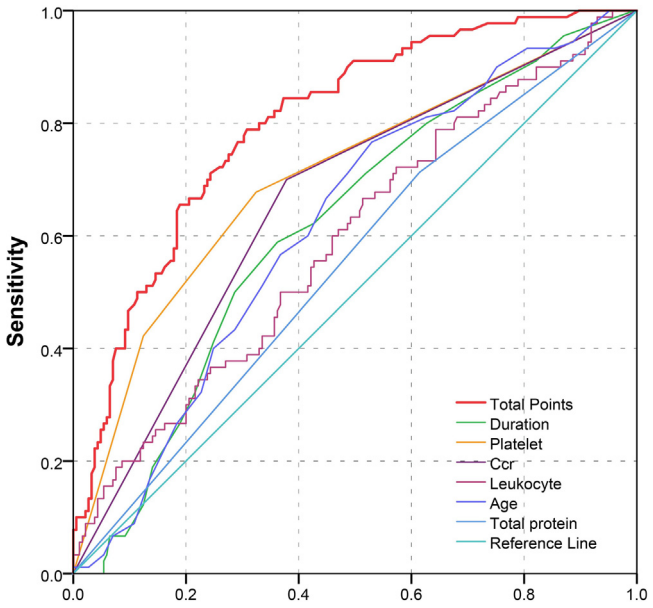

Figure 5. ROC curve for ADPLCP and other factors. AUC for ADPLCP was 0.802 (95% CI: 0.748–0.856).
ADPLCP: Age, duration, platelet, leukocyte, creatinine clearance, protein; AUC: Area under the curve; ROC: Receiver operating characteristic.

thrombocytopenia during linezolid treatment. The ADPLCP risk score scale can help us to assess the time and risk of LAT at an early stage to guide drug withdrawal and early intervention.

We included patients aged >65 years who had a 35.5% incidence of LAT, and the inclusion criteria were consistent with those from previous studies.[2–11] In a study of 50 elderly patients (age >60 years), the incidence of LAT was 48.0%; this value was slightly higher than that in our study, possibly because they did not exclude patients with baseline platelet count <100×10^9/L, and 48% of the included patients were malnourished.[8]

We found that patients aged >80 years had a 1.980-fold risk of LAT, which may be associated with slow linezolid metabolism or poor bone marrow hematopoietic function in elderly patients. A recent study showed that patients aged >80 years had concentrations thrice higher than those of patients aged <40 years, suggesting a positive correlation between linezolid concentrations and age.[15] Tinelli et al.[18] also found that the trough concentration of linezolid exceeded the normal threshold (8.0 mg/L) in elderly patients after they were given a conventional dose of linezolid (600 mg twice daily). Multiple pharmacokinetic studies have confirmed that the trough concentration of linezolid is associated with thrombocytopenia,[10,19,20] and so the risk of LAT increases with age.

In our study, LAT appeared after 12.0 ± 5.6 days of linezolid administration, which was consistent with the report of Nukui et al.[20] Studies have shown that a linezolid duration ≥14 days is associated with LAT.[5,6,9,20–22] We also found that the duration of linezolid was a risk factor for LAT, with a cut-off value of 10 days. This value was shorter than that in previous studies, possibly because the population we included was older, and all of them had severe infections.

A low baseline platelet count is a risk factor for LAT, which has been demonstrated in many studies,[3,4,7–10] and the threshold value of platelet count was 200×10^9/L.[4,7,8] We also found that the risk of LAT increased 8.205-fold when the baseline platelet count was <150×10^9/L, and 3.067-fold when the baseline platelet count was 150–199×10^9/L compared with baseline platelet count ≥200×10^9/L. The optimal cut-off value of platelet count was 200×10^9/L, which is highly consistent with that from previous studies. Since the criteria for defining LAT is a decrease in platelet count of ≥100×10^9/L or a 30% reduction, it is obvious that for lower baseline counts, a smaller decrease is required to meet the criteria for LAT. Therefore, the association between low platelet baseline count and higher risk for LAT is expected.

