论著·肝癌诊疗新策专题

5因子改良衰弱指数联合控制营养状态评分与不可切除肝癌患者介入治疗后总生存期的相关性分析

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［摘要］ **目的** 探究5因子改良衰弱指数(5-factor modified frailty index,mFI-5)联合控制营养状况评分(controlling nutritional status score,CONUT)、那不勒斯预后评分(Naples prognostic score,NPS)对不可切除肝细胞癌(unresectable hepatocellular carcinoma,uHCC)患者介入治疗后总生存期的相关性。**方法** 采用回顾性队列研究设计,纳入2017年10月至2021年12月陆军军医大学第二附属医院肝胆胰外科收治的292例接受介入治疗的uHCC患者。根据mFI-5(≥1分)、NPS(≥3分)和CONUT(≥4分)评分将患者分为高危组与低危组,通过倾向评分匹配(propensity score matching,PSM)平衡基线特征(匹配后*n*=186)。主要观察终点为总生存期(overall survival,OS),采用Kaplan-Meier法绘制生存曲线(Log-rank检验),采用受试者工作特征(receiver operating characteristic curve,ROC)曲线对联合指标预测效能进行评价,并采用Cox回归分析预后因素。**结果** PSM后2组在年龄、肿瘤指标、治疗相关指标等方面差异无统计学意义。生存分析结果显示,mFI-5+NPS高危组死亡风险增加2.252倍(95%*CI*:1.60~3.18,*P*<0.001)。mFI-5与NPS评分联合预测3年OS的曲线下面积(area under curve,AUC)为0.718,显著优于单一指标(*P*=0.007)。多因素Cox回归证实,mFI-5+NPS双阳性(*HR*=1.46,95%*CI*:1.01~2.11,*P*=0.044)、门静脉癌栓(*HR*=1.49,95%*CI*:1.03~2.16,*P*=0.035)、肿瘤直径>5 cm(*HR*=2.01,95%*CI*:1.27~3.17,*P*=0.003)、巴塞罗那临床肝癌分期(Barcelona clinic liver cancer,BCLC) C期(*HR*=2.05,95%*CI*:1.37~3.07,*P*<0.001)为独立不良预后因素,术后靶向-免疫联合治疗显著降低死亡风险(*HR*=0.57,95%*CI*:0.39~0.81,*P*=0.002)。**结论** mFI-5与NPS联合评估与uHCC患者介入治疗后OS显著相关,为临床风险分层和个体化治疗提供依据。

［关键词］ 不可切除肝癌;5因子改良衰弱指数;控制营养状况评分;那不勒斯预后评分;预后
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Association of 5-factor modified frailty index and controlling nutritional status score with overall survival in patients with unresectable hepatocellular carcinoma undergoing interventional therapy

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［**Abstract**］ Objective To investigate the correlation between the combined assessment of preoperative 5-factor modified frailty index (mFI-5) and Naples prognostic score (NPS) with overall survival in

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引用格式:陈代亮,李勇坤,刘磊,等.5因子改良衰弱指数联合营养状态评分与不可切除肝癌患者介入治疗后总生存期的相关性分析[J].陆军军医大学学报,2025,47(17):2061-2070. DOI:10.16016/j.2097-0927.202506011.

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patients with unresectable hepatocellular carcinoma (uHCC) following interventional therapy. **Methods** A retrospective cohort study enrolled 292 patients with uHCC who underwent interventional therapy at the Department of Hepatobiliary Pancreatic Surgery of the Second Affiliated Hospital in Army Medical University from October 2017 to December 2021. Patients were stratified into high-risk and low-risk groups based on mFI-5 (≥1), NPS (≥3), and CONUT (≥4) scores. Propensity score matching (PSM) was performed to balance baseline characteristics (post-matching n=186). The primary endpoint was overall survival (OS), analyzed using Kaplan-Meier curves with log-rank tests. The predictive performance of combined indicators was evaluated by receiver operating characteristic (ROC) curves, and prognostic factors were assessed *via* Cox regression analysis. **Results** After PSM, baseline characteristics (including age, tumor markers, and treatment-related parameters) showed no significant differences between the two groups. Survival analysis demonstrated a 2.252-fold higher risk of death in the mFI-5 plus NPS high-risk group (95%*CI*:1.60~3.18, P<0.001). The combination of mFI-5 and NPS scores yielded an area under curve (AUC) of 0.718 for predicting 3-year overall survival, significantly outperforming either index alone (P=0.007). Multivariable Cox regression analysis identified that dual positivity for mFI-5 and NPS (*HR*=1.46; 95%*CI*: 1.01~2.11, P=0.044), portal vein tumor thrombosis (*HR*=1.49; 95%*CI*: 1.03~2.16, P=0.035), tumor diameter >5 cm (*HR*=2.01; 95%*CI*:1.27~3.17, P=0.003), Barcelona clinic liver cancer (BCLC) stage C disease (*HR*=2.05; 95%*CI*: 1.37~3.07, P<0.001) were independent predictors of poor prognosis. Postoperative combination targeted therapy and immunotherapy was associated with significantly reduced mortality risk (*HR*=0.57; 95%*CI*: 0.39~0.81, P=0.002). **Conclusion** The combination of mFI-5 and NPS scores is significantly associated with overall survival in patients with unresectable hepatocellular carcinoma (uHCC) undergoing locoregional therapy, providing a validated tool for clinical risk stratification and personalized treatment planning.

