· 临床研究 ·

老年急性胰腺炎患者机体营养状况及其与免疫功能及预后的关系

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【摘 要】 **目的** 评估老年急性胰腺炎(AP)患者机体营养状况,并分析其与免疫功能及预后的关系。**方法** 选取 2021 年 7 月至 2023 年 12 月武汉大学中南医院肝胆胰腺外科收治的 122 例老年 AP 患者为研究对象。根据 AP 严重程度,分为轻症组 51 例、中度重症组 39 例、重症组 32 例,比较 3 组老年 AP 患者营养状态[白蛋白(ALB)、转铁蛋白(TRF)、老年营养风险指数(GNRI)]以及免疫功能($CD4^+$、$CD8^+$、$CD4^+/CD8^+$)差异。根据患者入院 28 d 内生存情况,分为生存组 110 例与死亡组 12 例。采用 SPSS 24.0 统计软件进行数据分析。采用 Pearson 相关系数分析相关性。采用受试者工作特征(ROC)曲线评估营养状态及免疫功能指标对老年 AP 患者死亡风险的预测价值。**结果** 不同严重程度老年 AP 患者入院时 ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$比较,差异均有统计学意义($P<0.05$)。其中,重症组患者上述指标均显著低于轻症组及中度重症组($P<0.05$),中度重症组显著低于轻症组($P<0.05$)。Pearson 相关系数分析显示,老年 AP 患者 ALB、GNRI、TRF 与 $CD4^+$、$CD4^+/CD8^+$均呈显著正相关($P<0.05$)。死亡组入院时 ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$均显著低于生存组,差异均有统计学意义(均 $P<0.05$)。ROC 曲线显示,入院时 ALB、GNRI、TRF、$CD4^+$及 $CD4^+/CD8^+$预测老年 AP 患者死亡风险的曲线下面积分别为 0.843(95%*CI* 0.717~0.969)、0.741(95%*CI* 0.597~0.884)、0.732(95%*CI* 0.594~0.870)、0.796(95%*CI* 0.669~0.923)及 0.911(95%*CI* 0.848~0.974);最佳截断点分别为 31.97 g/L、88.25、2.08 g/L、36.37%及 1.59。5 项指标联合检测的 ROC 曲线下面积值高达 0.947(95%*CI* 0.906~0.998,$P<0.05$)。**结论** 营养不良及免疫抑制可促进老年 AP 患者病情进展,且患者营养状态与免疫功能存在密切联系,入院时检测 ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$对预测患者死亡风险有价值。

【关键词】 老年人;急性胰腺炎;营养;免疫;严重程度;预后

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Nutritional status in elderly patients with acute pancreatitis and its relationship with immune function and prognosis

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【**Abstract**】 **Objective** To evaluate the nutritional status in elderly patients with acute pancreatitis (AP) and analyze its relationship with immune function and prognosis. **Methods** A total of 122 elderly AP patients admitted in Department of Hepatobiliary and Pancreatic Surgery of our hospital from July 2021 to December 2023 were recruited, and divided into mild, moderate and severe groups according to the severity of AP (51, 39 and 32 cases, respectively). The nutritional status [albumin (ALB) and transferrin (TRF) levels, geriatric nutritional risk index (GNRI)] and immune function ($CD4^+$ and $CD8^+$, and $CD4^+/CD8^+$) were compared among the three groups. Based on their clinical outcomes within 28 d after admission, they were assigned into survival group (110 cases) and death group (12 cases). SPSS statistics 24.0 software was used to process and analyze the data. Pearson correlation coefficient analysis was employed for correlation analysis, and receiver operating characteristic (ROC) curve was adopted to assess the predictive value of nutritional status and immune function indicators on death of elderly AP patients. **Results** There were statistical differences in ALB, GNRI, TRF, $CD4^+$ and $CD4^+/CD8^+$ at admission among elderly patients with different severities of AP ($P<0.05$), and the above indicators were significantly lower in the severe group than the mild group and moderate group ($P<0.05$), and in the moderate group than the mild group ($P<0.05$). Pearson correlation coefficient analysis showed that ALB, GNRI and TRF were positively correlated with $CD4^+$ and $CD4^+/CD8^+$ in elderly AP patients ($P<0.05$). At admission, the ALB, GNRI, TRF, $CD4^+$ and $CD4^+/CD8^+$ in death group were significantly lower than those in survival group, and the differences were statistically significant ($P<0.05$ for all). ROC curve revealed that AUC value of ALB, GNRI, TRF, $CD4^+$ and $CD4^+/CD8^+$ at admission in predicting death of elderly AP patients was 0.843 (95%*CI* 0.717-0.969, $P<0.05$), 0.741 (95%*CI* 0.597-0.884, $P<0.05$), 0.732 (95%*CI* 0.594-0.870, $P<0.05$),

