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在线全文

终末期肝病患者发生肺部真菌感染的危险因素及病原学分析

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【摘要】 目的 探讨终末期肝病患者合并肺部真菌感染的危险因素及病原学谱构成。**方法** 对211例终末期肝病患者临床资料进行回顾性分析。根据肺部影像学、临床表现及病原学检测结果，将患者分为3组：肺部真菌感染组（病例组）、肺部非真菌感染组（对照组1）和无肺部感染组（对照组2）。比较病例组与对照组1、对照组2之间临床特征的差异。以无肺部感染患者（对照组2）作为对照，采用单因素和多因素logistic回归分析筛选终末期肝病患者发生肺部真菌感染的独立危险因素，并基于此构建列线图预测模型。**结果** 211例患者中，76例（36.1%）有肺部真菌感染，46例（21.8%）有肺部非真菌感染，89例（42.2%）无肺部感染。多因素logistic回归显示入院时白细胞计数高（OR值=1.211，95%CI：1.011～1.460）、MELD-Na评分高（OR值=1.140，95%CI：1.021～1.282）、合并肝肾综合征（OR值=4.150，95%CI：1.050～17.300）、糖皮质激素累积使用时间超过7 d（OR值=26.832，95%CI：6.361～113.221）及入院时使用高级别抗生素治疗（OR值=6.601，95%CI：1.951～22.362）是肺部真菌感染的独立危险因素。基于上述危险因素构建了命名为TJLFPFI的列线图预测模型，其受试者工作特征曲线下面积为0.899（95%CI：0.853～0.945）。76例肺部真菌感染患者病原学分析显示，痰培养阳性36例（47.4%），痰培养阴性但G试验和（或）GM试验阳性40例（52.6%）。病原学曲霉检出率最高（25/36，59.5%）。**结论** 终末期肝病患者肺部真菌感染与入院时病情严重程度、高级抗生素的早期使用及较长时间糖皮质激素使用相关。曲霉是主要致病菌。TJLFPFI模型在识别高危人群方面有潜在应用价值，预测性能未来仍需进一步验证。

【关键词】 终末期肝病 真菌感染 危险因素 病原学 预测模型

Risk Factors and Etiology of Pulmonary Fungal Infection in Patients With End-Stage Liver Disease

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[Abstract] Objective To identify the risk factors and investigate etiological spectrum of pulmonary fungal infections (PFIs) in patients with end-stage liver disease (ESLD). **Methods** A retrospective analysis was performed on the clinical data of 211 ESLD patients. Based on pulmonary imaging, clinical manifestations, and microbiological test results, patients were categorized into three groups, including the PFI group (or the case group), the non-fungal pneumonia group (or the control group 1), and the group without pneumonia (or the control group 2). The clinical characteristics of patients in the the case group were then compared with those of patients in the two control groups. Taking patients without pneumonia as the control, univariate and multivariate logistic regression analyses were performed to identify independent risk factors for PFI, and a nomogram prediction model was constructed based on these risk factors. **Results** Among the 211 patients, 76 (36.1%) had PFIs, 46 (21.8%) had non-fungal pneumonia, and 89 (42.2%) did not have pneumonia. According to findings from the multivariate logistic regression, elevated white blood cell count upon admission (OR = 1.211; 95% CI, 1.011-1.460), higher Model for End-Stage Liver Disease-Sodium (MELD-Na) score (OR = 1.140; 95% CI, 1.021-1.282), concomitant hepatorenal syndrome (OR = 4.150; 95% CI, 1.050-17.300), cumulative glucocorticoid use for more than seven days (OR = 26.832; 95% CI, 6.361-113.221), and the administration of broad-spectrum antibiotics at the time of hospital admission (OR = 6.601; 95% CI, 1.951-22.362) were identified as independent risk factors for PFI. A predictive nomogram model named TJLFPFI was constructed based on these risk factors. The area under the receiver operating characteristic (AUC) curve of the model was 0.899 (95% CI, 0.853-0.945). Etiologic analysis of the 76 PFI cases revealed that 36 (47.4%) had positive results for culture, while 40 (52.6%) had negative results for sputum culture but tested positive by the 1,3-β-D-glucan test and/or galactomannan test. Aspergillus was the most frequently identified pathogen, detected in 25 of the 36 cases (59.5%). **Conclusion** PFI in ESLD patients is closely associated with disease severity at admission, early use of broad-spectrum antibiotics, and prolonged

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glucocorticoid therapy. Aspergillus is the predominant pathogen. The TJLFPFI model shows potential value in identifying high-risk patients, but prospective validation is still warranted.

