

· 临床研究 ·

NLR与SIRI术后与术前比值对经内镜逆行胰胆管造影术后急性胰腺炎的预测价值

赵子君, 朱颖婷, 缪林*

南京医科大学第二附属医院消化医学中心, 江苏 南京 210011

[摘要] 目的: 评估并对比胆总管结石患者术前中性粒细胞与淋巴细胞比值(neutrophil to lymphocyte ratio, NLR)、术后NLR、术后与术前NLR比值、术前全身炎症反应指数(systemic inflammatory response index, SIRI)、术后SIRI、术后与术前SIRI比值对内镜下逆行胰胆管造影术(endoscopic retrograde cholangiopancreatography, ERCP)后并发急性胰腺炎(post-ERCP pancreatitis, PEP)的预测价值。方法: 收集549例行ERCP的胆总管结石患者术前及术后血常规、ERCP术中操作、患者基本信息及既往病史等资料, 分为PEP组($n=43$)和无PEP组($n=506$), 比较两组术前、术后NLR、SIRI水平差异, 计算术后与术前NLR及SIRI比值, 比较两组间差异, 并通过受试者工作特征(receiver operating characteristic, ROC)曲线分析各指标对PEP的预测价值。结果: PEP组与无PEP组相比, 术前NLR、术后NLR、术前SIRI、术后SIRI, 术后/术前NLR、术后/术前SIRI差异均有统计学意义($P < 0.05$), 其中ERCP术后/术前NLR、术后/术前SIRI指标ROC曲线下面积均高于0.800, 术后/术前SIRI较其他指标具有更高的灵敏度(95.3%)和特异度(70.2%)。结论: 术后/术前NLR比值、术后/术前SIRI比值对于预测PEP具有参考价值。

[关键词] 急性胰腺炎; 经内镜逆行胰胆管造影术; 中性粒细胞与淋巴细胞比值; 全身炎症反应指数

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Predictive value of postoperative to preoperative ratios of NLR and SIRI for acute pancreatitis after endoscopic retrograde cholangiopancreatography

ZHAO Zijun, ZHU Yingting, MIAO Lin*

Department of Gastroenterology, the Second Affiliated Hospital of Nanjing Medical University, Nanjing 210011, China

[Abstract] **Objective:** To evaluate and compare the predictive values of preoperative neutrophil to lymphocyte ratio (NLR), postoperative NLR, postoperative/preoperative NLR ratio, preoperative systemic inflammatory response index (SIRI), postoperative SIRI, and postoperative/preoperative SIRI ratio for post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) in patients with choledocholithiasis. **Method:** Clinical data including preoperative and postoperative blood routine results, intraoperative ERCP conditions, basic information and medical history of 549 patients with choledocholithiasis undergoing ERCP were collected. The patients were divided into the PEP group ($n=43$) and the non-PEP group ($n=506$). The levels of NLR and SIRI before and after ERCP were compared between the two groups, the postoperative to preoperative ratios of NLR and SIRI were calculated, the differences in levels of these indicators between the two groups were compared, and the receiver operating characteristic (ROC) curve was used to analyze the predictive value of each indicator for PEP. **Results:** Significant differences were observed between the PEP group and the non-PEP group in preoperative NLR, postoperative NLR, preoperative SIRI, postoperative SIRI, postoperative/preoperative NLR ratio and postoperative/preoperative SIRI ratio (all $P < 0.05$). The areas under the ROC curve (AUC) of postoperative/preoperative NLR ratio and postoperative/preoperative SIRI ratio were both above 0.800, and the postoperative/preoperative SIRI ratio had a higher sensitivity of 95.3% and specificity of 70.2% than other indicators. **Conclusions:** The postoperative/preoperative NLR ratio and postoperative/preoperative SIRI ratio have reference value for predicting PEP in choledocholithiasis patients undergoing ERCP.