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0.796 (95%*CI* 0.669-0.923, $P<0.05$), and 0.911 (95%*CI* 0.848-0.974, $P<0.05$); optimum cut-off value was 31.97 g/L, 88.25、2.08 g/L, 36.37% and 1.59, respectively. The value was as high as 0.947 (95%*CI* 0.906-0.998, $P<0.05$) when the above five indicators combined together. **Conclusion** Malnutrition and immunosuppression promote the disease progression in elderly AP patients, and the nutritional status is closely associated with their immune function. Detecting ALB, GNRI, TRF, $CD4^+$ and $CD4^+/CD8^+$ at admission is of significance in prediction of death in the patients.

【Key words】 aged; acute pancreatitis; nutrition; immune; severity; prognosis

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急性胰腺炎(acute pancreatitis, AP)全球发病率为(4.9~73.4)/10万,以持续性向背部放射的上腹部剧烈疼痛为主要临床表现,部分患者呈休克表现,老年患者甚至可出现精神状态改变,且老年患者由于基础疾病多、器官功能退化,病死风险高于青中年AP患者[1]。AP的发生机制复杂且尚未明确,有报道指出,免疫细胞的迁移可能促进炎症过度反应,并参与AP的发生发展[2]。AP患者常伴肠道屏障功能受损,有研究发现,肠道微生物菌群失衡可能引起细菌异位及营养代谢失调,加重AP的炎症反应,加速病情进展[3]。而AP的全身应激状态又促进低蛋白血症等代谢性疾病的发生,诱发营养不良,导致负氮平衡,使免疫功能紊乱,进一步加剧AP的进展[4]。基于此,本研究评估老年AP患者的营养状况,并分析其与免疫功能及预后的关系,为老年AP患者的救治提供依据。

1 对象与方法

1.1 研究对象

前瞻性选取2021年7月至2023年12月武汉大学中南医院肝胆胰腺外科收治的122例老年AP患者为研究对象。纳入标准:符合《中国急性胰腺炎诊治指南(2021)》[5]中AP诊断标准,即首次AP发作,且发作24 h内入院治疗;年龄60~80岁;患者知情同意,并签署纸质版知情同意书。排除标准:既往胰腺手术治疗史;AP发作前存在肝、肾等器官功能衰竭;合并胰腺肿瘤;合并恶性肿瘤、免疫系统疾病。剔除标准:不遵医嘱治疗或住院中途自行出院。本研究经武汉大学中南医院医学伦理委员会审批(伦理批号:R-2021-027)。

1.2 方法

1.2.1 实验室指标检测 所有老年AP患者在入院2 h内采集2管外周肘静脉血,各3~4 ml。其中1管经离心半径8 cm转速3000转/min离心10 min,使用全自动生化分析仪(日本Hitachi公司,型号:7600-220)检测血清白蛋白(albumin, ALB)及转铁蛋白(transferrin, TRF)水平,评估营养状态。计算老年营养风险指数(geriatric nutritional risk index, GNRI)[6],GNRI=1.489×血清ALB(g/L)+41.7×实际体质量(kg)/理想体质量(kg)。将入院2 h内采集的另1管外周肘静脉血使用流式细胞仪(美国BD公司,型号:FACSCalibur)检测T细胞亚群$CD4^+$、$CD8^+$的百分比,并计算$CD4^+/CD8^+$,评估免疫功能。

