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Hans汉斯

术前NLR、PLR对评估结直肠息肉病理级别的临床价值分析

王占军[1,2]，韩志伟[1]，李芃萌[1]，宣碧碧[1]，刘希双[2*]

[1]青岛大学医学院，山东 青岛
[2]青岛大学附属医院消化内科，山东 青岛

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摘 要

目的：分析术前NLR、PLR与结直肠息肉病理级别的相关性，评估其对判断结直肠息肉癌变的临床价值。方法：回顾性分析青岛大学附属医院5525例瘤变或癌变的结直肠息肉患者，根据病理级别分为低级别瘤变组、高级别瘤变组、癌变组，分别3990例、451例和1084例，对各组NLR、PLR进行统计学分析。结果：不同病例组间NLR ($H = 2243.238$, $P < 0.01$)、PLR ($H = 92007.94$, $P < 0.01$)差异有统计学意义。各组NLR中位数随病理级别的升高依次增大(1.76、2.56、2.88)，癌变组明显高于其他组；各组PLR中位数随病理级别的升高依次增大(119.83、155.65、176.02)，癌变组明显高于其他组。*Spearman*秩相关分析显示不同病理级别和NLR、PLR间存在正相关性($P < 0.01$)。在分层统计时，三组NLR均主要集中在0~4区段(85.4%、61.0%、59.6%)；PLR主要集中在100~200区段(54.2%、50.6%、44.4%)。结论：NLR、PLR可以作为结直肠息肉病理级别升高的预测指标，对结直肠息肉发生高级别瘤变或癌变有一定的警示作用，但对高级别瘤变和癌变的鉴别诊断的价值、与息肉病理级别的计量对应关系有待进一步研究。

关键词

结直肠息肉，中性粒细胞与淋巴细胞比值，血小板与淋巴细胞比值，瘤变，癌变

Clinical Value Analysis of Preoperative NLR and PLR in Evaluating the Pathological Grade of Colorectal Polyps

Zhanjun Wang[1,2], Zhiwei Han[1], Pengmeng Li[1], Bibi Xuan[1], Xishuang Liu[2]

[1]Medical College of Qingdao University, Qingdao Shandong
[2]Department of Gastroenterology, The Affiliated Hospital of Qingdao University, Qingdao Shandong

[*]通讯作者 Email: 17854239367@163.com

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Abstract

Objective: To analyze the correlation between preoperative NLR, PLR and the pathological grade of colorectal polyp, and to evaluate their clinical value in the judgment of colorectal polyp canceration. Methods: A total of 5525 cases of colorectal polyps with neoplasia or canceration were retrospectively analyzed in The Affiliated Hospital of Qingdao University. According to pathological grade, they were divided into low grade tumor group, high grade tumor group and canceration group, 3990 cases, 451 cases and 1084 cases, respectively. NLR and PLR were statistically analyzed in each group. Results: There were significant differences in NLR (H = 2243.238, P < 0.01) and PLR (H = 92007.94, P < 0.01) among different case groups. The median NLR of each group increased with the increase of pathological grade (1.76, 2.56, 2.88), and the cancer group was significantly higher than that of other groups; the median PLR of each group increased with the increase of pathological grade (119.83, 155.65 and 176.02), and the cancer group was significantly higher than other groups. Spearman rank correlation analysis showed that there was a positive correlation between different pathological grades and NLR and PLR (P < 0.01). In stratified statistics, the NLR of the three groups was mainly concentrated in the 0~4 section (85.4%, 61.0%, 59.6%); PLR is mainly concentrated in 100~200 sections (54.2%, 50.6%, 44.4%). Conclusion: NLR and PLR can be used as predictors of pathological grade elevation of colorectal polyps, suggesting high-grade neoplasia or canceration of colorectal polyps to some extent. However, the value of differential diagnosis of high-grade neoplasia and canceration as well as the quantitative relationship between them and pathological grade of polyps need to be further studied.