[Key words] acute pancreatitis; endoscopic retrograde cholangiopancreatography; neutrophil to lymphocyte ratio; systemic inflammation response index

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*通信作者(Corresponding author), E-mail: linmiao@njmu.edu.cn (ORCID: 0000-0003-0248-2544)

胆石症是全球重大的公共卫生问题,大多数胆石症患者终生无症状,但其中10%~25%的患者可能会出现胆道疼痛或并发症,大多与结石迁移至胆总管有关。经内镜逆行胰胆管造影(endoscopic retrograde cholangiopancreatography, ERCP)指在内镜下经十二指肠乳头插管注入造影剂,以逆行显示胰管及胆管结构的方法,可用于胆总管结石的诊断,同时也是目前胆总管结石患者主要的治疗手段之一。ESGE指南建议,对于所有胆总管结石患者,无论有无症状,只要患者可耐受,均推荐取石治疗^[1]。ERCP相关的术后并发症中,ERCP术后胰腺炎(post-ERCP pancreatitis, PEP)是ERCP术后最常见也是最严重的并发症之一,病死率为0.1%~0.7%,延长了患者的住院时间,加重了患者的经济负担,在美国由此造成的经济损失年度超过1.5亿美元^[2-3],因此,致力于早期识别和预测PEP对改善治疗效果非常重要,为指导ERCP术后用药及治疗,亟需新型预测因子用于PEP早期预测。中性粒细胞与淋巴细胞比值(neutrophil to lymphocyte ratio, NLR)及全身炎症反应指数(systemic inflammatory response index, SIRI)作为新型炎症复合标志物,可有效反映全身炎症状态,已被证实在急性胰腺炎及PEP早期预测及识别中具有一定价值^[4-7],但尚无研究探讨NLR及SIRI术后与术前的变化趋势对于PEP的预测价值。本研究通过回顾性收集并分析行ERCP治疗前后患者血常规变化特点,首次探讨NLR及SIRI在ERCP术后与术前比值在PEP预测中的价值。

1 对象和方法

1.1 对象

本研究收集2021年1月1日—2023年12月31日在南京医科大学第二附属医院接受ERCP治疗的549例胆总管结石患者,其中接受ERCP手术后发生PEP患者43例。纳入标准:①年龄 ≥ 18 岁;②术前影像学及实验学检查证实为胆总管结石患者。排除标准:①术前影像学及实验学检查证实合并胰腺炎或淀粉酶升高;②合并胰腺外伤及手术史;③合并血液系统恶性肿瘤或其他系统恶性肿瘤致骨髓受累;④未成功取石;⑤关键临床数据缺失影响后续研究。所有患者术前均签署相关治疗同意书,本研究经南京医科大学第二附属医院医学伦理委员会批准(审查批号:2025-KY-473-01)。

1.2 方法

1.2.1 一般资料收集

收集的基线资料包括:①患者基本资料,包括

患者年龄、性别、心脑血管病史、糖尿病病史、恶性肿瘤病史、既往ERCP手术史;②实验室检查数据,包括ERCP术前24 h及术后3 h全血细胞计数(中性粒细胞计数、淋巴细胞计数、单核细胞计数)、术后淀粉酶;③影像学数据,包括胆总管结石直径、是否合并多发胆管结石;④ERCP术中常见操作包括内镜下乳头球囊扩张术(endoscopic papillary balloon dilation, EPBD)、内镜下鼻胆管引流术(endoscopic nasobiliary drainage, ENBD)、内镜下乳头括约肌切开术(endoscopic sphincterotomy, EST)、胰管支架置入、麻醉方式。NLR=中性粒细胞计数/淋巴细胞计数;SIRI=中性粒细胞计数 \times 单核细胞计数/淋巴细胞计数。

1.2.2 诊治流程

所有患者入院后24 h内采集术前血常规,完善腹部CT或者MRCP,并接受抗感染、抑酸护胃、保肝利胆等对症治疗。术前禁食8~12 h,完善麻醉评估,告知患者手术相关注意事项,所有患者均于手术前签署相关知情同意书。术后告知患者平卧,注意监测患者生命体征、鼻胆管引流情况、腹部症状,术后患者常规接受抑酸、抑酶、补液等规范治疗,术后3 h采血检查血常规、淀粉酶。若患者术后24 h内实验学检查指标无异常,未发生恶心、呕吐、新发腹痛或原有腹痛加重等症状,则准予进食少量流食并予择期出院。