[Key words] End-stage liver disease　Fungal infection　Risk factors　Etiology　Predictive model

终末期肝病(end-stage liver disease, ESLD)是多种肝病进展的最终阶段,包括急性、亚急性、慢加急性肝衰竭、失代偿期肝硬化及肝癌等[1]。由于免疫功能障碍、肠道菌群移位及医源性因素,患者易发生感染[2]。其中,肺部真菌感染(pulmonary fungal infection, PFI)临床表现不典型,诊断困难且预后不良[3]。本研究通过回顾性分析ESLD合并PFI患者与肺部非真菌感染及无肺部感染患者的临床资料,探讨PFI的危险因素,为早期干预提供临床依据。

1　资料与方法

1.1　研究对象

收集2021年1月–2024年1月在武汉同济医院治疗的211例ESLD患者临床资料。根据肺部影像学、临床症状及病原学检测结果,将患者分为PFI组、肺部非真菌感染组和无肺部感染组。本研究PFI诊断标准包括:①肺部CT提示感染(如肿块、结节、斑片、实变、空洞、晕征、空气新月征);②伴或不伴发热、咳嗽、咳痰等呼吸道感染症状,查体温及呼吸音粗、干湿啰音等;③血清或呼吸道标本提示真菌感染;④抗生素治疗>72 h无效后静脉应用抗真菌药物[4]。肺部非真菌感染的诊断参考美国感染病学会肺部感染指南[5]。

纳入标准:符合中国《终末期肝病合并感染诊治专家共识》ESLD的诊断标准[6]。排除标准:住院时间<7 d,合并其他系统恶性肿瘤、肺结核、人体免疫缺陷病毒感染、COVID-19感染、年龄<18岁及失访。本研究经华中科技大学同济医学院附属同济医院医学伦理委员会批准(伦理批文号:TJ-IRB202404035)。

1.2　研究方法

通过电子病历系统收集患者一般资料,糖尿病和肝硬化病史,肝衰竭原因,并发症,实验室检查、MELD-Na评分[7],病原学结果、治疗、住院天数及随访30 d存活情况。

1.3　统计学方法

符合正态分布的计量资料以$\bar{x}\pm s$表示,组间差异采用独立样本t检验分析;不符合正态分布的采用中位数(四分位间距)表示,组间差异采用Kruskal-Wallis H检验分析。分类变量组间差异采用卡方检验或Fisher检验分析。为识别肺部真菌感染的独立危险因素,以肺部真菌感染组为病例组,无肺部感染组为对照组,进行单因素、多因素logistic回归分析。基于多因素分析结果构建预测模型,并评估拟合效果:通过受试者工作特征(ROC)曲线下面积(AUC)评估模型在原始数据中对肺部真菌感染的区分能力,通过校准曲线检验预测概率与实际结局间的一致性,利用决策曲线分析评估临床应用价值。所有数据采用R 4.4.2(R Foundation for Statistical Computing, Vienna, Austria)进行统计分析。P<0.05时差异有统计学意义。

2　结果

2.1　人口学资料与临床特征

211例患者发生肺部感染122例,其中PFI感染率36.1%(76/211),肺部非真菌感染率21.8%(46/211),无肺部感染率42.2%(89/211)。3组患者性别、年龄、吸烟、饮酒、糖尿病、肝硬化病史方面差异无统计学意义(P>0.05)。肝衰竭病因方面,PFI组与无感染组相比,PFI组病毒性肝炎占比低,自身免疫性肝炎占比高(P<0.05)。在入院查血方面,PFI组总胆红素显著高于肺部非真菌感染组(P<0.05),PFI组白细胞计数、中性粒细胞计数、中性粒细胞与淋巴细胞比值、超敏C反应蛋白、降钙素原及MELD-Na评分显著高于无感染组(P<0.05),见表1。

2.2　临床结局

住院期间PFI组中使用糖皮质激素超过7 d及入院使用广谱抗生素比例显著高于肺部非真菌感染组(P<0.05),PFI组接受有创操作、激素使用时间长及入院使用广谱抗生素比例显著高于无感染组(P<0.05)。PFI组肝肾综合征和肝性脑病发病率显著高于肺部非真菌感染组(P<0.05),PFI组消化道出血、自发性细菌性腹膜炎、肝肾综合征、肝性脑病发生率显著高于无感染组(P<0.05)。预后方面,PFI组住院时间显著长于对照组(P<0.05),30 d死亡率显著高于无肺部感染组(P<0.05),较肺部非真菌感染组亦有升高趋势,但差异无统计学意义(P>0.05),见表2。

2.3　病原学分析

患者病原学诊断主要依赖痰培养及血清G、GM试验。在76例ESLD合并PFI患者中,36例(47.4%)痰培养真菌阳性,40例(52.5%)痰培养真菌阴性但G试验和(或)GM试验阳性,见表3。病原学谱显示,曲霉为最常见致病真菌,共检出25株(59.5%);其次为念珠菌,共检出13株(28.9%);卡氏肺孢子虫核酸阳性4例(9.5%)。部分患者同时检出多种真菌,如痰中同时检出烟曲霉、念珠菌和卡氏肺孢子虫,见表4。