Keywords

Colorectum Polyp, Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio, Neoplasia, Canceration

1. 引言

结直肠癌是最常见的恶性肿瘤之一，2020 年其发病率在全球居于恶性肿瘤第 3 位(10.0%)，死亡率高居第 2 位(9.4%)，是占全球发病和死亡首位的消化系统恶性肿瘤[1]。对于结直肠癌的预后，I 期结直肠癌患者预后较好，5 年生存率超过 91%，IV 期结直肠癌患者即使手术切除，5 年生存率仅 12% [2]，因此对早期结直肠癌的治疗获益更大，做好结直肠癌的早期筛查对人们生活质量的提高尤为重要。近来研究表明中性粒细胞与淋巴细胞比值**(Neutrophil to lymphocyte ratio, NLR)**、血小板与淋巴细胞比值**(Platelet-lymphocyte ratio, PLR)**可作为炎症、心血管系统疾病和恶性肿瘤新的炎症标志物，用于疾病的诊断及预后评估[3] [4] [5]。常用于疾病预后的监测，是较为稳定的炎症状态反应指标，有容易获取、医疗资源消耗低等优势。虽已有少量研究认为 NRL、PLR 可能是结直肠癌不同阶段诊断和早期识别的有用标志物[5]，但对结直肠癌与其相关性仍没有定论，为了进一步探讨 NLR、PLR 与结直肠息肉癌变的关系，评估其对提示结直肠息肉癌变的临床价值，本研究选取了青岛大学附属医院的部分病例资料，分析了结直肠息肉术前 NLR、PLR 与结直肠息肉病理级别的相关性。

2. 一般资料

2.1. 研究对象

选取青岛大学附属医院2013-05-01至2020-08-31期间收治的5525例瘤变或癌变的结直肠息肉患者，所有患者均接受结直肠镜检查并获取病理组织学结果，均无急性和化脓性感染、急性大出血、急性溶血、各种中毒、组织损伤、恶性肿瘤、血液病、自身免疫性疾病、缺铁性贫血、脾切除术、血液病等疾病，根据病理级别将以上病例分为低级别瘤变组、高级别瘤变组、癌变组，低级别瘤变组3990例，其中男性2639例，女性1351例，年龄(62.88 ± 10.78)岁；高级别瘤变组451例，其中男性328例，女性123例，年龄(64.75 ± 10.04)岁；癌变组1084例，其中男性712例，女性372例，年龄(65.78 ± 11.34)岁。

2.2. 观察指标

记录各病例术(息肉切除术或ESD/EMR)前的血常规结果，包括中性粒细胞计数、血小板计数、淋巴细胞计数，计算中性粒细胞与淋巴细胞比值(NLR)和血小板与淋巴细胞比值(PLR)。

2.3. 统计方法

运用*SPSS25.0*对各组病例进行统计学分析，计量资料以$\bar{X} \pm S$和中位数(*M*)表示；各病例组间的比较采用多样本的*K-W*检验(*Kruskal-Wallis test*)，两两比较时采用*Bonferroni*法调整显著性($P < 0.0167$)；NLR、PLR与不同病理组间相关性分析采用*Spearman*秩相关分析；对NLR、PLR资料进行分层统计分析，采用*K-W*检验($P < 0.05$)，两两比较时采用*Bonferroni*法调整显著性($P < 0.0167$)。检验水准：$\alpha = 0.05$。

3. 结果

3.1. 各病理组基本情况(n为各组病例数)

各病例组经过*K-S*检验，低级别瘤变组NLR ($Z = 0.298$, $P < 0.01$) PLR ($Z = 0.203$, $P < 0.01$)；高级别瘤变组NLR ($Z = 0.243$, $P < 0.01$) PLR ($Z = 0.200$, $P < 0.01$)；癌变组NLR ($Z = 0.225$, $P < 0.01$) PLR ($Z = 0.145$, $P < 0.01$)。各组样本$P < 0.05$，故各组NLR、PLR均不符合正态分布。

不同病理组间在NLR、PLR的比较上差异有统计学意义($P < 0.05$)。在NLR的统计分析中，各组中位数随病理级别的升高依次增大(1.76、2.56、2.88)，癌变组中位数明显高于其他组，癌变组平均数明显高于低级别瘤变组(6.03 *vs* 3.02)，并且任两组间差异均有统计学意义($P < 0.01$)。在PLR的统计分析中，各组PLR中位数随病理级别的升高依次增大(119.83、155.65、176.02)，癌变组中位数明显高于其他组，癌变组平均数明显高于其他组(217.65 *vs* 146.36、207.78)，并且任两组间差异均有统计学意义($P < 0.01$)，详见表1。