[**Key words**] unresectable hepatocellular carcinoma; 5-factor modified frailty index; controlling nutritional status score; Naples prognostic score; prognosis

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肝细胞癌(hepatocellular carcinoma, HCC)是全球范围内致死率排名第三的恶性肿瘤[1],约70%的患者初诊时因肿瘤体积大、多灶性分布或合并严重肝硬化等原因被归类为不可切除肝癌[2]。以经导管动脉化疗栓塞术(transarterial chemoembolization, TACE)及肝动脉灌注化疗(hepatic arterial infusion chemotherapy, HAIC)为主的肝癌介入治疗因其可靠的疗效及微创性,已成为这类患者延长生存期的重要手段[3-4]。然而临床实践表明,即使采用相同治疗方案,患者的术后并发症发生率及生存结局仍存在显著异质性[5]。研究发现,除肿瘤分期、分子特征外,自身的机体状态可能成为影响治疗预后的关键因素[6]。不可切除肝癌(unresectable hepatocellular carcinoma, uHCC)患者常伴随骨骼肌减少、代谢紊乱、慢性炎症以及营养不良等多种机体状态的异常[7-10]。近年来,快速、标准化的消耗状态评估工具在优化治疗决策中的价值逐渐受到关注[11]。5因子改良衰弱指数(5-factor modified frailty index, mFI-5)通过综合评价患者的生理储备能力,可有效预测肝切除及肝移植术后并发症及死亡率[12];客观性营养筛查指标,如控制营养状况评分(controlling nutritional status score, CONUT)、那不勒斯预后评分(Naples prognostic score, NPS),则被证实与肝癌患者生存期独立相关[13-14]。然而,上述指标在uHCC介入治疗中的应用报道较少,不同指标与患者术后总生存期之间的相关性亦不明确。基于此,本研究旨在探讨衰弱指数、术前营养状况及恶病质等客观评分与不可切除肝癌患者介入治疗术后总生存期的相关性,初步探讨其对未来个体化治疗策略制定的指导价值,以期实现对肝癌患者的精准干预。

1 资料与方法

1.1 研究对象

采用回顾性队列研究设计,收集2017年10月至2021年12月间陆军军医大学第二附属医院肝胆胰外科接受介入治疗的292例uHCC患者的临床资料。纳入标准:①年龄≥18岁;②依据《原发性肝癌诊疗规范》临床诊断为HCC[15];③介入前未接受其他抗肿瘤治疗。排除标准:①临床资料不完整;②合并其他系

统恶性肿瘤。本研究符合《赫尔辛基宣言》相关要求,通过了陆军军医大学第二附属医院伦理审查委员会的批准(2024-研第336-01)。

1.2 观察指标和评价标准

患者的观察指标包括一般情况指标:性别、年龄、体质指数(body mass index, BMI)、吸烟史、饮酒史;术前合并症:慢性乙肝、肝硬化、高血压、2型糖尿病、慢性阻塞性肺疾病/慢性肺炎;术前血清学指标:甲胎蛋白(Alpha-fetoprotein, AFP)、血红蛋白、血小板、谷草转氨酶(aspartate aminotransferase, AST)、谷丙转氨酶(alanine aminotransferase, ALT)、血清白蛋白(serum albumin, ALB)、凝血酶原时间(prothrombin time,PT)、血清肌酐、总胆红素、淋巴细胞绝对值、单核细胞绝对值、血红蛋白、血小板计数、胆固醇;肿瘤相关特征:肿瘤最大直径、肝外转移情况、门静脉癌栓(portal vein tumor thrombus, PVTT)、巴塞罗那临床肝癌(Barcelona clinic liver cancer,BCLC)分期情况。以mFI-5评分评价患者衰弱程度。mFI-5评分标准由慢性阻塞性肺疾病或慢性肺炎病史、2型糖尿病史、非独立功能状态、术前30 d内的充血性心力衰竭病史、需要药物治疗的高血压病史5项因素组成。基于既往研究,将患者以mFI-5评分=0分或≥1分分为非衰弱组与衰弱组[16]。CONUT评分通过血清白蛋白浓度、外周血淋巴细胞计数和总胆固醇浓度计算,以CONUT评分<4分或≥4分分为低CONUT组与高CONUT组[17]。NPS评分基于血清白蛋白、总胆固醇、中性粒细胞与淋巴细胞比率(neutrophil-to-lymphocyte ratio, NLR)和淋巴细胞与单核细胞比率(lymphocyte-to-monocyte ratio,LMR)计算,NPS评分以<3分或≥3分分为低NPS组及高NPS组[18]。mFI-5评分、CONUT评分及NPS评分诊断过程由2名高年资(工作时间>10年)主治医师进行,确保数据准确性。