1.2.2 AP严重程度评估 参考《中国急性胰腺炎诊治指南(2021)》,在入院确诊后给予患者液体治疗及营养支持,针对病因及早期并发症治疗,并以无器官衰竭、无局部或全身并发症判断为轻症,以一过性器官功能障碍(<48 h)或局部并发症判断为中度重症,以持续性器官功能障碍(≥48 h)判断为重症。122例老年AP患者根据严重程度,分为轻症组51例、中度重症组39例、重症组32例。

1.2.3 预后评估 以入院28 d内生存情况评估预后,并分为生存组110例与死亡组12例。

1.3 统计学处理

采用SPSS 24.0统计软件(美国IBM公司)进行数据分析。计量资料以($\bar{x}\pm s$)表示,多组间比较采用单因素方差分析,组内两两比较采用LSD-t检验;计数资料以例数(百分率)表示,组间比较采用χ^2检验。相关性分析采用Pearson相关系数。采用受试者工作特征(receiver operating characteristic, ROC)曲线评估营养状态及免疫功能指标对老年AP患者预后死亡的预测价值。$P<0.05$为差异有统计学意义。

2 结 果

2.1 不同严重程度老年AP患者一般资料比较

122例老年AP患者均遵医嘱治疗,无剔除病例。3组老年AP患者性别、年龄、发病至入院时间、AP类型、基础疾病等一般资料比较,差异均无统计学意义(均$P>0.05$;表1)。

2.2 不同严重程度老年AP患者入院时营养状态、免疫功能比较

不同严重程度老年AP患者入院时ALB、GNRI、TRF、$CD4^+$及$CD4^+/CD8^+$比较,差异均有统计学意义(均$P<0.05$)。其中,重症组上述指标均低于轻症组及中度重症组,中度重症组则低于轻症组,差异均有统计学意义(均$P<0.05$;表2)。

表 1 不同严重程度老年 AP 患者一般资料比较

Table 1 Comparison of general data between elderly AP patients with different severity

Group	n	Male/female (n)	Age (years, $\bar{x}\pm s$)	Time from onset to admission (h, $\bar{x}\pm s$)	AP type[n(%)]			Hypertension [n(%)]	Diabetes mellitus [n(%)]	Hyperlipidemia [n(%)]
					Acute biliary pancreatitis	Hypertriglyceridemic AP	Acute alcoholic pancreatitis			
Mild	51	28/23	68.40±5.23	6.85±1.44	41(80.39)	5(9.80)	5(9.80)	20(39.22)	5(9.80)	6(11.76)
Moderately severe	39	22/17	68.61±5.09	6.93±1.36	31(79.49)	6(15.38)	2(5.13)	16(41.03)	3(7.69)	7(17.95)
Severe	32	17/15	68.89±5.40	7.12±1.47	23(71.88)	7(21.87)	2(6.25)	13(40.63)	4(12.50)	9(28.13)
F/χ^2		0.077	0.086	0.358		2.889		0.034	0.458	3.561
P value		0.962	0.917	0.700		0.576		0.983	0.795	0.169

AP: acute pancreatitis.

表 2 不同严重程度老年 AP 患者入院时营养状态、免疫功能比较

Table 2 Comparison of nutritional status and immune function at admission between elderly AP patients with different severity ($\bar{x}\pm s$)

Group	n	ALB(g/L)	GNRI	TRF(g/L)	$CD4^+$(%)	$CD8^+$(%)	$CD4^+/CD8^+$
Mild	51	39.12±5.39	93.90±5.21	2.42±0.42	41.81±6.89	24.26±2.98	1.96±0.34
Moderately severe	39	36.23±5.90*	88.46±5.87*	2.23±0.41*	38.40±7.21*	25.24±3.20	1.64±0.31*
Severe	32	31.25±5.98*#	85.69±5.39*#	1.98±0.37*#	29.98±7.05*#	25.59±3.04	1.33±0.28*#
F		18.671	24.402	11.681	28.153	2.156	39.942
P value		<0.001	<0.001	<0.001	<0.001	0.120	<0.001

AP: acute pancreatitis; ALB: albumin; GNRI: geriatric nutritional risk index; TRF: transferrin. Compared with mild group, *P<0.05; compared with moderately severe group, #P<0.05.

