



· 论 著 ·

# <sup>18</sup>F-FDG PET/CT代谢参数对接受CAR-T治疗的弥漫大B细胞淋巴瘤患者预后价值的队列研究

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**[摘要]** 背景与目的: 复发或难治性弥漫大B细胞淋巴瘤 (diffuse large B-cell lymphoma, DLBCL) 可采用嵌合抗原受体T细胞 (chimeric antigen receptor T-cell, CAR-T) 疗法进行治疗。基于影像学的特征有助于筛选可能对该免疫疗法产生临床应答的患者。本研究旨在建立一个基于<sup>18</sup>氟脱氧葡萄糖正电子发射断层显像 (18-fluoro-2-deoxy-D-glucose positron emission tomography-computed tomography, <sup>18</sup>F-FDG PET/CT) 参数的模型, 用于评估接受CAR-T疗法的复发或难治性DLBCL患者的无进展生存期 (progression-free survival, PFS) 和总生存期 (overall survival, OS)。方法: 回顾性分析2017年3月—2022年1月于苏州大学附属第一医院接受CAR-T治疗的DLBCL患者的临床和影像学资料。纳入标准: ① 年龄≥18岁; ② 病理学检查证实为复发或难治性DLBCL; ③ CAR-T治疗前行<sup>18</sup>F-FDG PET/CT检查; ④ 临床病理学数据完整; ⑤ 患者必须有可测量的病灶。排除标准: ① 患者的临床或影像学数据不完整; ② 患有其他类型的恶性肿瘤; ③ 在PET/CT扫描前1个月内接受过粒细胞集落刺激因子治疗。本研究通过苏州大学附属第一医院伦理委员会的审查 (编号: 2025256)。利用受试者工作特征曲线 (receiver operating characteristic curve, ROC) 确定最大标准摄取值 (maximum standard uptake value, SUV<sub>max</sub>)、肿瘤代谢体积 (metabolic tumour volume, MTV) 和总糖酵解量 (total lesion glycolysis, TLG) 的最佳阈值, 并将患者分为高风险组和低风险组。采用单因素和多因素Cox回归分析来确定潜在的影响预后的因素并构建预测模型, 绘制列线图进行可视化分析。计算受试者工作特征曲线下面积评估各模型的性能。结果: 本研究共纳入了61例 (男性37例, 女性24例, 年龄26~75岁) 在CAR-T输注前接受<sup>18</sup>F-FDG PET/CT检查的DLBCL患者。中位随访时间为14个月, 36例 (59.02%) 患者出现疾病进展, 25例 (40.98%) 患者死亡。多因素分析显示, 细胞因子释放综合征 (cytokine release syndrome, CRS) 分级 [风险比 (HR)=3.671, P=0.003] 和MTV (HR=0.171, P=0.004) 是影响OS的独立预后因素; 东部肿瘤协作组 (Eastern Cooperative Oncology Group, ECOG) 评分 (HR=2.411, P=0.019)、CRS分级 (HR=2.499, P=0.027) 和MTV (HR=0.338, P=0.007) 是影响PFS的独立预后因素。综合模型 (MTV、ECOG评分、CRS分级) 在预测PFS和OS方面比临床模型 (ECOG评分、CRS分级)、代谢参数模型 (MTV) 更佳。结论: <sup>18</sup>F-FDG PET/CT代谢参数MTV联合传统的临床风险因素 (ECOG评分、CRS分级) 可识别出超高风险的DLBCL患者。

**[关键词]** 弥漫大B细胞淋巴瘤; PET/CT; 肿瘤代谢体积; CAR-T; 预后

中图分类号: R733.4 文献标志码: A

DOI: 10.19401/j.cnki.1007-3639.2025.08.002

基金项目: 无。

利益冲突: 作者声明无利益冲突。

伦理批件: 2025256。

知情同意: 不需要。

引用本文: 何 超, 周夜夜, 章 斌, 等. <sup>18</sup>F-FDG PET/CT代谢参数对接受CAR-T治疗的弥漫大B细胞淋巴瘤患者预后价值的队列研究 [J]. 中国癌症杂志, 2025, 35(8): 743-751.

Funding: no.

Conflicts of interest: authors declare no conflicts of interest.

Ethical approval: 2025256.

Informed consent: not required.

Cite this article: HE C, ZHOU Y Y, ZHANG B, et al. A cohort study of prognostic value of <sup>18</sup>F-FDG PET/CT metabolic parameters in patients with diffuse large B-cell lymphoma treated with CAR-T [J]. China Oncol, 2025, 35(8): 743-751.