1.3 结局与随访方法

本研究以总生存期(overall survival,OS)为主要结局指标,患者从接受介入术后第1个月开始通过打电话和查阅门诊复查病历的方式随访,后每3个月随访1次,直至患者死亡或退出随访。首次介入治疗后视患者一般情况,决定是否重复介入治疗或采用其他治疗方式(如手术、放疗或全身治疗),如果一般情况较差,则给予支持性治疗及护理。OS为患者首次接受介入治疗至死亡或随访截止的时间间隔。随访截止日期为2024年11月。

1.4 统计学分析

符合正态分布且具备方差齐性的计量资料以$\bar{x}\pm s$描述,计数资料则以阳性病例数(%)描述,对连续变量采用独立样本t检验或者非参数检验,对分类变量采用χ^2检验进行分析。为排除术前衰弱及营养状态以外的混杂因素的影响,进行1∶1倾向评分匹配(propensity score matching,PSM),采用最近邻匹配法,卡钳值设为0.1。采用Log-rank检验比较Kaplan-Meier生存曲线。采用X-tile软件计算各评分分组截断值。采用时间依赖性受试者工作特征(receiver operating characteristic curve, ROC)曲线下面积(area under the curve, AUC)评估评分对预后的预测效能,Delong test比较曲线间差异。采用单因素Cox回归筛选变量,单因素具有统计学意义的变量纳入Cox多因素回归分析,计算风险比(*HR*),并在计算95%*CI*讨论影响OS的因素。本研究涉及的所有统计学检验均为双侧,$P<0.05$为差异具有统计学意义。所有数据使用SPSS 23.0、R 4.1.12、X-tile软件进行统计分析。

2 结果

2.1 倾向性评分匹配前后患者基线资料

采用PSM(卡钳值为0.1)对292例患者的基线特征进行均衡性检验。PSM前分析显示,mIF-5≥1分组患者年龄较大($t=-8.05$,$P<0.001$),且肌酐($t=-2.68$,$P=0.008$)、AST($t=2.71$,$P=0.007$)、NPS评分≥3分($\chi^2=18.92$,$P<0.001$)、CONUT评分≥4分($\chi^2=9.42$,$P=0.002$)及门静脉癌栓发生率($\chi^2=5.77$,$P=0.016$)存在显著差异(表1)。经PSM匹配后($n=186$),mIF-5≥1组和NPS评分≥3组比例仍较高($P<0.001$),且白蛋白水平较低($t=2.25$,$P=0.026$),其余基线变量(如年龄、最大肿瘤直径、性别、AFP水平等)均差异无统计学意义(表2)。提示PSM有效平衡了样本间除营养状态外的主要混杂因素。

2.2 PSM后不同评分与生存结局的相关性

通过Kaplan-Meier生存曲线评估不同评分组的生存差异。结果显示:本研究人群经PSM后的中位OS为16.8个月。低mFI-5组和高mFI-5组的中位OS分别为21.2个月和14.83个月。与低mFI-5组比较,高mFI-5组($P=0.014$)、高CONUT组($P=0.024$)及高NPS组($P=0.03$)的总生存期显著更短,表明高mFI-5、高CONUT和高NPS评分与患者不良预后显著相关。mFI-5与CONUT指标双阳性($P=0.008$)以及mFI-5与NPS指标双阳性($P<0.001$)均与患者不良预后显著相关(图1)。结果提示改良衰弱指数与营养状态评分与患者术后较差的OS相关。

表1 PSM前患者基线资料[例(%),$\bar{x}\pm s$]