In our study, the risk of LAT increased 2.580-fold when the leukocyte count at baseline ≥16×10^9/L. Ichie et al.[6] also found that leukocyte count at baseline was a risk factor for LAT, which was consistent with our findings, suggesting that the initial gradient of infection may be related to LAT. However, Ichie et al.[6] found that when the leukocyte count at baseline >12×10^9/L, the risk of LAT was increased by 9.399 times, which was significantly higher than that in this study. This may be because of younger patients and a smaller number of patients (n=47) in Ichie's study.[6]

Pharmacokinetic studies of linezolid have indicated that 30% of linezolid is eliminated unchanged via the kidneys,[20] and the clearance rate of linezolid decreases by 20% in renal failure,[23] which leads to an increase in the plasma concentration of linezolid,[20] thereby inducing LAT. Several studies have shown a significant association between renal function impairment and LAT. [[2,5,7,9,13,14]] Takahashi et al.[5] found that when the Ccr was <50 mL/min, the risk of LAT was 2.32 times, and LAT occurred earlier (6.7 ± 4.4 days *vs.* 8.5 ± 5.2 days, P=0.039). In this study, Ccr was also found to be correlated with LAT. When Ccr <50 mL/min, the risk of LAT was 2.323 times compared to Ccr ≥50 mL/min, which was highly consistent with the study of Takahashi et al.[5] Ccr may be correlated to age, while in our study, we performed Spearman correlation analysis between age and Ccr, but no linear relationship was found. In addition, before the multivariate analysis, we made a collinearity diagnosis of all the factors, and no collinearity problems were found. Therefore, there was no correlation between age and Ccr in patients aged >65 years in our study.

Interestingly, in our study albumin was not found to be associated with LAT; instead, plasma TP <60 g/L was a risk factor for LAT. We speculate that this effect may be related to the immune function of globulin, but the specific mechanism is not clear.

According to the ADPLCP risk score scale, when the cut-off value was 108, the sensitivity and specificity of LAT were 78.9% and 69.2%, respectively; and the false negative (omission diagnostic rate) was 21.1% and the false positive (mistake diagnostic rate) was 30.8%, and so the false positive rate cannot be negligible. Actually, if we want to reduce the false positive rate, we can improve the cut-off value. For example, when the cut-off value was 130, the false positive value was 11.2%, the sensitivity was 45.2%, and the specificity was 88.8%. Therefore, according to whether we want to improve the sensitivity or specificity, we can adjust the cut-off value appropriately, but when the cut-off value is 108, the AUC of ROC curve was the largest and the diagnostic efficiency was the best.

The physician should not withhold linezolid solely based on this risk score. Based on our scoring scale, we can determine a patient's risk of LAT and thus determine the frequency of monitoring platelets. According to the incidence of LAT, patients

were classified into low risk, medium risk, and high risk. In low risk, we did not need to monitor blood routine closely; in high risk, we needed to monitor platelets daily and stop linezolid as soon as possible, because according to our experience, platelets still showed a downward trend 3 days after the discontinuation of linezolid. In addition, before the use of linezolid, the patient's age, baseline platelets, baseline leukocyte count, Ccr, and TP were known. We could calculate how long after the use of linezolid the patient had a total point >108 (LAT was likely to occur). This would help us to estimate the duration of linezolid.

To our knowledge, we analyzed the risk factors for LAT in a large sample size of elderly individuals for the first time and established the nomogram prediction model called the ADPLCP risk score scale, which is helpful for early judgment of LAT. However, there are some limitations in this study. First, it was a retrospective study that did not incorporate monitoring of the blood concentration of linezolid. Second, part of the information of the included patients was not described in detail, and so assessing the severity of the disease by SOFA score was not possible. Third, we temporarily lack effective external validation data with which to evaluate the generalization performance of the model.

Conclusions

We analyzed the incidence and risk factors for LAT in 428 enrolled patients aged >65 years. We also established a nomogram prediction model called the ADPLCP (age, duration, platelet, leukocyte, creatinine clearance, protein) risk score scale, and the included factors were easy to obtain. Through the ADPLCP risk score scale, we can quickly and simply identify the risk of LAT at an early stage, which provides help for the judgment of LAT and early intervention.

Ethics Statement

As a retrospective study, no manual interventions were applied and all indicators were observational. Hence, informed consent was waived, and the study protocol was approved by the ethics committee of Chinese People's Liberation Army (PLA) General Hospital (Ethical approval No. S2020-141-01).

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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