1.2.3 诊断标准

根据急性胰腺炎定义和分类的亚特兰大国际共识^[8],PEP的诊断至少需满足以下3个标准中的2个:①腹痛符合急性胰腺炎特征(持续、严重的上腹部疼痛急性发作,通常放射至背部);②血清脂肪酶或淀粉酶活性较正常上限至少高3倍;③增强CT、磁共振成像或腹部超声具有急性胰腺炎的特征性表现。

1.3 统计学方法

使用SPSS 27.0软件进行数据处理。对所有定量数据进行正态性检验,符合正态分布的计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,组间比较采用独立样本 t 检验;不符合正态分布的计量资料以中位数(四分位数)[$M(P_{25}, P_{75})$]表示,采用非参数检验进行分析。 $P < 0.05$ 为差异有统计学意义。采用受试者工作特征(receiver operating characteristic, ROC)曲线分析各指标对PEP的预测效果,通过Youden指数确定最佳的诊断阈值。

2 结果

2.1 PEP组与无PEP组一般资料比较

ERCP术中是否行ENBD操作及胆总管结石直径

在PEP组及无PEP组间差异有统计学意义,其他一般资料在两组间差异均无统计学意义($P > 0.05$,表1)。

2.2 PEP组与无PEP组术前及术后NLR、SIRI比较

PEP组术前NLR、术前SIRI均低于无PEP组,组间比较差异具有统计学意义;PEP组术后NLR、术后SIRI、术后/术前NLR、术前SIRI指标高于无PEP组,组间比较差异有统计学意义。两组术前及术后NLR、SIRI指标及其比值见表2。

2.3 ERCP后发生胰腺炎相关指标ROC分析

通过分析,可得ERCP术后/术前NLR、术后/术前SIRI指标ROC曲线下面积(area under the curve, AUC)均高于0.800,其中术后/术前SIRI较其他指标具有更高的敏感度(95.3%)和特异度(70.2%)。术后/术前NLR最佳阈值为2.594,术后/术前SIRI最佳阈值为2.263(表3,图1)。

3 讨论

自1968年问世以来,ERCP已成为胆胰疾病的

重要诊治手段。尽管ERCP发展日趋成熟,但实际操作中与ERCP术后并发症相关的多种风险因素仍不可避免。PEP作为ERCP术后最常见及最严重的并发症之一,仍未得到理想的控制,本研究通过研究ERCP术前及术后NLR及SIRI变化特点对于PEP的预测价值,为预测PEP提供早期、高效、兼具敏感度及特异度的生物学标志物提供了参考,有助于加强PEP早期干预、改善PEP预后。

急性胰腺炎是一种多方面的炎症性疾病,其发生机制受到多种因素的影响,如胰蛋白酶激活、钙离子过载、炎症级联反应激活、肠道微生态环境失调、线粒体功能障碍^[9],PEP属于急性胰腺炎的一种,其发病机制被证实与胰腺中胰蛋白酶过度激活及炎症级联反应相关,在Akshintala等^[10]关于PEP发生机制的概述中,ERCP术中操作如十二指肠乳头插管、胰管支架置入、乳头括约肌切开术等均可造成胰管压力增高,进而诱发胰腺的炎症级联反应。基于急性胰腺炎及PEP的病理生理机制,若干