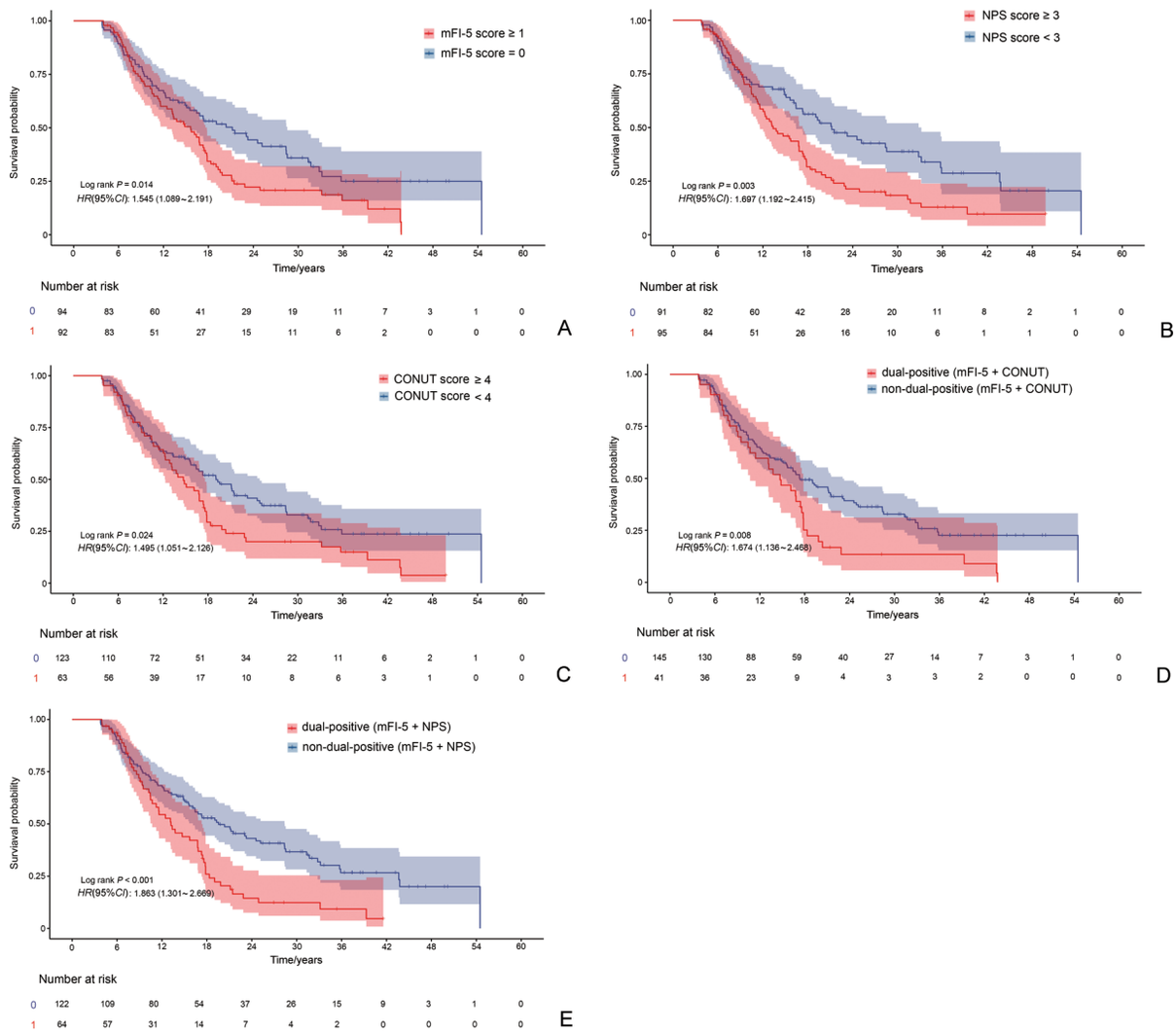
Table 1 Baseline characteristics of patients before PSM[n(%),$\bar{x}\pm s$]