2.3 老年 AP 患者入院时营养状态与免疫功能的相关性

Pearson 相关系数分析显示,老年 AP 患者 ALB、GNRI、TRF 与 $CD4^+$、$CD4^+/CD8^+$均呈显著正相关(P<0.05;表 3)。

表 3 老年 AP 患者入院时营养状态与免疫功能的相关性分析

Table 3 Correlation analysis between nutritional status and immune function of elderly AP patients at admission (r)

Item	ALB	GNRI	TRF
$CD4^+$(%)	0.567*	0.622*	0.498*
$CD4^+/CD8^+$	0.611*	0.671*	0.567*

AP: acute pancreatitis; ALB: albumin; GNRI: geriatric nutritional risk index; TRF: transferrin. *P<0.001.

2.4 不同预后老年 AP 患者入院时营养状态、免疫功能比较

入院时死亡组 ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$均显著低于生存组,差异均有统计学意义(均 P<0.05;表 4)。

2.5 入院时营养状态及免疫功能对老年 AP 患者死亡风险的预测价值

ROC 曲线显示,入院时 ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$均对预测老年 AP 患者死亡风险具有统计学意义(P<0.05),最佳截断点分别为 31.97 g/L、88.25、2.08 g/L、36.37%、1.59,5 项指标联合预测的 ROC 曲线下面积(area under curve, AUC)值高达 0.947(表 5,图 1)。

表 4 不同预后老年 AP 患者入院时营养状态、免疫功能比较

Table 4 Comparison of nutritional status and immune function at admission between elderly AP patients with different prognosis ($\bar{x}\pm s$)

Group	n	ALB(g/L)	GNRI	TRF(g/L)	$CD4^+$(%)	$CD8^+$(%)	$CD4^+/CD8^+$
Death	12	28.75±5.99	85.95±4.90	1.93±0.39	29.84±7.75	26.32±3.11	1.26±0.25
Survival	110	36.94±5.23	90.45±5.31	2.28±0.39	38.47±6.48	24.77±2.98	1.74±0.27
t		5.074	2.809	2.936	4.299	1.704	5.933
P value		<0.001	0.006	0.004	<0.001	0.091	<0.001

AP: acute pancreatitis; ALB: albumin; GNRI: geriatric nutritional risk index; TRF: transferrin.

表5 入院时营养状态及免疫功能对老年AP患者死亡风险的预测价值

Table 5 Predictive value of nutritional status and immune function at admission on death of elderly AP patients

Indicator	Cut-off value	Sensitivity(%)	Specificity(%)	AUC	95%*CI*	*P* value
ALB	31.97 g/L	75.00	82.73	0.843	0.717-0.969	<0.001
GNRI	88.25	75.00	68.18	0.741	0.597-0.884	<0.001
TRF	2.08 g/L	75.00	68.18	0.732	0.594-0.870	<0.001
$CD4^+$	36.37%	83.33	62.73	0.796	0.669-0.923	<0.001
$CD4^+/CD8^+$	1.59	100.00	70.00	0.911	0.848-0.974	<0.001
Combination of five indicators	-	66.67	86.36	0.947	0.906-0.998	<0.001

AP: acute pancreatitis; AUC: area under curve; ALB: albumin; GNRI: geriatric nutritional risk index; TRF: transferrin. -: no datum.

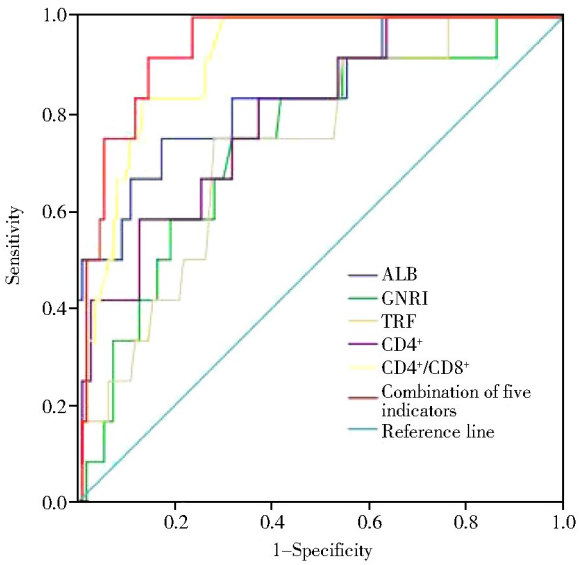

图1 入院时ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$预测老年AP患者死亡风险的ROC曲线

Figure 1 ROC curves of ALB, GNRI, TRF, $CD4^+$ and $CD4^+/CD8^+$ at admission for predicting death of elderly AP patients

ALB: albumin; GNRI: geriatric nutritional risk index; TRF: transferrin; AP: acute pancreatitis; ROC: receiver operating characteristic.