表 1 终末期肝病患者发生肺部真菌感染的人口学资料与临床特征

Table 1 Demographic and clinical characteristics of PFIs in ESLD patients

Variable	ESLD with PFI (*n*=76)	ESLD with non-fungal pneumonia (*n*=46)	ESLD without pneumonia (*n*=89)	P^a	P^b
Male/case (%)	63 (82.9)	38 (82.6)	78 (87.6)	0.968	0.389
Age#/yr.	52 (47, 59)	54 (42, 66)	50 (36, 56)	0.384	0.074
Smoking/case (%)	27 (35.5)	15 (32.6)	35 (39.3)	0.742	0.582
Alcohol consumption/case (%)	25 (32.9)	12 (26.1)	24 (26.9)	0.428	0.587
Diabetes/case (%)	6 (7.9)	9 (19.6)	12 (13.5)	0.057	0.275
Cirrhosis/case (%)	51 (67.1)	30 (65.2)	61 (68.5)	0.831	0.832
Etiology of liver failure/case (%)					
Viral hepatitis	62 (81.6)	39 (84.8)	85 (95.5)	0.650	0.004
Alcoholic hepatitis	5 (6.6)	1 (2.2)	1 (1.1)	0.276	0.062
Autoimmune hepatitis	6 (7.8)	3 (6.5)	1 (1.1)	0.779	0.031
Unknown	3 (4.0)	3 (6.5)	2 (2.3)	0.524	0.525
Blood test at admission					
White blood cell#/($\times10^9$ L^{-1})	7.93 (5.33, 11.39)	6.46 (4.92, 8.70)	5.87 (4.32, 7.68)	0.061	< 0.001
Neutrophil count#/($\times10^9$ L^{-1})	5.36 (3.41, 8.50)	4.70 (3.19, 6.51)	3.89 (2.81, 5.27)	0.124	< 0.001
Lymphocyte count#/($\times10^9$ L^{-1})	1.02 (0.74, 1.46)	1.04 (0.78, 1.52)	1.20 (0.78, 1.58)	0.531	0.400
NLR#	4.62 (2.8, 8.512)	3.776 (2.40, 5.66)	3.24 (2.35, 4.69)	0.082	0.002
Hemoglobin#/(g/L)	115 (99, 129)	98 (77, 119)	130 (116, 145)	< 0.001	0.001
Platelet count#/($\times10^9$ L^{-1})	100 (61, 140)	80 (57, 130)	111 (71, 153)	0.174	0.285
C-reactive protein#/(mg/L)	13.1 (8.4, 36.0)	11.6 (7.7, 24.1)	10.3 (7.4, 15.3)	0.237	0.009
Procalcitonin#/(ng/mL)	0.72 (0.46, 1.30)	0.60 (0.36, 0.86)	0.63 (0.37, 0.81)	0.053	0.017
Total bilirubin/(μmol/L)	343.2 ± 158.9	275.9 ± 132.8	304.1 ± 140.2	0.019	0.104
Albumin#/(g/L)	31.4 (29.2, 34.5)	32.8 (27.9, 36.8)	34.5 (31.2, 36.8)	0.540	< 0.001
Prothrombin activity#/%	37 (32, 47)	37 (31, 42)	40 (35, 61)	0.657	0.018
MELD-Na score#	27.5 (23.8, 31.9)	28.3 (24.7, 32.7)	24.7 (21.5, 26.5)	0.973	< 0.001

NLR: neutrophil-to-lymphocyte ratio. #: The quantitative data in the above table are described by median (P_{25}, P_{75}). P^a: the difference between the ESLD patients with PFI and those with non-fungal pneumonia. P^b: the difference between the group of ESLD with PFI and those without PFI.

表 2 终末期肝病患者住院期间干预措施与预后比较

Table 2 Clinical outcomes of ESLD patients

Variable	ESLD with PFI (*n* = 76)	ESLD with non-fungal pneumonia (*n* = 46)	ESLD without pneumonia(*n* = 89)	P^a	P^b
Treatment measures/case (%)					
Artificial liver support	52 (68.4)	24 (52.2)	39 (43.8)	0.073	0.002
Abdominal paracentesis	14 (18.4)	9 (19.6)	4 (4.5)	0.876	0.003
Cumulative corticosteroid use > 7 d	36 (47.4)	3 (6.5)	4 (4.5)	< 0.001	< 0.001
Use of broad-spectrum antibiotics at admission	33 (43.4)	3 (6.5)	11 (13.4)	< 0.001	< 0.001
Complications/case (%)					
Gastrointestinal bleeding	10 (13.2)	2 (4.4)	3 (3.4)	0.113	0.020
Spontaneous bacterial peritonitis	36 (47.4)	21 (45.7)	22 (28.1)	0.854	0.006
Hepatorenal syndrome	24 (31.6)	6 (13.0)	10 (11.2)	0.021	0.001
Hepatic encephalopathy	36 (47.4)	13 (28.3)	13 (14.6)	0.037	< 0.001
Outcomes					
Length of hospital stay #	29 (19, 47)	21 (14, 33)	18 (11, 28)	0.002	< 0.001
30-day mortality/case (%)	43 (56.6)	20 (43.5)	12 (13.5)	0.161	< 0.001

#: The quantitative data in the above table are described by median (P_{25}, P_{75}). P^a: ESLD with PFI vs. ESLD with non-fungal pneumonia. P^b: ESLD with PFI vs. ESLD without pneumonia.