Variables	Before PSM				
	Total(n=292)	mIF-5=0(n=192)	mIF-5≥1(n=100)	t/χ^2	P
Age/years	55.14±10.68	51.74±9.16	61.67±10.40	−8.05	<0.001
Gender				0.05	0.815
Female	39(13.36)	25(13.02)	14(14.00)		
Male	253(86.64)	167(86.98)	86(86.00)		
BMI/(kg/m^2)	23.38±3.10	23.35±3.18	23.44±2.96	−0.24	0.810
Maximum tumor diameter/cm	6.16±2.50	6.12±2.52	6.24±2.48	−0.38	0.705
Serum creatinine/(μmol/L)	71.43±17.06	69.52±13.27	75.12±22.27	−2.68	0.008
ALT/(U/L)	60.84±43.95	61.62±38.43	59.34±53.14	0.42	0.675
AST/(U/L)	72.35±52.91	78.34±56.66	60.84±42.80	2.71	0.007
Albumin/(g/L)	40.86±4.73	41.28±4.78	40.06±4.54	2.10	0.037
Total bilirubin/(μmol/L)	23.02±19.58	22.45±12.91	24.11±28.35	−0.69	0.492
Hemoglobin/(g/L)	138.57±19.73	140.09±19.42	135.68±20.09	1.82	0.070
Platelet/(×10^9/L)	178.49±93.50	182.74±94.54	170.36±91.39	1.07	0.284
Prothrombin time/s	12.53±1.26	12.62±1.28	12.35±1.20	1.73	0.085
NPS score				18.92	<0.001
<3	142(48.63)	111(57.81)	31(31.00)		
≥3	150(51.37)	81(42.19)	69(69.00)		
CONUT score				9.42	0.002
<4	184(63.01)	133(69.27)	51(51.00)		
≥4	108(36.99)	59(30.73)	49(49.00)		
Child-Pugh B				0.07	0.786
No	259(88.70)	171(89.06)	88(88.00)		
Yes	33(11.30)	21(10.94)	12(12.00)		
Cirrhosis				0.00	0.989
No	140(47.95)	92(47.92)	48(48.00)		
Yes	152(52.05)	100(52.08)	52(52.00)		
AFP>400 ng/mL				9.71	0.002
No	150(51.37)	86(44.79)	64(64.00)		
Yes	142(48.63)	106(55.21)	36(36.00)		
BCLC Stage C				3.19	0.074
No	160(54.79)	98(51.04)	62(62.00)		
Yes	132(45.21)	94(48.96)	38(38.00)		
Extrahepatic metastasis				3.20	0.074
No	157(53.77)	96(50.00)	61(61.00)		
Yes	135(46.23)	96(50.00)	39(39.00)		
PVTT				5.77	0.016
No	192(65.75)	117(60.94)	75(75.00)		
Yes	100(34.25)	75(39.06)	25(25.00)		
Targeted-immunotherapy combination				2.70	0.100
No	104(35.62)	62(32.29)	42(42.00)		
Yes	188(64.38)	130(67.71)	58(58.00)		

表2 PSM后患者基线资料[例(%),$\bar{x}\pm s$]

Table 2 Baseline characteristics of patients after PSM[n(%),$\bar{x}\pm s$]

Variables	After PSM				
	Total(n=186)	mIF-5=0(n=102)	mIF-5≥1(n=84)	t/χ^2	P
Age /years	55.68±8.52	55.26±8.81	56.11±8.23	−0.68	0.496
Gender				0.34	0.557
Female	25(13.44)	15(14.71)	10(11.90)		
Male	161(86.56)	87(85.29)	74(88.10)		
BMI/(kg/m^2)	23.59±3.11	23.28±2.62	23.91±3.52	−1.40	0.164
Maximum tumor diameter/cm	6.19±2.50	6.06±2.54	6.33±2.47	−0.72	0.471
Serum creatinine/(μmol/L)	69.62±12.90	68.74±12.94	70.52±12.87	−0.94	0.350
ALT/(U/L)	62.44±47.85	58.56±38.20	66.40±55.96	−1.12	0.265
AST/(U/L)	70.43±54.34	69.39±58.11	71.49±50.50	−0.26	0.793
Albumin/(g/L)	40.51±4.79	41.28±4.89	39.72±4.57	2.25	0.026
Total bilirubin/(μmol/L)	24.12±23.69	26.12±31.88	22.09±9.66	1.16	0.247
Hemoglobin/(g/L)	137.76±19.21	138.81±18.05	136.68±20.38	0.75	0.452
Platelet/(×10^9/L)	178.96±93.77	170.65±86.60	187.46±100.33	−1.22	0.223
Prothrombin time/s	12.50±1.22	12.38±1.24	12.63±1.18	−1.39	0.167
NPS score				24.91	<0.001
<3	91(48.92)	63(67.02)	28(30.43)		
≥3	95(51.08)	31(32.98)	64(69.57)		
CONUT score				4.49	0.034
<4	123(66.13)	69(73.40)	54(58.70)		
≥4	63(33.87)	25(26.60)	38(41.30)		
Child-Pugh B				0.62	0.431
No	160(86.02)	79(84.04)	81(88.04)		
Yes	26(13.98)	15(15.96)	11(11.96)		
Cirrhosis				0.54	0.462
No	92(49.46)	49(52.13)	43(46.74)		
Yes	94(50.54)	45(47.87)	49(53.26)		
AFP>400 ng/mL				0.10	0.756
No	103(55.38)	51(54.26)	52(56.52)		
Yes	83(44.62)	43(45.74)	40(43.48)		
BCLC Stage C				3.09	0.079
No	107(57.53)	60(63.83)	47(51.09)		
Yes	79(42.47)	34(36.17)	45(48.91)		
Extrahepatic metastasis				0.81	0.369
No	131(70.43)	69(73.40)	62(67.39)		
Yes	55(29.57)	25(26.60)	30(32.61)		
PVTT				0.52	0.470
No	120(64.52)	63(67.02)	57(61.96)		
Yes	66(35.48)	31(32.98)	35(38.04)		
Targeted-immunotherapy combination				0.32	0.570
No	67(36.02)	32(34.04)	35(38.04)		
Yes	119(63.98)	62(65.96)	57(61.96)		