表1 PEP组与无PEP组一般资料组间比较

Table 1 Comparison of general data between the PEP group and the non-PEP group

Variable	PEP group(n=43)	Non-PEP group(n=506)	P
Age[years, $M(P_{25}, P_{75})$]	71.00(63.00, 77.00)	70.00(59.00, 80.00)	0.804
Male[n(%)]	22(51.2)	300(59.3)	0.299
Diabetes[n(%)]	8(18.6)	106(20.9)	0.716
Cardio-cerebrovascular disease[n(%)]	26(60.5)	270(53.4)	0.370
History of malignancy[n(%)]	4(9.3)	82(19.2)	0.232
History of previous ERCP[n(%)]	6(14.0)	134(26.5)	0.070
Diameter of common bile duct stone[mm, $M(P_{25}, P_{75})$]	6.00(5.00, 10.00)	8.00(5.00, 13.00)	0.028
Combined with multiple choledocholithiasis[n(%)]	22(51.2)	263(52.0)	0.918
Duodenal diverticulum[n(%)]	20(46.5)	187(37.0)	0.251
ENBD[n(%)]	39(90.7)	390(77.1)	0.038
EST[n(%)]	31(72.1)	323(63.8)	0.277
EPBD[n(%)]	32(74.4)	335(66.2)	0.272
Pancreatic duct stenting[n(%)]	10(22.3)	78(15.4)	0.178
Endotracheal anesthesia[n(%)]	8(18.6)	107(21.1)	0.694

表2 PEP组与无PEP组炎症复合标志物组间比较

Table 2 Comparison of inflammation composite markers between the PEP group and non-PEP group

Variable	PEP group(n=43)	Non-PEP group(n=506)	U	P
Preoperative NLR	2.20(1.51, 3.17)	4.02(2.23, 8.59)	5 840	<0.001
Postoperative NLR	11.17(7.02, 19.76)	8.70(5.68, 14.64)	8 033	0.004
Postoperative to preoperative NLR	4.89(2.99, 9.42)	2.11(1.06, 3.81)	3 970	<0.001
Preoperative SIRI	0.80(0.52, 1.21)	1.68(0.84, 4.12)	5 651	<0.001
Postoperative SIRI	3.74(2.38, 9.25)	2.62(1.14, 4.84)	7 479	<0.001
Postoperative to preoperative SIRI	4.27(2.86, 8.62)	1.33(0.60, 2.61)	3 148	<0.001

表3 炎症复合标志物的ROC分析

Table 3 The ROC analysis of inflammation composite markers

Variable	AUC(95%CI)	Cut-off value	Sensitivity	Specificity
Preoperative NLR	0.731(0.667-0.794)	0.825	0.977	0.002
Postoperative NLR	0.631(0.552-0.710)	8.405	0.721	0.489
Preoperative SIRI	0.741(0.681-0.803)	0.289	0.977	0.016
Postoperative SIRI	0.656(0.584-0.728)	1.915	0.907	0.396
Postoperative to preoperative NLR	0.817(0.762-0.872)	2.594	0.930	0.584
Postoperative to preoperative SIRI	0.855(0.809-0.901)	2.263	0.953	0.702

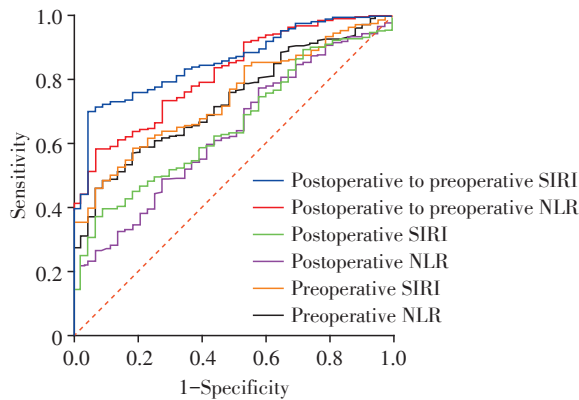


图1 炎症复合标志物ROC曲线

Figure 1 The ROC curve of inflammation composite markers

生物标志物可用于疾病预测及严重程度分级,例如炎症因子及趋化因子及胰腺特异性标志物等^[11],但由于临床实践中条件有限,上述因子难以在实际中获得;同时,在血液系统中多种细胞参与急性胰腺炎及PEP炎症发生与发展的过程,NLR、SIRI被证实是评估性炎症状态及感染水平的重要参数,在全身炎症性疾病中,相比单一类型的血细胞计数指标具有更好的预测性能^[12-16],同时又极易获取,因此有望成为PEP预测的初筛指标。