表 3　终末期肝病合并肺部真菌感染患者病原学诊断结果

Table 3　Etiology diagnosis evidence for PFIs in ESLD patients

Test category	Single positive/case (%)	Dual positive/case (%)	Triple positive/case (%)	Total
Culture-positive group				36
Culture only	15 (19.7)	—	—	
Culture + G test	—	6 (7.9)	—	
Culture + GM test	—	3 (3.9)	—	
Culture + G + GM test	—	—	12 (15.8)	
Culture-negative group				40
G test only	25 (25.0)	—	—	
GM test only	9 (3.9)	—	—	
G + GM tests	—	6 (7.9)	—	
Total	49 (64.5)	15 (19.7)	12 (15.7)	76

G test: detection of 1, 3-β-d-glucan (BDG); GM test: detection of galactomannan antigen.

表 4　终末期肝病合并肺部真菌感染患者病原学谱

Table 4　Etiological pathogens of PFIs in ESLD patients

Pathogen	Sputum	Throat swab	BALF	Total
Aspergillus spp. (*n* = 25)			—	
Aspergillus fumigatus	20	—	—	20
Aspergillus flavus	2	—	1	3
Aspergillus spp.	2	—	—	2
Candida spp. (*n* = 13)				
Candida albicans	4	3	—	7
Candida glabrata		1	—	1
Candida parapsilosis	1	2	—	3
Candida spp.	1	1	—	2
Pneumocystis jirovecii (*n* = 4)	4	—	—	4
Total	34	7	1	42

BALF: bronchoalveolar lavage fluid.

2.4　ESLD患者发生肺部真菌感染的危险因素分析

以无肺部感染ESLD患者作为对照，分析筛选ESLD患者发生肺部真菌感染的危险因素。单因素分析显示，年龄偏大、自身免疫性肝炎、入院白细胞计数高、超敏C反应蛋白高、降钙素原高、血清白蛋白低、凝血酶原活动度低、MELD评分高、接受人工肝、腹腔穿刺术治疗、累积激素治疗>7 d、入院时使用高级抗生素，以及消化道出血、肝性脑病、肝肾综合征和自发性腹膜炎均与PFI发生相关(P<0.05)。将单因素回归分析中有统计学意义的因素纳入进行多因素回归分析，结果显示入院时白细胞计数高、MELD-Na评分高、合并肝肾综合征、累积激素治疗>7 d及入院时使用高级抗生素治疗是ESLD患者发生PFI的独立危险因素，见表5。

2.5　列线图预测模型的建立

基于回归分析结果，将入院时使用高级抗生素、累积激素治疗>7 d、合并肝肾综合征、白细胞计数和MELD-Na评分5个独立危险因素，建立列线图预测模型(图1)，命名为TJLFPFI，用于评估ESLD患者发生肺部真菌感染的风险。由于样本量有限，本研究未进行训练集与验证集划分，仅对模型在原数据集中的拟合性能进行了评估：在区分度验证中，列线图ROC曲线下面积(AUC)为0.899(95%CI: 0.853 ~ 0.945)，灵敏度为89.5%，特异性为76.4%，表明模型能有效的肺部真菌感染高风险和低风险患者，有较强的临床应用价值，见图2；校准度分析中，校准曲线显示模型预测概率与实际观测情况具有良好的一致性，Hosmer-Lemeshow检验P值为0.605，提示模型拟合优度较好，见图3。临床实用性评估中，决策曲线分析表明，模型指导可以有显著的净临床获益，有较强的临床决策支持能力，见图4。

3　讨论

ESLD患者因免疫功能受损、长期住院及侵入性医疗干预等因素，是肺部真菌感染(PFI)高风险人群[8-9]。本研究分析ESLD患者临床资料，探讨其发生PFI的危险因素并构建预测模型，为临床识别高危患者提供依据。

不同病因ESLD患者PFI风险存在差异，自免肝患者风险高，病毒肝患者风险相对较低。自免肝患者因长期接受免疫抑制治疗，免疫应答受损，易发生机会性感染[10-11]。

PFI组入院时白细胞、NLR比值、CRP及PCT高均明显升高。一方面，免疫细胞通过吞噬、释放炎症因子和活性氧等机制清除病原体；另一方面，过度炎症反应可导致微循环障碍、组织灌注不足和多器官功能损伤[12-13]。此外，PFI组白蛋白水平显著低于无感染组，血清白蛋白水平下降及其结构和功能异常转变，影响其抗氧化、毒素清除、免疫调节和内皮保护作用，增加感染风险[14-15]。PFI组肝肾综合征、肝性脑病发生率也明显较高。前者通过毒素蓄积加重免疫抑制，后者则因误吸风险增加，易发生PFI[16-18]。