**A cohort study of prognostic value of <sup>18</sup>F-FDG PET/CT metabolic parameters in patients with diffuse large B-cell lymphoma treated with CAR-T** HE Chao, ZHOU Yeye, ZHANG Bin, DENG Shengming (Department of Nuclear Medicine, the First Affiliated Hospital of Soochow University, Suzhou 215006, Jiangsu Province, China)

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[ **Abstract** ] **Background and purpose:** Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) can be treated with chimeric antigen receptor T-cell (CAR-T) therapy. Imaging-based biomarkers may help identify patients likely to achieve clinical response to this immunotherapy. In this study, an 18-fluoro-2-deoxy-D-glucose positron emission tomography-computed tomography ( $^{18}\text{F}$ -FDG PET/CT) based model was developed to assess the progression-free survival (PFS) and overall survival (OS) of patients with relapsed or refractory (R/R) DLBCL who received CAR-T therapy. **Methods:** We retrospectively analyzed clinical and imaging data from patients with DLBCL who underwent CAR-T therapy at the First Affiliated Hospital of Soochow University between March 2017 and January 2022. Inclusion criteria: ① age  $\geq 18$  years old; ② pathologically confirmed R/R DLBCL; ③  $^{18}\text{F}$ -FDG PET/CT performed before CAR-T cell therapy; ④ complete clinicopathologic data; ⑤ patients must have measurable lesions. Exclusion criteria: ① patients with incomplete clinical or imaging data; ② patients with other types of malignant tumors; ③ patients who have received granulocyte colony-stimulating factor treatment within 1 month prior to PET/CT scan. This study was reviewed by the Ethics Committee of the First Affiliated Hospital of Soochow University (ID: 2025256). Receiver operating characteristic (ROC) curves were used to determine the optimal thresholds for maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ), tumor metabolic volume (MTV), and total glycolysis (TLG), and the patients were classified into high-risk and low-risk groups. Univariate and multivariate Cox regression analyses were used to identify potential prognostic factors and construct predictive models, which were visualized by drawing nomogram. Area under the ROC curve was used to assess the performance of each model. **Results:** A total of 61 patients (37 male patients and 24 female patients, aged 26-75 years) with DLBCL who underwent  $^{18}\text{F}$ -FDG PET/CT prior to CAR-T infusion were included. The median follow-up was 14 months; 36 patients (59.02%) had disease progression and 25 patients (40.98%) died. Multivariate analysis showed that grade of cytokine release syndrome (CRS) [Hazard ratio (HR)=3.671;  $P=0.003$ ] and MTV (HR=0.171,  $P=0.004$ ) were independent prognostic factors for OS; Eastern Cooperative Oncology Group (ECOG) score (HR=2.411,  $P=0.019$ ), grade of CRS (HR=2.499;  $P=0.027$ ), and MTV (HR=0.338,  $P=0.007$ ) were independent prognostic factors for PFS. The combined model (MTV, ECOG score, grade of CRS) was better than the clinical model (ECOG score, grade of CRS), and metabolic parameter model (MTV) in predicting PFS and OS. **Conclusion:**  $^{18}\text{F}$ -FDG PET/CT metabolic parameter MTV in combination with traditional clinical risk factors (ECOG score, Grade of CRS) could identify patients with ultra-high risk of DLBCL.

[ **Key words** ] Diffuse large B-cell lymphoma; PET/CT; MTV; CAR-T; Prognosis

弥漫大B细胞淋巴瘤 (diffuse large B-cell lymphoma, DLBCL) 是一种可通过一线治疗方案R-CHOP治愈的疾病, 但有30%~40%的患者仍处于难治性状态, 或在初始反应后复发。嵌合抗原受体T细胞 (chimeric antigen receptor T-cell, CAR-T) 疗法是治疗复发或难治性 (relapsed or refractory, R/R) B细胞淋巴瘤的有效疗法, 其完全缓解率约为43%<sup>[1-3]</sup>。然而, 这种疗法也会引起一定的不良反应, 包括细胞因子释放综合征 (cytokine release syndrome, CRS) 和免疫效应细胞相关神经毒性综合征 (immune effector cell-associated neurotoxicity syndrome, ICANS), 这些不良事件可能危及生命<sup>[4]</sup>。

$^{18}\text{F}$ 氟脱氧葡萄糖正电子发射断层显像 (18-fluoro-2-deoxy-D-glucose positron emission tomography-computed tomography,  $^{18}\text{F}$ -FDG PET/CT) 代谢参数可预测DLBCL的预后, 如最大标准摄取值 (maximum standard uptake value,  $\text{SUV}_{\text{max}}$ )、肿瘤代谢体积 (metabolic tumour volume, MTV) 和总糖酵解量 (total lesion glycolysis, TLG)<sup>[5-8]</sup>。本研究中, 我们回顾性分析接受CAR-T治疗的DLBCL患者的临床指标及代谢参数, 以确定 $^{18}\text{F}$ -FDG PET/CT是否可以提