A: Comparison of survival curves between high mFI-5 and low mFI-5 groups; B: Comparison of survival curves between high NPS and low NPS groups; C: Comparison of survival curves between high CONUT and low CONUT groups; D: Comparison of survival curves between dual-positive (mFI-5 + CONUT) and non-dual-positive groups; E: Comparison of survival curves between dual-positive (mFI-5 + NPS) and non-dual-positive groups

图1 PSM后不同评分评估的肝癌患者的总体生存曲线比较

Figure 1 Overall survival curves after PSM stratified by frailty and nutritional scoring systems in patients with HCC

2.3 不同指标预测HCC介入术后3年OS的ROC曲线分析

采用时间依赖性ROC曲线分析各评分对HCC患者介入术后3年OS的预测效能,结果显示:mFI-5评分预测HCC患者介入术后3年OS的AUC为0.664,NPS评分AUC为0.661,二者均显著高于CONUT评分(AUC:0.546,Z=2.662 5,P=0.007)。在联合评分中,mFI-5+NPS评分预测HCC术后3年OS的AUC为0.718,显著高于mFI-5+CONUT评分(AUC:0.605,Z=3.279 3,P=0.001,图2)。结果提示,联合评分模型具有最优生存预测价值。

2.4 PSM后患者预后危险因素分析

通过单因素Cox回归分析显示,门静脉癌栓、肿瘤直径>5 cm、肝外转移、AFP>400 ng/mL、BCLC分期C期及mFI-5+NPS双阳性与总生存期缩短显著相关,而术后靶免联合治疗为保护性因素。多因素分析进一步校正混杂变量后,门静脉癌栓、肿瘤直径>5 cm、肝外转移、AFP>400 ng/mL、BCLC分期C期及mFI-5+NPS双阳性仍为独立不良预后因素,术后靶免联合治疗的保护作用更为显著。性别、年龄、肝硬化、肝功能指标(ALT、AST、ALB等)及凝血功能指标在多因素模型中均差异无统计学意义。以上结果提示,肿瘤负荷(直

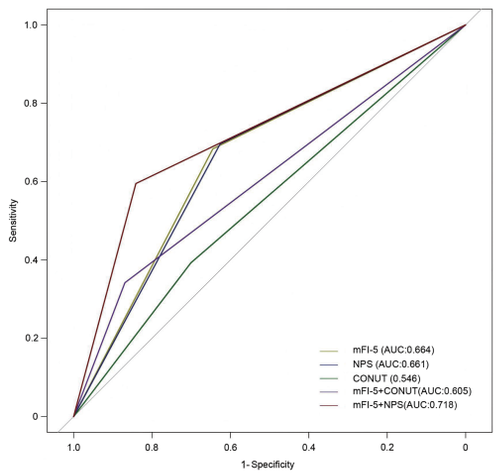


图2 不同指标预测HCC介入术后3年总生存期的ROC曲线

Figure 2 ROC curves for scoring systems predicting 3-year overall survival after locoregional therapy in HCC

径、转移)、AFP水平、BCLC分期及mFI-5+NPS双阳性是影响预后的关键独立风险因素,而术后靶免联合治疗可显著改善患者生存结局(表3)。

2.5 PSM后亚组分析

通过森林图进行交互作用分析,检验mFI-5联合NPS评分在不同临床亚组中的预后一致性。亚组分析结果表明,在年龄≤60岁、男性、BCLC分期B期、门静脉癌栓阳性、肿瘤单发或多发、最大肿瘤直径>5 cm、无肝外转移、AFP≤400 ng/mL以及介入术后联合靶免治疗的亚组中,CONUT评分与OS具有显著相关性(P<0.05)。然而,除门脉癌栓亚组(P=0.035)和BCLC分期亚组(P=0.014)外,mFI-5联合NPS评分在不同亚组间的预后价值未表现出显著差异(图3)。提示mFI-5+NPS联合评分的预后价值在不同临床特征亚组中具有一致性。