表 5 终末期肝病患者发生肺部真菌感染的危险因素分析

Table 5 Analysis of risk factors for PFIs in patients with ESLD

Variable	Univariable logistic analysis		Multivariable logistic analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Male	0.683 (0.287-1.629)	0.391		
Age	1.027 (1.006-1.055)	0.046	1.030 (0.982-1.080)	0.251
Smoking	0.850 (0.451-1.602)	0.616		
Alcohol consumption	1.205 (0.614-2.364)	0.407		
Diabetes	0.550 (0.196-1.544)	0.256		
Cirrhosis	0.936 (0.486-1.803)	0.844		
Etiology of liver failure				
Viral hepatitis	0.208 (0.065-0.664)	0.008	0.194 (0.028-1.180)	0.083
Alcoholic hepatitis	6.200 (0.971-120.0)	0.099		
Autoimmune hepatitis	7.540 (1.250-144.0)	0.064		
Unknown	1.788 (0.291-10.990)	0.531		
Blood test at admission				
White blood cell count	1.262 (1.122-1.419)	< 0.001	1.211 (1.011-1.460)	0.036
NLR	1.033 (0.987-1.081)	0.166		
C-reactive protein	1.035 (1.001-1.059)	0.005	0.990 (0.952-1.030)	0.608
Procalcitonin	1.790 (1.190-3.230)	0.023	1.040 (0.783-1.380)	0.795
Total bilirubin	1.002 (0.999-1.004)	0.105		
Albumin	0.904 (0.844-0.969)	0.004	0.968 (0.851-1.100)	0.610
Prothrombin activity	0.978 (0.961-0.996)	0.017	1.010 (0.975-1.050)	0.584
MELD-Na score	1.106 (1.048-1.167)	< 0.001	1.140(1.021-1.282)	0.021
Treatment measures				
Artificial liver support	2.78 (1.465-5.267)	0.002	1.440 (0.466-4.510)	0.525
Abdominal paracentesis	4.798 (1.507-15.282)	0.008	0.950 (0.179-5.700)	0.953
Corticosteroid use > 7 d	19.125 (6.371-57.410)	< 0.001	26.832(6.361-113.221)	< 0.001
Use of broad-spectrum antibiotics	5.442 (2.501-11.839)	< 0.001	6.601 (1.951-22.362)	0.003
Complications				
Gastrointestinal bleeding	4.343 (1.149-16.414)	0.030	1.400 (0.215-10.200)	0.727
Spontaneous bacterial peritonitis	2.304 (1.208-4.393)	0.011	0.787 (0.243-2.420)	0.680
Hepatorenal syndrome	3.646 (1.611-8.250)	0.002	4.150 (1.050-17.300)	0.044
Hepatic encephalopathy	5.262 (2.508-11.037)	< 0.001	1.160 (0.323-4.130)	0.815

NLR: neutrophil-to-lymphocyte ratio.

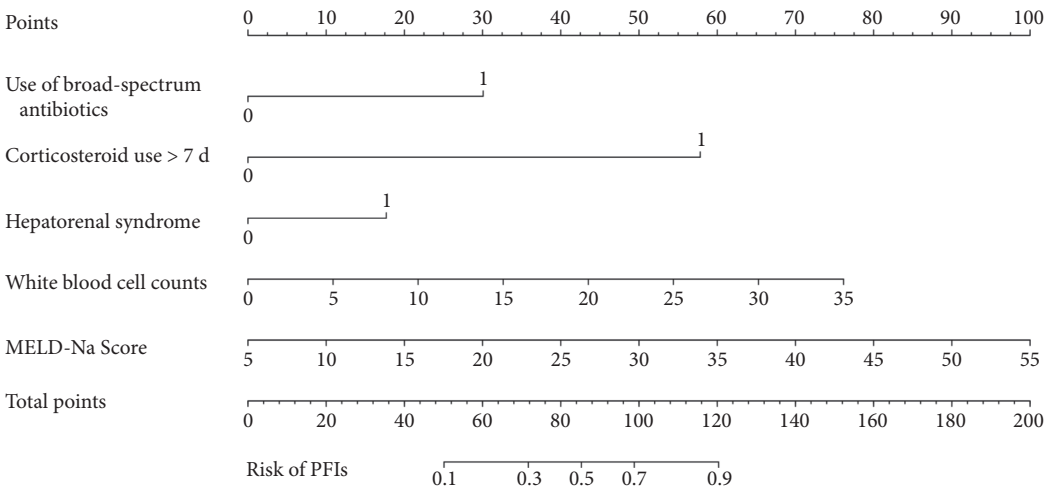

图 1 预测终末期肝病患者发生肺部真菌感染的列线图

Fig 1 TJLFPFI model for predicting the risk of PFIs in ESLD patients

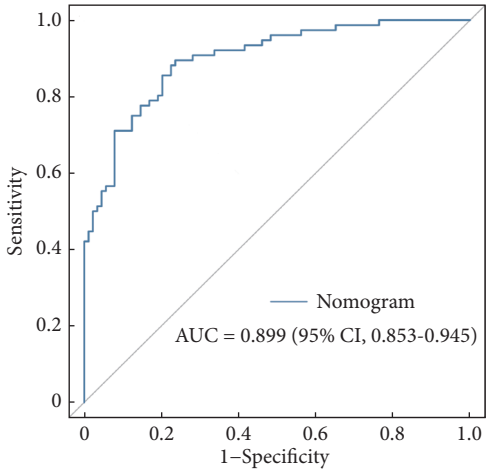

图 2 TJLFPFI预测模型预测终末期肝病患者发生肺部真菌感染的受试者工作特征曲线

Fig 2 Receiver operating characteristic (ROC) curve of the TJLFPFI model for predicting PFIs in ESLD patients