供预后预测相关信息。

## 1 资料和方法

### 1.1 研究对象

本研究回顾性分析了2017年3月—2022年1月于苏州大学附属第一医院接受CAR-T治疗的DLBCL患者的病历及影像学资料, 所采用的CAR-T由优卡迪生物医药科技 (上海) 有限公司提供。患者纳入标准为: ① 患者年龄 $\geq 18$ 岁; ② 病理学检查证实为R/R DLBCL; ③ CAR-T治疗前行 $^{18}\text{F}$ -FDG PET/CT检查; ④ 临床病理学数据完整; ⑤ 患者必须有可测量病灶。排除标准为: ① 患者的临床或影像学数据不完整; ② 患有其他类型的恶性肿瘤; ③ 在PET/CT扫描前1个月内接受过粒细胞集落刺激因子治疗。收集患者的临床病例资料, 包括: 年龄、性别、Ann Arbor分期、B症状、乳酸脱氢酶 (lactate dehydrogenase, LDH) 水平、美国东部肿瘤协作组 (Eastern Cooperative Oncology Group, ECOG) 评分、国际预后指数 (international prognostic index, IPI) 评分、骨髓有无累及、c-Myc与Bcl-2双表达。采用美国移植与细胞治疗学会指南对CRS进行分级<sup>[9]</sup>。本研究经苏州大学附属第一医院伦理委

员会批准（编号：2025256），伦理审批环节已豁免知情同意。

## 1.2 显像方法

采用GE Discovery STE 16型PET/CT扫描仪进行图像采集。注射 $^{18}\text{F}$ -FDG前血糖水平要求低于11 mmol/L，空腹时间大于6 h。注射 $^{18}\text{F}$ -FDG（4.07~5.55 MBq/kg）40~60 min后，从颅顶到股中段进行扫描。CT扫描参数为140 kV、120 mA、横轴FOV 70 cm、切片厚度3.75 mm。

## 1.3 图像分析

$^{18}\text{F}$ -FDG PET/CT图像分析使用LIFE<sub>x</sub>软件（版本6.30，<https://www.lifexsoft.org/>）<sup>[10]</sup>。通过在三维平面上手动调整来设置感兴趣区域（region of interest, ROI），以排除生理性摄取。记录病灶的SUV<sub>max</sub>、总MTV、总TLG及最远病灶距离（the maximum tumor dissemination, D<sub>max</sub>）。如患者仅有单个病灶，将D<sub>max</sub>计为0 cm。采用41%SUV<sub>max</sub>阈值对所有单个病灶的代谢体积求和计算MTV。TLG的计算公式为MTV×SUV<sub>mean</sub>。

## 1.4 随访

随访自CAR-T输注当日开始至2022年1月31日截止。所有患者定期复诊，包括体格检查、实验室检查、CT或PET/CT等检查。随访方法包括门诊和住院病历随访及电话随访。无进展生存期（progression-free survival, PFS）为从首次输注CAR-T到疾病进展的时间；总生存期（overall survival, OS）为从首次输注CAR-T到因任何原因导致死亡或未次随访时间。研究截止时未知终点事件的患者，按删失数据处理。

## 1.5 统计学处理

SUV<sub>max</sub>、MTV、TLG、D<sub>max</sub>值为连续性

变量，为计量资料；年龄、性别、Ann Arbor分期、B症状、LDH水平、ECOG评分、IPI评分、骨髓有无累及、CRS分级、ICANS、既往化疗线数、是否移植、c-Myc/Bcl-2蛋白双表达作为分类变量，为定性资料。对于组间比较，如独立样本数据符合正态分布且方差齐，则采用 $t$ 检验；若方差不齐，则采用校正 $t$ 检验；非正态分布则采用Mann-Whitney  $U$ 检验比较两组分类变量间的差异。采用卡方检验或Fisher精确概率法对分类变量进行分析。利用ROC曲线确定SUV<sub>max</sub>、MTV、TLG的最佳阈值，并将患者分为高风险组和低风险组。采用单因素和多因素Cox回归分析来确定潜在的预后因素并构建预测模型，绘制列线图进行可视化分析。采用Kaplan-Meier法绘制生存曲线，组间比较采用log-rank检验。受试者工作特征（receiver operating characteristic, ROC）曲线下面积（area under curve, AUC）用于评估各模型的性能。 $P < 0.05$ 为差异有统计学意义。统计学分析采用SPSS 26.0和R 4.2.2软件进行。使用R 4.2.2软件进行图形绘制。

## 2 结果

### 2.1 临床特征

61例接受CAR-T治疗的DLBCL患者纳入本研究，患者纳入和排除流程图见图1。本研究包括37例男性和24例女性，中位年龄为53岁（26~75岁）。中位随访时间为14个月，36例（59.02%）患者疾病进展，25例（40.98%）患者死亡。1年和3年PFS率分别是45.90%、40.98%，1和3年OS率分别为65.57%和60.66%。患者在CAR-T输注前的临床特征见表1。