3 讨论

3.1 宿主因素在肝癌个体化治疗中的重要性

随着精准医学的发展,越来越多的研究开始关注宿主因素与肿瘤治疗之间的相互作用[19-20]。综合评估患者的肿瘤特征和机体状态引导的个体化治疗策略有望在不可切除肝癌的治疗中发挥更大的作用[21]。目前,已有大量研究证实这些因素不仅影响肿瘤患者的整体生存状况,还可能通过多种机制影响肿瘤的进展和治疗反应[22-24]。结合患者的营养状态、肌肉质量以及炎症标志物等指标,制定个性化的治疗方案,可能有助于优化治疗效果并改善患者的长期生存[25-26]。目前针对肝癌患者机体状态的评估大多为营养、炎症状态的评估,部分工具评估流程复杂且使用较多主观指标,不利于临床推广应用。

表3 PSM后影响患者预后的Cox单因素和多因素分析

Table 3 Univariate and multivariate analyses of prognostic factors in patients after PSM

Variables	Univariate Analysis					Multivariate Analysis				
	β	SE	Z	P	HR(95%CI)	β	SE	Z	P	HR(95%CI)
Gender(Male/Female)	0.14	0.25	0.56	0.575	1.15(0.70~1.90)					
Age>60 years(yes/no)	−0.20	0.20	−1.00	0.317	0.82(0.55~1.21)					
Cirrhosis(present/absent)	−0.04	0.18	−0.22	0.823	0.96(0.68~1.36)					
Portal vein tumor thrombus(present/absent)	0.79	0.18	4.43	<0.001	2.21(1.56~3.15)	0.40	0.19	2.10	0.035	1.49(1.03~2.16)
Tumor diameter(>5 cm)	1.01	0.22	4.48	<0.001	2.74(1.76~4.26)	0.70	0.23	2.99	0.003	2.01(1.27~3.17)
Tumor number(multiple/single)	0.26	0.18	1.47	0.141	1.30(0.92~1.85)					
Extrahepatic metastasis(present/absent)	1.12	0.19	5.96	<0.001	3.05(2.11~4.40)	0.62	0.21	2.96	0.003	1.86(1.23~2.80)
ALT>40 U/L(yes/no)	0.09	0.19	0.49	0.623	1.10(0.76~1.57)					
AST>40 U/L(yes/no)	0.35	0.21	1.67	0.095	1.42(0.94~2.13)					
ALB≤35 g/L(yes/no)	0.10	0.27	0.37	0.711	1.10(0.65~1.86)					
TB>34 μmol/L(yes/no)	−0.04	0.28	−0.16	0.874	0.96(0.56~1.64)					
HB>120 g/L(yes/no)	0.38	0.26	1.46	0.143	1.46(0.88~2.44)					
PLT>150×10^9/L(yes/no)	0.16	0.18	0.87	0.386	1.17(0.82~1.67)					
PT>14.5 s(yes/no)	−0.11	0.35	−0.32	0.746	0.89(0.45~1.77)					
AFP>400 ng/mL(yes/no)	0.55	0.18	3.11	0.002	1.74(1.23~2.46)	0.40	0.19	2.14	0.033	1.49(1.03~2.14)
Child-Pugh classification(B/A)	0.06	0.25	0.26	0.794	1.07(0.66~1.73)					
BCLC stage(C/B)	1.21	0.19	6.49	<0.001	3.34(2.32~4.81)	0.72	0.21	3.48	<0.001	2.05(1.37~3.07)
Targeted-immunotherapy combination(yes/no)	−0.45	0.18	−2.49	0.013	0.64(0.45~0.91)	−0.57	0.18	−3.09	0.002	0.57(0.39~0.81)
mFI-5+NPS dual-positive(yes/no)	0.62	0.18	3.40	<0.001	1.86(1.30~2.67)	0.38	0.19	2.01	0.044	1.46(1.01~2.11)