Table 1. Basic information of three groups of samples
表1. 三组NLR、PLR的比较

项目	*n*	NLR		PLR	
		$\bar{X} \pm S$	*M*	$\bar{X} \pm S$	*M*
低级别瘤变组	3990	3.02 ± 4.24	1.76	146.36 ± 116.37	119.83
高级别瘤变组	451	6.13 ± 7.91	2.56	207.78 ± 167.28	155.65
癌变组	1084	6.03 ± 7.31	2.88	217.65 ± 153.26	170.02
H		2243.24		92007.94	
P		<0.01		<0.01	

3.2. NLR、PLR 之间秩相关性分析

对所有病理组的 NLR、PLR 分别进行 *Spearman* 秩相关分析显示不同病理级别和 NLR 间存在正相关性($r = 0.262$, $P < 0.01$)，不同病理级别和 PLR 间存在正相关性($r = 0.288$, $P < 0.01$)，NLR 与 PLR 间存在正相关性($r = 0.705$, $P < 0.01$)，详见表 2。

Table 2. Correlation analysis of NLR and PLR between different pathological groups
表 2. 不同病理组间间 NLR、PLR 的相关性分析

指标	组别		NLR		PLR	
	r 值	*P* 值	*r* 值	*P* 值	*r* 值	*P* 值
组别	-	-	0.262	<0.01	0.288	<0.01
NLR	0.262	<0.01	-	-	0.705	<0.01
PLR	0.288	<0.01	0.705	<0.01	-	-

3.3. NLR、PL R 分层的统计学分析

依 NLR 数值的大小分为<4、4~8、8~12、12~16、≥16 共 5 个区段，各病理组均主要分布在 0~4 区段内(85.4%、61.0%、59.6%)，虽然三组间、低级别瘤变组与高级别瘤变组间($H = -700.33$, $P < 0.01$)差异有统计学意义，但低级别瘤变组与癌变组间($H = -733.37$, $P < 0.01$)、高级别瘤变组与癌变组间($H = -33.05$, $P = 0.608$)差异均无统计学意义。详见表 3。

依 PLR 数值大小分为<100、100~200、200~300、300~400、≥400 共 5 个区段，对三组 NLR、PLR 进行分层后统计分析，各病理组均主要分布在 100~200 区段(54.2%、50.6%、44.4%)，但在 PLR 的分布上差异有统计学意义($P < 0.05$)，且任两组间差异仍有统计学意义($P < 0.01$)。详见表 4。

Table 3. Stratified statistical analysis of NLR (%)
表 3. NLR 的分层统计学分析 例(%)

区段	低级别瘤变组	高级别瘤变组	癌变组	*H*	*P*
<4	3406 (85.4)	275 (61.0)	646 (59.6)		
4~8	299 (7.5)	70 (15.5)	175 (16.1)		
8~12	118 (3.0)	34 (7.5)	96 (8.9)	440.33	<0.01
12~16	81 (2.0)	25 (5.5)	67 (6.2)		
≥16	86 (2.2)	47 (10.4)	100 (9.2)		

Table 4. Stratified statistical analysis of PLR (%)
表 4. PLR 的分层统计学分析 例(%)

区段	低级别瘤变组	高级别瘤变组	癌变组	*H*	*P*
<100	1248 (31.3)	76 (16.9)	151 (13.9)		
100~200	2161 (54.2)	228 (50.6)	481 (44.4)		
200~300	367 (9.2)	60 (13.3)	243 (22.4)	2719.54	<0.01
300~400	99 (2.5)	46 (10.2)	107 (9.9)		
≥400	115 (2.9)	41 (9.1)	102 (9.4)		