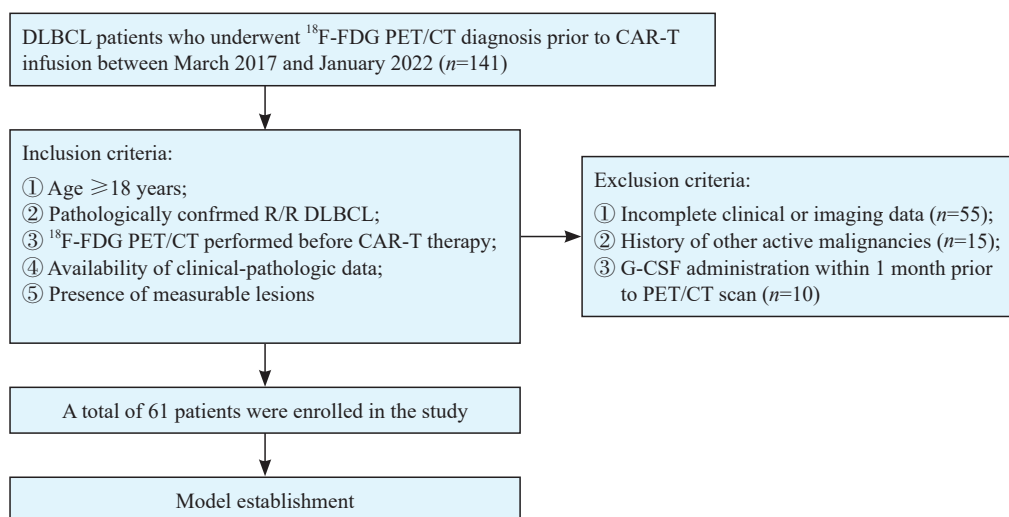


图1 患者纳入和排除标准流程图

Fig. 1 Flowchart of patients' inclusion and exclusion criteria

表1 患者的临床特征

Tab. 1 Clinical characteristics of patients

Characteristic	Case	[n(%)]
Age/year median (range)	53 (26-75)	
Gender		
Male	37 (60.7)	
Female	24 (39.3)	
Ann Arbor stage		
I - II	7 (11.5)	
III-IV	54 (88.5)	
B symptom	26 (42.6)	
LDH>ULN	31 (50.8)	
ECOG		
0-1	46 (75.4)	
$\geq 2$	15 (24.6)	
IPI (at diagnosis)		
Low-risk (0-2)	35 (57.4)	
High-risk (3-5)	26 (42.6)	
BM	16 (26.2)	
Prior lines of chemotherapy>2	19 (31.1)	
Prior ASCT	17 (27.9)	
Grade of CRS		
1-2	50 (82.0)	
3-4	11 (18.0)	
ICANS	6 (9.8)	
DE	35 (57.4)	

LDH: Lactate dehydrogenase; ULN: Upper limit of normal; ECOG: Eastern Cooperative Oncology Group; IPI: International prognostic index; BM: Bone marrow infiltration; ASCT: Autologous stem cell transplant; DE: Bcl-2/c-MYC double expression.

## 2.2 $^{18}\text{F}$ -FDG PET/CT特征

中位 $\text{SUV}_{\text{max}}$ 为17.20 (1.51~46.39), 中位TLG为496.00 (0.11~4 902.38), 中位MTV为103.00  $\text{cm}^3$  (1.00~846.00  $\text{cm}^3$ ), 中位 $\text{D}_{\text{max}}$ 为28.70 cm (0~76.00)。本研究利用ROC曲线确定 $\text{SUV}_{\text{max}}$ 、MTV、TLG和 $\text{D}_{\text{max}}$ 的最佳阈值, 并将患者分为高风险组和低风险组。在PFS中,  $\text{SUV}_{\text{max}}$ 、MTV、TLG和 $\text{D}_{\text{max}}$ 的最佳阈值分别为5.160 (AUC=0.707,  $P=0.004$ )、70.000  $\text{cm}^3$  (AUC=0.688,

$P=0.014$ )、244.038 (AUC=0.708,  $P=0.005$ )、6.200 cm (AUC=0.561,  $P=0.455$ ); 在OS中,  $\text{SUV}_{\text{max}}$ 、MTV、TLG和 $\text{D}_{\text{max}}$ 的最佳阈值分别为5.820 (AUC=0.664,  $P=0.017$ )、35.500  $\text{cm}^3$  (AUC=0.665,  $P=0.019$ )、421.164 (AUC=0.702,  $P=0.003$ )和6.400 (AUC=0.586,  $P=0.247$ )。

## 2.3 完全缓解组和非完全缓解组之间的比较

根据Lugano疗效评价标准, 27例患者(44.26%)经CAR-T治疗后达到完全缓解, 34例患者(55.74%)表现为非完全缓解, 其中11例患者获得部分缓解, 4例患者为疾病稳定, 19例发生疾病进展。比较完全缓解组和非完全缓解组, LDH水平、ICANS、MTV、TLG及 $\text{SUV}_{\text{max}}$ 差异有统计学意义( $P<0.05$ ); MTV、TLG及 $\text{SUV}_{\text{max}}$ 在非完全缓解组的患者中明显较高(表2)。