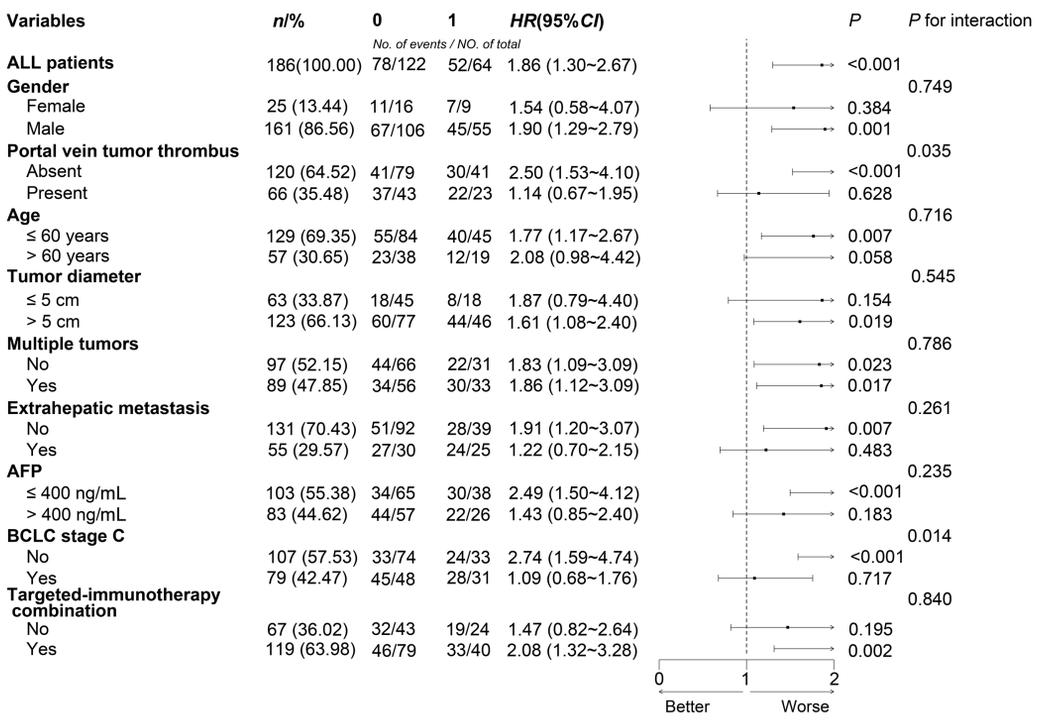


图3 mFI-5联合NPS评分预后价值的亚组分析森林图

Figure 3 Forest plot of subgroup analysis for the prognostic value of the mFI-5 combined NPS score

3.2 衰弱与营养炎症评分的临床指导价值

mFI-5评分、CONUT评分、NPS评分是近年来出现的客观炎症-营养筛查工具,具有简易、低成本、较全面等优势,已经广泛应用于其他疾病的营养筛查,大量研究已证实其有效性[27-29]。本研究初步探索了mFI-5评分、NPS和CONUT营养评分对不可切除肝细胞癌患者介入治疗预后的预测价值。研究结果表明,mFI-5、NPS和CONUT营养评分均与患者较差的预后相关。不仅如此,Cox多因素回归分析结果显示mFI-5与NPS联合后为患者预后较差的独立危险因素(*HR*=1.46,95%*CI*:1.01~2.11,*P*=0.044)。亚组分析进一步揭示,mFI-5在无门静脉癌栓、BCLC分期B期的患者中风险分层作用更加突出,提示患者机体状态可能与肿瘤进展存在潜在关联。NPS评分中包含的中性粒细胞-淋巴细胞比值和血清白蛋白等指标,直接反映了"炎症-免疫-代谢"轴的异常激活[30-31]。其次,有文献报道mFI-5评估的衰弱状态直接影响了患者对治疗应激的耐受能力[32]。更重要的是,衰弱和炎症之间存在正向反馈循环:炎症因子(如IL-6、TNF-α)通过NF-κB通路促进肌肉蛋白分解,而肌肉减少又进一步加剧炎症反应[33-34]。这种"炎症-衰弱"的恶性循环可能是导致高危患者预后更差的核心机制。

3.3 不可切除肝癌未来个体化干预策略的展望

发展针对"炎症-衰弱-营养不良"复杂网络的综合干预方案是未来肝癌个体化治疗的潜在方向[35]。有学者提出的"预康复"模式值得借鉴,即在治疗前4~6周开始联合运动训练、营养支持和心理干预,初步研究显示该方案可提高患者术前储备功能[36-37]。未来预康复策略(如抗阻训练+营养支持)或靶向恶病质药物(如Anamorelin)联合介入治疗的可行性还有待评估。本研究存在以下不足:首先,作为单中心回顾性研究,尽管采用严格的纳入标准和多因素校正,仍不能完全避免选择偏倚;其次,各评分系统的最佳截断值需要在前瞻性队列中进一步验证。

综上所述,本研究揭示了衰弱与营养评价指标在不可切除肝癌介入治疗中的预后预测作用,为从"以肿瘤为中心"向"以患者为中心"的诊疗模式转变提供了理论依据。未来需通过多学科协作,将肝癌患者衰弱及营养状态监测纳入临床路径,最终实现肝癌患者的精准干预。

利益冲突 本文所有作者声明不存在利益冲突

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