4. 讨论

结合国内外报道，炎症反应在癌症的发展和进展中起着重要作用[6] [7] [8]，炎症明显有助于许多癌症的发展[9] [10]，已被列为癌症的标志[11]，其中炎性细胞因子和趋化因子可由肿瘤和相关宿主细胞(白细胞)产生，并导致恶性进展[12]，炎症发生后，中性粒细胞和血小板升高，淋巴细胞较少，但他们容易受到机体状态的影响，如脱水等。中性粒细胞作为一种炎症细胞，通过抑制免疫细胞如淋巴细胞、活化的 T 细胞和自然杀伤细胞的溶细胞活性来抑制免疫系统[13] [14]。另外，淋巴细胞的重要性在多项研究中得到了强调，在这些研究中，肿瘤中淋巴细胞浸润的增加与癌症患者对细胞毒性治疗的更好反应和预后有关[15] [16] [17]。此外，PLR 在多种不同炎症状态中的意义均有报道[18]。

不同病理级别和 NLR 间存在正相关性，并且随病理级别的升高中位数依次增大，癌变组 NLR 明显高于其他组；在各分层 NLR 的比较中，各病例组 NLR 均主要集中在 0~4 区段(85.4%、61.0%、59.6%)，且高级别瘤变组与癌变组间差异无统计学意义。结合国外研究，中性粒细胞与淋巴细胞比值(NLR)已被证明与多种恶性肿瘤存在相关，NLR 升高被认为是各种癌症的不良预后指标[19]。在许多实体瘤中，高 NLR 与不利的 OS (Overall survival)相关[20]。此外，中性粒细胞与淋巴细胞比率(NLR)被发现与心血管和神经血管疾病患者的不良事件相关[21] [22]，Wang Lu 等人的一项回顾性研究表明，较高的可预测急性缺血性卒中患者的短期不良结局[23]。因此，NLR 可以认为是结直肠息肉瘤变或癌变的危险因素，但对高级别瘤变和癌变的鉴别诊断价值不大，并且反映结直肠息肉发生瘤变或癌变的临界值有待进一步研究，两者的计量对应关系暂不明显。

不同病理级别和 PLR 间存在正相关性，并且随病理级别的升高中位数依次增大，癌变组 PLR 明显高于其他组；在各分层 PLR 的分布上各病例组 PLR 均主要集中在 100~200 区段(54.2%、50.6%、44.4%)，但任两组间差异仍有统计学意义($P < 0.01$)。关于血小板与淋巴细胞比值(PLR)，在包括胃癌在内的多种肿瘤患者中，高 PLR 与肿瘤侵袭性相关[24] [25] [26] [27]。部分研究表明，结合以上两者根据 NLR-PLR 评分的低成本分层可能是预测晚期胃癌患者肿瘤反应和预后的一种有前景的方法[28]，因此，PLR 可以认为是结直肠息肉瘤变或癌变的危险因素，但对高级别瘤变和癌变的鉴别诊断价值不大。目前对 NLR 与结直肠息肉癌变的研究较少，有待更多的临床证据验证其临床价值。

NLR 与 PLR 间存在正相关性($r = 0.705$, $P < 0.01$)，且相关系数较大，相关性较强，考虑与两者的计算方法有关，其中 NLR 为中性粒细胞计数与淋巴细胞计数的比值，PLR 为血小板计数与淋巴细胞计数的比值，两者均与淋巴细胞相关，而这可能导致两者的强相关性，并有程迎迎等[29]研究认为 PLT 为反映炎症的常用指标，感染和血栓形成过程中释放的细胞因子可影响其结果，认为 PLR 的升高可能是 NLR 升高的继发反应。

5. 研究的不足

对三个病例组的 NLR、PLR 进行 *Spearman* 秩相关分析时不同病理级别和 NLR、PLR 间存在正相关性($P < 0.01$)，但相关系数较小(0.262、0.288)，考虑可能与其他混杂因素相关，例如结直肠癌家族史[30]、炎症性肠病[31]、肉类摄入[32]、糖尿病[33]、肥胖[34]、心理因素[35]、肠道菌群失调[36]、胆囊息肉[37]等，有待控制唯一变量后进一步研究。

6. 结论

NLR、PLR 可以作为结直肠息肉病理级别升高的预测指标，对结直肠息肉发生高级别瘤变或癌变有一定的提示作用，但对高级别瘤变和癌变的鉴别诊断的价值、与息肉病理级别的计量对应关系有待进一步研究。

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