## 2.4 单因素及多因素分析

本研究采用单因素和多因素Cox回归分析评估了临床特征和代谢参数与生存率之间的关系(表3、4)。在单因素分析中, LDH ( $P=0.024$ )、ECOG评分 ( $P=0.011$ )、CRS分级 ( $P=0.002$ )、ICANS ( $P=0.003$ )、c-Myc/Bcl-2蛋白双表达 ( $P=0.011$ )、MTV ( $P=0.001$ )、TLG ( $P=0.004$ )、 $\text{SUV}_{\text{max}}$  ( $P=0.002$ )和 $\text{D}_{\text{max}}$  ( $P=0.005$ )与OS相关。LDH ( $P=0.045$ )、ECOG评分 ( $P<0.001$ )、CRS分级 ( $P=0.006$ )、ICANS ( $P=0.020$ )、MTV ( $P=0.001$ )、TLG ( $P=0.003$ )和 $\text{SUV}_{\text{max}}$  ( $P=0.002$ )和 $\text{D}_{\text{max}}$  ( $P=0.010$ )与PFS相关。较高的MTV与较差的PFS和OS显著相关(图2)。

将单因素分析中有统计学意义的变量纳入多变量模型, 在进一步进行多因素分析后, 我们发现CRS分级 ( $P=0.003$ )和MTV ( $P=0.004$ )仍是影响OS的具有统计学意义的预后因素。ECOG评分 ( $P=0.019$ )、CRS分级 ( $P=0.027$ )和MTV ( $P=0.007$ )作为PFS的独立影响因素, 仍具有显著的预后价值。

## 2.5 模型的构建与评估

基于从PFS (ECOG评分、CRS分级和MTV)和OS (CRS分级和MTV)的Cox多因素分析中获得的独立风险因素构建新的预测模型, 并使用列线图进行可视化分析(图3、4)。ROC曲线表明, 在预测PFS和OS方面, 综合模型比临床模型 (ECOG评分、CRS分级)、代谢参数模型 (MTV)具有更高的AUC(图5)。

表2 完全缓解组和非完全缓解组之间的比较

Tab. 2 Comparison between complete and incomplete metabolic response groups

Variable	Complete metabolic response (n=27)	Not complete metabolic response (n=34)	$\chi^2$ value	P value
Age/year			0.091	0.763
≤60	20 (74.07)	24 (70.59)		
>60	7 (25.93)	10 (29.41)		
Gender			0.528	0.467
Male	15 (55.56)	22 (64.71)		
Female	12 (44.44)	12 (35.29)		
Ann Arbor stage			2.365	0.224
I - II	5 (18.52)	2 (5.88)		
III-IV	22 (81.48)	32 (94.12)		
B symptom			0.066	0.798
Yes	12 (44.44)	14 (41.18)		
No	15 (55.56)	20 (58.82)		
LDH > ULN			8.703	0.003
Yes	8 (29.63)	23 (67.65)		
No	19 (70.37)	11 (32.35)		
ECOG			2.496	0.114
0-1	23 (85.19)	23 (67.65)		
≥ 2	4 (14.81)	11 (32.35)		
IPI (at diagnosis)			3.344	0.067
Low-risk (0-2)	19 (70.37)	16 (47.06)		
High-risk (3-5)	8 (29.63)	18 (52.94)		
BM			0.002	0.962
Yes	7 (25.93)	9 (26.47)		
No	20 (74.07)	25 (73.53)		
Grade of CRS			1.570	0.317
1-2	24 (88.89)	26 (76.47)		
3-4	3 (11.11)	8 (23.53)		
ICANS			5.284	0.030
Yes	0 (0.00)	6 (17.65)		
No	27 (100.00)	28 (82.35)		
Prior lines of chemotherapy			0.052	0.820
>2	8 (29.63)	11 (32.35)		
≤2	19 (70.37)	23 (67.65)		
Prior ASCT			0.075	0.785
Yes	8 (29.63)	9 (26.47)		
No	19 (70.37)	25 (73.53)		
DE			3.313	0.069
Yes	12 (44.44)	23 (67.65)		
No	15 (55.56)	11 (32.35)		
MTV, median	32.00 (1.00-846.00)	148.00 (1.00-655.00)		0.021 <sup>#</sup>
TLG, median	86.29 (0.11-4902.38)	844.48 (9.00-4840.00)		0.006 <sup>#</sup>
SUV <sub>max</sub> , ( $\bar{x} \pm s$ )	11.500 ± 7.786	20.352 ± 10.415		0.001 <sup>*</sup>
D <sub>max</sub> , median	32.30 (0.00-75.80)	26.35 (0.00-76.30)		0.864 <sup>#</sup>

\* : Independent-samples *t*-test; <sup>#</sup>: Mann-Whitney *U* test.