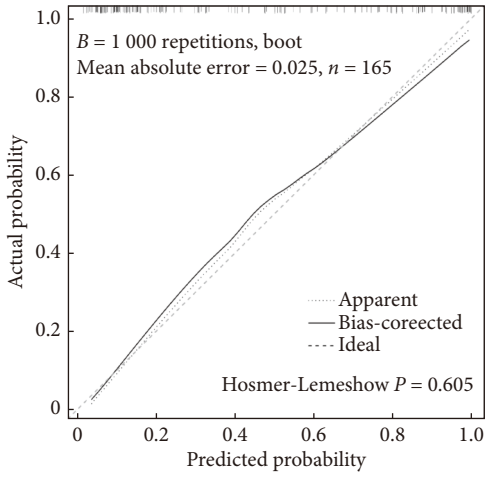

图 3 TJLFPFI预测模型预测终末期肝病患者发生肺部真菌感染的校准曲线

Fig 3 Calibration curve of the TJLFPFI model for predicting PFIs in ESLD patients

医源性因素是PFI风险升高的重要原因[19-20]。单因素分析显示, PFI风险与激素、高级别抗生素使用及侵入性操作有关, 多因素分析显示激素及高级别抗生素应用为独立危险因素。糖皮质激素可抑制免疫功能[11], 在肝病患者中使用相对谨慎。长期应用多见于自身免疫性肝炎患者, 重症肝炎早期短期用抑制超强免疫应答、减轻肝细胞损伤、避免肝细胞崩解坏死[21]。本队列中激素主要与人工肝治疗时的抗过敏处理相关, 可以尽量采用最低有效剂量或其他可替代药物[22]。广谱抗生素治疗破坏菌群平衡促进真菌定植[23], 然而, ESLD患者易发生细菌感染, 抗生素使用难以避免[24], 因此制定合理治疗方案, 动态监测炎症指标, 指导抗生素降阶梯治疗, 可能是兼顾抗感染疗效与真菌防控的有效措施。人工肝、腹腔穿刺引流等

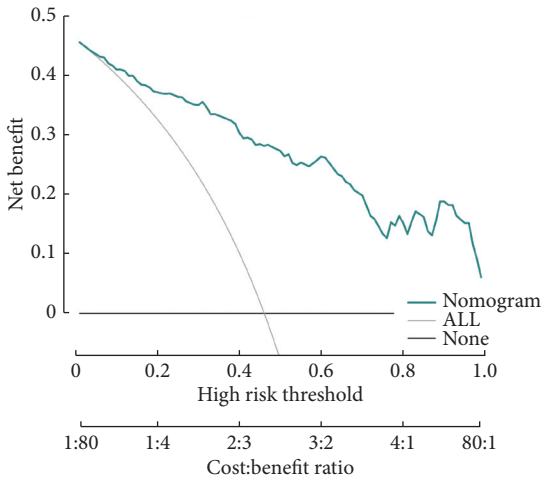

图 4 列线图预测终末期肝病发生肺部真菌感染的决策曲线分析

Fig 4 Decision curve analysis of the TJLFPFI model for predicting PFIs in ESLD patients

操作在挽救生命的同时, 也可能增加感染风险[25], 应严格遵循无菌操作。

需要注意的是, 这些医源性因素与患者病情严重程度相关。本研究中PFI组入院时MELD-Na评分明显高于无感染组, 反应其病情更严重, 可能存在更加显著的免疫障碍和营养不良, 感染风险更高, 因此, 在解读这些因素与PFI的关联时, 应综合考虑患者基础病情。

本队列中, PFI病原学以曲霉检出率最高59.5%(25/36)。曲霉广泛存在于空气和水源中, 吸入后可引起侵袭性肺部真菌感染[26]。本组念珠菌感染占31%(13/36), 另有卡氏肺孢子菌占9.5%(4/36)。曲霉和念珠菌的检出情况与既往文献基本一致[27-28], 而卡氏肺孢子菌感染在ESLD患者中报道较少, 多见于实体器官移植、免疫抑制治疗者, 提示ESLD患者存在免疫抑制状态[29]。