本研究通过回顾性收集ERCP术后与术前全血细胞计数并分析,探究NLR及SIRI在PEP预测中的临床应用价值。本研究发现,PEP组术前NLR、术前SIRI均低于无PEP组,而PEP组术后NLR、术后SIRI、术后/术前NLR、术前SIRI指标显著高于无PEP组,提示术后NLR及SIRI升高可能是由于PEP发生过程中伴随着炎症细胞的聚集及炎症因子的大量释放,这与胰腺炎炎症发展过程中多种炎症细胞迁移及聚集有关。中性粒细胞作为白细胞的主要亚型,在免疫反应及炎症反应中发挥重要作用,是第一批进入胰腺组织的白细胞,大量研究报告表明胰腺组织中中性粒细胞聚集是胰腺炎发展的重要因素^[17],胰腺炎发生发展过程中肠道菌群的变化

也会促进中性粒细胞亚群的扩展^[18]。淋巴细胞作为免疫细胞,参与机体炎症反应及免疫调节, Malheiro等^[19]在研究中发现循环淋巴细胞在胰腺炎中表现出衰竭趋势。术后SIRI相比术后NLR、术后/术前SIRI相比术后/术前NLR具有较好的预测性能,与其纳入了单核细胞计数有关。单核细胞在机体免疫中发挥重要作用, Manohar等^[20]发现其与胰腺炎炎症活动程度呈正相关。NLR及SIRI作为新型炎症复合标志物纳入中性粒细胞、单核细胞、淋巴细胞,反映了患者ERCP术前及术后机体炎症状态,既往研究提出无症状胆结石患者发生PEP风险高于有症状胆结石患者,这为解释本研究结果中术前炎症水平较低的患者更容易发生PEP提供了依据^[21]。同时,本研究发现,与单纯的术前及术后NLR及SIRI指标相比,术后与术前NLR及SIRI比值在PEP预测上具有更高的敏感度及特异度,术后/术前NLR的AUC为0.817,最佳阈值为2.594,敏感度及特异度分别为93.0%和58.4%。术后/术前SIRI的AUC为0.855,最佳阈值为2.263,敏感度及特异度分别为95.3%和70.2%,其预测性能远优于术后及术前单个时间点炎症标志物的预测性能,这是由于PEP的发展是一个动态的过程,个体的免疫功能和机体状态差异巨大,单纯的横向对比无法排除年龄、性别、基础病史、合并感染对于机体炎症反应的影响,而大量研究表明,炎症反应与许多常见基础疾病如糖尿病、冠心病、肥胖症等息息相关^[22-25]。

同时,本研究存在一定的局限性:①本研究为回顾性分析,纳入样本在时间范围及地域上存在一定局限性,可能在信息收集过程中存在选择偏倚、信息偏倚;②本研究为单中心分析,研究结果缺乏外部验证;③本研究主要探讨术前及术后3h炎症复合标志物对PEP的预测性能,未收集术后更长时间段的相关数据,对于PEP远期发生与发展变化曲线缺乏研究;④本研究由于样本量较少,未对PEP的严重程度分级,可能影响NLR及SIRI预测的灵敏度

和特异度。

综上所述,术后/术前NLR及术后/术前SIRI在PEP患者中显著升高,对于早期诊断及预防PEP具有一定的参考价值,尤其是术后/术前SIRI,其高灵敏度为PEP筛查提供了新型预测指标,同时具有易获取、经济成本低的特点。期待更多的研究将该指标纳入PEP的预测中,与其他指标联用或纳入前瞻性的分析,提高术后/术前NLR及术后/术前SIRI的实际临床应用价值。

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所有作者声明无利益冲突。

Conflict of Interests:

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ZHAO Zijun was responsible for data collection, data analysis and initial draft preparation; ZHU Yinting was responsible for creating charts and graphs; MIAO Lin was responsible for data supervision and manuscript revision.

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