表3 单因素Cox回归分析结果

Tab. 3 The results of the univariate Cox regression analysis

Variable	OS		PFS	
	HR (95% CI)	P value	HR (95% CI)	P value
Age > 60	0.560 (0.223-1.407)	0.217	0.769 (0.351-1.684)	0.511
Male	1.361 (0.604-3.067)	0.457	1.352 (0.670-2.727)	0.400
Ann Arbor stage III-IV	1.259 (0.389-4.074)	0.701	0.695 (0.269-1.794)	0.452
B symptom	1.012 (0.447-2.291)	0.978	1.053 (0.527-2.105)	0.884
LDH > ULN	0.396 (0.177-0.887)	0.024	0.493 (0.246-0.986)	0.045
ECOG $\geq$ 2	0.268 (0.098-0.736)	0.011	0.175 (0.067-0.456)	<0.001
IPI (at diagnosis) $\geq$ 3	0.670 (0.294-1.525)	0.340	0.553 (0.271-1.126)	0.102
BM	1.136 (0.457-2.824)	0.784	1.422 (0.666-3.034)	0.363
Grade of CRS 3-4	0.140 (0.041-0.480)	0.002	0.212 (0.071-0.637)	0.006
ICANS	0.080 (0.015-0.428)	0.003	0.164 (0.036- 0.748)	0.020
Prior lines of chemotherapy > 2	0.746 (0.300-1.854)	0.528	0.658 (0.300-1.444)	0.297
Prior ASCT	1.851 (0.745-4.599)	0.185	1.414 (0.652-3.065)	0.380
DE	0.350 (0.156-0.784)	0.011	0.529 (0.265-1.056)	0.071
MTV	3.815 (1.692-8.600)	0.001	3.218 (1.607-6.444)	0.001
TLG	3.305 (1.475-7.409)	0.004	2.892 (1.440-5.811)	0.003
SUV <sub>max</sub>	-	0.002	3.393 (1.573-7.316)	0.002
D <sub>max</sub>	3.356 (1.436-7.846)	0.005	2.604 (1.255-5.405)	0.010

表4 多因素Cox回归分析结果

Tab. 4 The results of the multivariate Cox regression analysis

Variable	OS		PFS	
	HR (95%CI)	P value	HR (95%CI)	P value
LDH > ULN	0.899 (0.314-2.575)	0.820	1.013 (0.447-2.296)	0.975
ECOG $\geq$ 2	1.537 (0.511-4.626)	0.444	2.411 (1.158-5.022)	0.019
Grade of CRS 3-4	3.671 (1.556-8.659)	0.003	2.499 (1.109-5.631)	0.027
ICANS	0.613 (0.112-3.340)	0.571	0.485 (0.135-1.738)	0.267
DE	2.118 (0.810-5.542)	0.126	1.750 (0.841-3.641)	0.134
MTV	0.171 (0.051-0.574)	0.004	0.338 (0.155-0.741)	0.007
TLG	1.275 (0.332-4.897)	0.723	2.554 (0.397-16.426)	0.323
SUV <sub>max</sub>	-	0.050	0.259 (0.046-1.459)	0.126
D <sub>max</sub>	0.621 (0.124-3.104)	0.562	1.336 (0.397-4.495)	0.640