本研究基于入院MELD-Na评分、白细胞计数、是否合并肝肾综合征、累积激素治疗>7 d以及入院时高级别抗生素5个变量, 构建了用于预测ESLD患者发生PFI风险的列线图模型。模型在原始数据中显示出较好的临床实用性和判别力, 可以区分PFI高风险与低风险患者, 指导临床干预并优化患者管理。由于本研究尚未纳入外部验证队列, 其泛化能力需要进一步评估, 后续研究将通过扩大样本量并引入独立外部队列进行模型验证, 以提高模型的稳定性和应用价值。

*　　*　　*

作者贡献声明　柳琴文负责论文构思、数据审编、正式分析、调查研究、可视化和初稿写作, 李晶晶负责论文构思、数据审编、正式分析和调查研究, 王文涛负责审读与编辑写作, 赵西平负责研究方法、研究项目管理和审读与编辑写作。所有作者已经同意将文章提交给本刊, 且对将

要发表的版本进行最终定稿,并同意对工作的所有方面负责。

Author Contribution LIU Qingwen is responsible for conceptualization, data curation, formal analysis, investigation, visualization, and writing--original draft. LI Jingjing is responsible for conceptualization, data curation, formal analysis, and investigation. WANG Wentao is responsible for writing--review and editing. ZHAO Xiping is responsible for methodology, project administration, and writing--review and editing. All authors consented to the submission of the article to the Journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

利益冲突 所有作者均声明不存在利益冲突

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参 考 文 献

[1] CHEN T, CHEN G, WANG G, *et al*. Expert consensus on the diagnosis and treatment of end-stage liver disease complicated by infections. Hepatol Int, 2024, 18(3): 817-832. doi: 10.1007/s12072-023-10637-3.

[2] BAJAJ J S, KAMATH P S, REDDY K R. The evolving challenge of infections in cirrhosis. New N Engl J Med, 2021, 384(24): 2317-2330. doi: 10.1056/NEJMra2021808.

[3] Bajaj J S, Reddy R K, Tandon P, *et al*. Prediction of fungal infection development and their impact on survival using the NACSELD cohort. Am J Gastroenterol, 2018, 113(4): 556-563. doi: 10.1038/ajg.2017.471.

[4] DONNELLY J P, CHEN S C, KAUFFMAN C A, *et al*. Revision and update of the consensus definitions of invasive fungal disease from the european organization for research and treatment of cancer and the mycoses study group education and research consortium. Clin Infect Dis, 2020, 71(6): 1367-1376. doi: 10.1093/cid/ciz1008.

[5] METLAY J P, WATERER G W, LONG A C, *et al* . Diagnosis and treatment of adults with community-acquired pneumonia. JAMA, 2019, 200(7): e45-e67. doi: 10.1164/rccm.201908-1581ST.

[6] 中华医学会感染病学分会. 终末期肝病合并感染诊治专家共识(2021年版). 临床肝胆病杂志, 2022, 38(2): 304-310. doi: 10.3969/j.issn.1001-5256.2022.02.010.
Society of Infectious Diseases. Chinese Medical Association. Expert consensus on diagnosis and treatment of end-stage liver disease complicated with infections(2021 version). J Clin Hepatol, 2022, 38(2): 304-310. doi: 10.3969/j.issn.1001-5256.2022.02.010.

[7] MAZUMDER N R, FONTANA R J. MELD 3.0 in advanced chronic liver disease. Annu Rev Med, 2024, 75: 233-245. doi: 10.1146/annurev-med-051322-122539.

[8] ALEXOPOULOU A, VASILIEVA L, AGIASOTELLI D, *et al*. Fungal infections in patients with cirrhosis. J Hepatol, 2015, 63(4): 1043-1045.

[9] PIANO S, BUNCHORNTAVAKUL C, MARCIANO S, *et al*. Infections in cirrhosis. Lancet Gastroenterol Hepatol, 2024, 9(8): 745-757.

[10] GHEMBAZA A, VAUTIER M, CACOUB P, *et al*. Risk factors and prevention of pneumocystis jirovecii pneumonia in patients with autoimmune and inflammatory diseases. Chest, 2020, 158(6): 2323-2332. doi: 10.1016/j.chest.2020.05.558.

[11] EPELBAUM O, DE MORAES A G, OLSON J C, *et al*. Invasive fungal infections in patients with liver disease: immunological and clinical considerations for the intensive care unit. Intensive Care Med, 2025, 51(2): 364-377. doi: 10.1007/s00134-025-07797-1.

[12] KIENLE K, GLASER K M, EICKHOFF S, *et al*. Neutrophils self-limit swarming to contain bacterial growth in vivo Science, 2021, 372(6548): eabe7729. doi: 10.1126/science.abe7729.

[13] SIKORA J P, KARAWANI J, SOBCZAK J. Neutrophils and the systemic inflammatory response syndrome (SIRS). Int J Mol Sci, 2023, 24(17): 13469. doi: 10.3390/ijms241713469.

[14] BERNARDI M, ANGELI P, CLARIA J, *et al*. Albumin in decompensated cirrhosis: New concepts and perspectives. Gut, 2020, 69(6): 1127-1138. doi: 10.1136/gutjnl-2019-318843.