3 讨 论

老年AP患者病死率高于青中年患者,入院早期评估病情并预测预后,对指导临床治疗有利[7]。血清ALB、TRF作为评估机体营养状态的常用指标,在机体营养不良时显著下降[8]。GNRI是近年评估老年营养状态的常用工具,结合了老年人理想与实际体质量及ALB,可综合评估营养不良风险,也被用于预测老年癌症、心力衰竭等重症疾病的预后[9]。本研究结果显示,老年AP重症患者入院时血清ALB、GNRI、TRF水平均低于轻症及中度重症患者,而中度重症患者低于轻症,提示入院时ALB、GNRI、TRF越低者,病情越严重,即营养状态可能参与老年AP病情进展。分析原因可能为营养状态与肠道功能直接相关,营养状态越差者肠黏膜屏障损伤越严重,肠源性感染风险升高,从而促进病情进展[10]。需要注重的是,AP患者入院治疗常需持续胃肠减压伴禁食[11],可进一步影响营养状态,是临床易忽视之处。因此,老年AP患者入院后应注意对营养状态的监测及干预,必要时联合营养师制定个性化营养干预方案,以减轻营养不良对疾病进展的影响。

免疫功能紊乱在AP患者中常见,有报道指出,AP患者的T淋巴细胞亚群较健康人群减少,且$CD4^+/CD8^+$平衡向$CD8^+$漂移,导致免疫抑制,增加继发感染风险,使患者病死率升高[12]。也有研究发现,AP患者的全身应激及炎症反应可诱导自身过度自噬反应,导致T淋巴细胞凋亡,诱导平衡$CD4^+/CD8^+$紊乱,引起病情加重[13,14]。本研究中,不同严重程度的老年AP患者入院时$CD4^+$、$CD4^+/CD8^+$具有显著差异,且越严重者$CD4^+$、$CD4^+/CD8^+$越低,提示$CD4^+/CD8^+$向$CD8^+$漂移的这种免疫抑制可能参与了老年AP的病情进展,免疫抑制更严重者,更易发生器官功能衰竭,与上述报道结果相似。不仅如此,本研究还发现,老年AP患者ALB、GNRI、TRF与$CD4^+$、$CD4^+/CD8^+$均呈显著正相关,提示老年AP患者营养不良与免疫抑制密切相关,两者相互影响。考虑原因为营养不良导致机体免疫力低下,更易发生免疫功能紊乱,而免疫抑制可加剧炎症及应激反应,引起代谢障碍,影响ALB、TRF等蛋白的生成,从而诱导营养不良[15,16]。

除了病情严重程度外,本研究也对老年AP患者预后展开分析。122例患者入院28 d内死亡12例(9.84%),死亡组入院时ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$均低于生存组,提示入院时营养状态差及免疫功能受损严重者死亡风险也较高,可能与营养不良及免疫抑制增加了感染、器官功能损伤风险,加剧病情进展,使患者死亡风险升高有关[17,18]。ROC曲线分析也显示,ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$单项检测均能预测老年AP患者死亡风险,表明上述入院时的营养状态及免疫功能

指标可辅助预测患者预后,对指导临床治疗有利。此外,值得注意的是,本研究结果显示,5 项指标联合预测的 AUC 值最高,提示入院时综合评估营养状态与免疫功能,对预测预后更有利。分析其原因可能为营养不良与免疫抑制相互影响,并协同促进了感染及各组织器官损伤的发生,使死亡风险升高[19,20]。

综上,ALB、GNRI、TRF、$CD4^+$、$CD4^+/CD8^+$的下降可能促进老年 AP 患者的病情进展,入院时上述指标越低者预后死亡风险越高,5 项联合检测对预测死亡风险更有利。

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