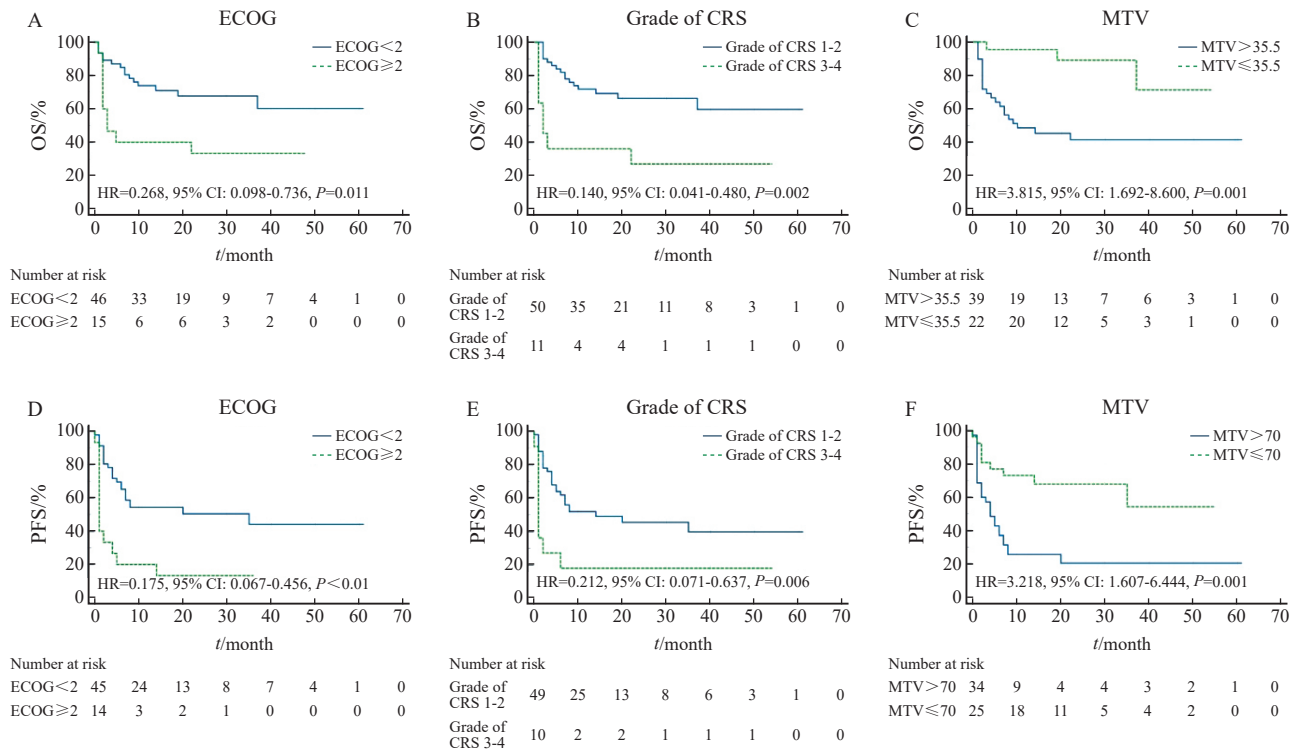


图2 生存分析曲线

Fig. 2 Kaplan-Meier survival curve analysis

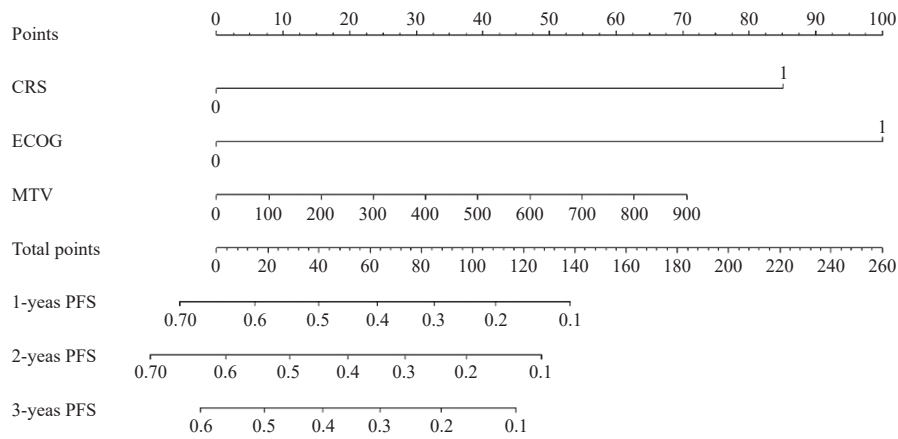


图3 预测PFS的列线图模型

Fig. 3 The nomogram model for predicting PFS

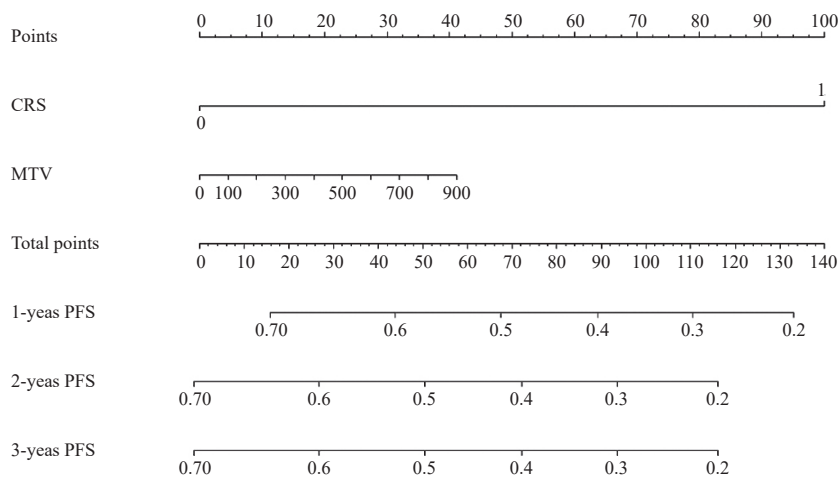


图4 预测OS的列线图模型

Fig. 4 The nomogram model for predicting OS

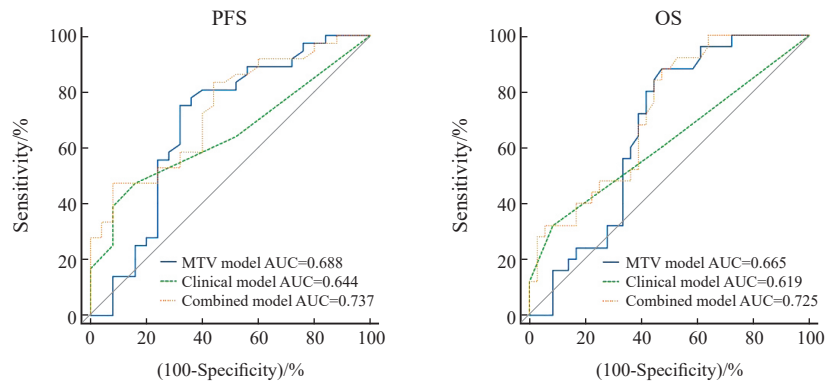


图5 不同模型预测PFS和OS的ROC曲线

Fig. 5 ROC curves for different models to predict PFS and OS

### 3 讨 论

本研究评估了 $^{18}\text{F}$ -FDG PET/CT的代谢特征、患者的临床特征在接受CAR-T治疗的R/R DLBCL患者中的潜在预后价值。ECOG评分、CRS分级以及MTV均显示出独立的预后价值。与单独的临床模型、代谢参数模型相比,综合模型的预后能力在OS和PFS方面均更胜一筹。

由于DLBCL具有高度异质性、侵袭性强以及对CAR-T治疗敏感性不同的生物学特征,一些接受CAR-T治疗后的患者可能预后不佳<sup>[11]</sup>。在这种情况下, $^{18}\text{F}$ -FDG PET/CT代谢参数,如 $\text{SUV}_{\max}$ 、MTV和TLG,对判断疗效和预后具有重要意义。与获得完全缓解的患者相比,非完全缓解的患者在基线参数中具有更高的 $\text{SUV}_{\max}$ 、MTV和TLG。本研究还发现,非完全缓解患者的LDH水平及ICANS发生率也较高。多项研究<sup>[12-14]</sup>证实,PET/CT体积参数MTV是DLBCL和其他淋巴瘤亚型PFS和OS的独立预后因素。本研究中,MTV在预测PFS中的最佳阈值是 $70\text{ cm}^3$ ,在OS中的最佳阈值为 $35.5\text{ cm}^3$ 。CAR-T输注前较高的MTV值与较短的PFS和OS相关。Voorhees等<sup>[15]</sup>的研究结果表明,高 $\text{MTV}>60\text{ mL}$ 与CAR-T治疗后的PFS显著相关。Leithner等<sup>[16]</sup>的研究结果表明,MTV是接受CAR-T治疗的大B细胞淋巴瘤患者的不良PFS和OS的关键参数。MTV作为肿瘤负荷的一个指标可以有效地预测治疗效果。

