炎症反应相关评分系统在判断胰腺癌预后中的意义

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摘要：胰腺癌预后极差，炎症反应与肿瘤发生发展相关，影响胰腺癌预后。基于临床常规化验指标的炎症相关评分系统可以预测胰腺癌患者预后，具有简单、易用及方便获取的特点，可兼顾胰腺癌患者的炎症、免疫、营养等特征。本文就文献中常用于判断胰腺癌预后的炎症相关评分系统进行综述。

关键词：胰腺癌；炎症；预后
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Inflammatory response related scoring systems in predicting the prognosis of patients with pancreatic adenocarcinoma

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Abstract: Pancreatic adenocarcinoma is characterized by poor prognosis, which also associates with systemic inflammation response. It has been confirmed that the prognosis can be evaluated through inflammatory response related scoring systems based on routine laboratory test items. These scoring system can be obtained easily and conveniently, and it can also reflect tumor characteristics and host systemic inflammatory. In this paper, we will review the published scoring systems that related to pancreatic adenocarcinoma.
Keywords: pancreatic adenocarcinoma; inflammation; prognosis

胰腺癌是消化系统常见恶性肿瘤之一，是我国第7大癌症相关致死疾病[1-3]。近年来，胰腺癌的综合治疗水平明显提高，但预后依然较差，5年生存率 < 7%[4]。机体炎症与恶性肿瘤发生发展密切相关，影响肿瘤预后[5]。多种基于临床化验指标的评分系统可以反映机体炎症反应情况，与恶性肿瘤预后相关。本文就这些评分系统在判断胰腺癌预后中的意义进行综述。

1 中性粒细胞/淋巴细胞比值(neutrophil-to-lymphocyte ratio，NLR)

NLR为中性粒细胞与淋巴细胞计数的比值，可反映二者的相对变化，能够在一定程度上体现肿瘤炎症反应与抗肿瘤免疫的平衡。中性粒细胞是机体主要的炎症细胞之一，在肿瘤发生发展中发挥重要作用，其生成的配体可促进肿瘤增殖浸润[6-7]。此外，中性粒细胞通过释放促血管生成因子促进肿瘤血管生成，通过释放炎症介质促进肿瘤微环境的形成[8-9]。而肿瘤所产生的细胞因子亦可以刺激中性粒细胞升高[10]。淋巴细胞是抗肿瘤免疫的主要组分，淋巴细胞的减少提示淋巴细胞介导的抗肿瘤免疫反应降低，影响肿瘤患者的预后[11-12]。

NLR升高对于胰腺癌预后不良的预测作用在多项研究中得到证实，但各项研究采用的NLR截断值不尽相同，范围为2 ~ 5[13-16]。Garcea等[16]分析了74例行根治手术的胰腺癌患者，以5为术前NLR截断值，结果显示NLR > 5是胰腺癌术后无病生存预后不良的独立预测指标。Ben等[14]以2为NLR截断值，分析了来自两个中心的381例行胰腺癌根治术的患者，结果显示术前NLR > 2是判断胰腺癌根治术后生存不良的独立预测指标。An等[13]分析了95例无法行手术切除的进展期胰腺癌患者，发现NLR升高(> 5)的患者中位生存时间较NLR正常的患者明显缩短。Cheng等[15]对NLR在判断胰腺癌预后中的意义进行了Meta分析，共纳入来自9个队列的2 035例胰腺癌患者，结果显示NLR升高可以提示胰腺癌预后不良。NLR值通过临床常用的血常规化验即可获得，具有简单、方便、易于在临床中应用等特点，可作为胰腺癌治疗疗效监测及预后判断的有效工具。

2 血小板/淋巴细胞比值(platelet-to-lymphocyte ratio，PLR)

恶性肿瘤患者常呈现反应性血小板增多，尤其是进展期肿瘤[17-18]。血小板在肿瘤微血管内聚集和脱颗粒，释放细胞因子促进肿瘤细胞生长和播散[19]。而肿瘤细胞可以产生血小板生成样激素以及炎症介质，刺激血小板增殖[20]。肿瘤患者常呈现为高凝状态，肿瘤细胞与血小板相互作用形成血小板–肿瘤细胞栓子复合体，在肿瘤血行转移中发挥重要作用[21]。此外，肿瘤细胞诱导血小板聚集，可避免

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肿瘤细胞受主要组织相容性复合物识别，实现免疫逃逸[22]。肿瘤患者血小板升高提示严重的炎症反应，影响肿瘤预后。