[15] BALDASSARRE M, NALDI M, ZACCHERINI G, *et al*. Determination of effective albumin in patients with decompensated cirrhosis: clinical and prognostic implications. Hepatology, 2021, 74(4): 2058-2073. doi: 10.1002/hep.31798.

[16] TAPPER E B, PARIKH N D. Diagnosis and management of cirrhosis and its complications: A review. JAMA, 2023, 329(18): 1589-1602. doi: 10.1001/jama.2023.5997.

[17] HÄUSSINGER D, DHIMAN R K, FELIPO V, *et al*. Hepatic encephalopathy. Nat Rev Dis Primers, 2022, 8(1): 43. doi: 10.1038/s41572-022-00366-6.

[18] THOMSON M J, TAYLOR A, SHARMA P, *et al*. Limited progress in hepatorenal syndrome (HRS) reversal and survival 2002-2018: A systematic review and meta-analysis. Dig Dis Sci, 2020, 65(5): 1539-1548. doi: 10.1007/s10620-019-05858-2.

[19] THOMAS-RÜDDEL D O, SCHLATTMANN P, PLETZ M, *et al*. Risk factors for invasive candida infection in critically ill patients: A systematic review and meta-analysis. Chest, 2022, 161(2): 345-355. doi: 10.1016/j.chest.2021.08.081.

[20] SHAH K, DESHPANDE M, SHAH P. Healthcare-associated fungal infections and emerging pathogens during the COVID-19 pandemic. Front Fungal Biol, 2024, 5: 1339911. doi: 10.3389/ffunb.2024.1339911.

[21] 王鑫, 徐红瑞, 王亚东, 等. 肝功能衰竭与糖皮质激素抵抗. 中华肝脏病杂志, 2020, 28(10): 888-892. doi: 10.3760/cma.j.cn501113-20200629-00349.
WANG X, XU H R, WANG Y D, *et al*. Liver failure and glucocorticoid resistance. Chin J Hepatol, 2020, 28(10): 888-892. doi: 10.3760/cma.j.cn501113-20200629-00349.

[22] POFI R, CARATTI G, RAY D W, *et al*. Treating the side effects of exogenous glucocorticoids; can we separate the good from the bad? Endocr Rev, 2023, 44(6): 975-1011. doi: 10.1210/endrev/bnad016.

[23] BARTOLETTI M, RINALDI M, PASQUINI Z, *et al*. Risk factors for candidaemia in hospitalized patients with liver cirrhosis: a multicentre case–control–control study. Clin Microbiol Infect, 2021, 27(2): 276-282. doi: 10.1016/j.cmi.2020.04.030.

[24] WONG F, PIANO S, SINGH V, *et al*. Clinical features and evolution of bacterial infection-related acute-on-chronic liver failure. J Hepatol, 2021, 74(2): 330-339. doi: 10.1016/j.jhep.2020.07.046.

[25] 中国研究型医院学会肝病专业委员会重症肝病学组, 中华医学会肝病学分会重型肝病与人工肝学组. 重症肝病合并侵袭性真菌感染诊治专家共识. 中华肝脏病杂志, 2022, 30(2): 159-168. doi: 10.3760/cma.j.cn501113-20220130-00053.
Severe Liver Disease Group, Hepatology Professional Committee of the Chinese Society of Research Hospitals; Severe Liver Disease and Artificial Liver Group, Hepatology Branch of the Chinese Medical Association. Consensus on diagnosis and treatment of invasive fungal infection in patients with severe liver disease. Chin J Hepatol, 2022, 30(2): 159-168. doi: 10.3760/cma.j.cn501113-20220130-00053.

[26] 牛雨溪, 刘博华, 杨苏乔, 等. 半乳甘露聚糖试验诊断侵袭性曲霉病假阳性原因研究进展. 中华结核和呼吸杂志, 2020, 43(10): 862-866. doi: 10.3760/cma.j.cn112147-20191216-00832.
NIU Y X, LIU B H, YAGN S Q, *et al*. Research progress on the positive causes of invasive aspergillus sick leave by galactomannan test. Zhonghua Jie He He Hu Xi Za Zhi, 2020, 43(10): 862-866. doi: 10.3760/cma.j.cn112147-20191216-00832.

[27] VERMA N, SINGH S, SINGH M, *et al*. Global epidemiological burden of fungal infections in cirrhosis patients: a systematic review with meta-analysis. Mycoses, 2022, 65(3): 266-284. doi: 10.1111/myc.13387.

[28] 杨中原, 陈韬. 肝衰竭合并真菌感染的诊断和治疗. 内科急危重症杂志, 2019, 25(3): 185-188.

[29] SAADATZADEH T, ANGARONE M, STOSOR V. Pneumocystis jirovecii in solid organ transplant recipients: Updates in epidemiology, diagnosis, treatment, and prevention. Curr Opin Infect Dis, 2024, 37(2): 121-128. doi: 10.1097/QCO.0000000000001002.

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