肿瘤MTV的计算方法基于一定的阈值,阈值的选择有多种方法: $\text{SUV}\geq 2.5$ 、 $41\%\text{SUV}_{\max}$ 、 $\text{SUV}\geq$ 肝脏平均摄取背景。而不论其使用的方法如何,其预测PFS和OS的准确性相似<sup>[17]</sup>。本研究中,我们采用的 $41\%\text{SUV}_{\max}$ 方法是基于欧洲核医学协会的建议<sup>[18]</sup>。

ECOG评分是评估患者整体健康状况和日常

活动能力的实用工具,是预测DLBCL患者生存率最常用的变量<sup>[19]</sup>。本研究结果表明,ECOG评分是DLBCL患者预后的独立预测因子,这与以前的研究一致<sup>[20-21]</sup>。MTV允许准确量化肿瘤负荷以确定预后。与单独使用传统的临床风险因素相比,结合ECOG评分和MTV变量,可更加精确地定义经CAR-T治疗的DLBCL患者的预后。

CRS是CAR-T治疗最常见的不良反应。在探索CAR-T治疗R/R侵袭性淋巴瘤的多中心研究<sup>[22]</sup>中,CRS的严重程度与肿瘤负荷的程度有明显的关联。本研究中, $\geq 3$ 级CRS患者的OS更短。

本研究存在一些局限性。首先,本研究是单中心、回顾性设计,选择偏倚和信息偏倚难以避免。其次,尽管患者数量与其他已发表研究相当,但由于该疗法的新颖性和复杂性,导致可纳入的病例数量相对有限。然而,正因为目前接受该疗法的患者总体数量有限,而且相关研究也很零散,开展针对早期数据的深入分析对于优化以患者为中心的疗法非常重要。再次,患者在接受CAR-T治疗前接受了异质性的初始治疗方案(如化疗线数、是否移植等),这些因素可能影响CAR-T疗效。最后,缺乏外部验证的患者队列,相关结果仍需在更大规模、多中心的前瞻性队列研究中进行验证。

综上, $^{18}\text{F}$ -FDG PET/CT代谢参数在预测CAR-T疗法对DLBCL患者的疗效方面具有重要作用。MTV联合传统的临床风险因素(ECOG评分、CRS分级)可以改善患者的风险分层,更早、更好地识别超高危DLBCL患者。

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(收稿日期: 2025-02-18 修回日期: 2025-06-17)

(责任编辑: 王琳辉)