PLR是血小板和淋巴细胞的比值，可以反映二者的相对变化，多数研究按照PLR < 150、150 ~ 300及> 300进行分层预后分析。但其在胰腺癌的预后预测中的意义还存在争议。Shirai等[23]分析了131例行胰腺癌根治术的患者，以150为PLR的截断值，结果显示术前PLR是胰腺癌术后无病生存及整体生存的独立预测因素，且可以指导术后治疗。Jamieson等[24]分析了135例胰腺癌根治术患者，结果显示，PLR > 150组患者生存期较PLA < 150组患者短，但差异无统计学意义。此外，尚无关于PLR与胰腺癌预后相关的Meta分析。PLR在胰腺癌预后预测中的应用还需要更多的多中心、大样本研究证据支持。

3 淋巴细胞/单核细胞比值(lymphocyte to monocyte ratio，LMR)

LMR为淋巴细胞计数与单核细胞计数的比值。单核细胞可为肿瘤细胞发生发展提供所需营养[25]。肿瘤微环境中的单核细胞可表达T细胞共抑制配体B7-H1，促进调节性T细胞增殖，抑制抗肿瘤免疫[26]。聚集在肿瘤组织中的单核细胞可以进化为巨噬细胞，与肿瘤细胞相互作用，产生细胞因子及炎症趋化因子，促进肿瘤发生发展[27]。淋巴细胞则如上所述，是机体抗肿瘤免疫的主要组分。Fujiwara等[28]分析了111例行胰腺癌根治术患者的预后因素，发现LMR是判断胰腺癌术后生存的独立指标。Stotz等[29]对474例胰腺癌患者进行单因素及多因素生存分析，显示LMR是独立预测因素。目前关于LMR在胰腺癌预后判断中作用的研究较少，在截断值及可信度方面尚无一致意见。

4 营养预后指数(nutritional prognostic index，NPI)

炎症反应被认为是肿瘤相关营养不良的原因之一[30]。肿瘤患者体内的炎性细胞因子增加，如IL-1、IL-6及TNF-α，这些细胞因子可以抑制白蛋白合成，促进脂肪消耗，造成肿瘤患者营养不良[31]。肿瘤患者术前的营养状态与术后并发症、肿瘤进展及预后相关[32-33]。

NPI计算公式：10 × 血清白蛋白(g/dl) + 0.005 × 淋巴细胞计数(/mm^2)。其中白蛋白是血浆蛋白的主要组分，维持胶体渗透压，其水平可以反映营养状态。淋巴细胞亦是机体免疫和营养状态的重要指标。研究中常用的NPI截断值为45，Kanda等[34]分析了268例胰腺癌切除术后患者，显示NPI < 45提示预后不良，且与术后胰漏相关。此外，营养不良可以导致体质量指数下降、免疫功能受损、对化疗不敏感及预后不良。Geng等[35]对321例行姑息治疗的进展期胰腺癌患者进行预后分析，结果显示NPI与全身炎症反应相关，可用于预测进展期胰腺癌的预后。

5 Glasgow预后评分(Glasgow prognostic score，GPS)

GPS是基于血清C反应蛋白(C-reactive protein，CRP)和白蛋白的炎症相关评分，具体评分方法：CRP > 1.0 mg/dl，且白蛋白 < 3.5 g/dl，则GPS为2；仅具有其中一项，则GPS为1；二者均正常则GPS为0[36-37]。CRP是临床上常用来观察全身炎症反应的化验指标，白蛋白亦可以反映炎症反应。多项研究显示GPS与胰腺癌预后相关。La Torre等[38]分析了101例胰腺癌切除术患者，结果显示术前GPS为0、1和2的患者的中位生存期分别为37.2个月、11.5个月及7.3个月，三者比较差异具有统计学意义，提示术前GPS与胰腺癌切除术后预后相关。对于无法根治性切除的进展期胰腺癌患者，Glen等[39]对187例行姑息手术的胰腺癌患者的预后因素进行了单因素和多因素分析，结果提示GPS是预测进展期胰腺癌患者预后的独立危险因素。

6 结语

传统的临床病理因素在临床中广泛用于肿瘤预后预测，但对于同期肿瘤的预后判断效能较差，且部分指标在术前无法获取，如病理分期、类型及分化程度。炎症相关的评分系统基于临床常规化验项目，兼顾炎症、免疫、营养等肿瘤相关特征，具有简单、易用、廉价的特点，且在术前或化疗前即可获取，可指导治疗并判断疗效。但部分评分系统在判定肿瘤预后方面尚存在争议，联合应用多个系统可以更加精确地判断肿瘤预后。

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