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血清 Aib、PA、NLR 水平在直肠癌术后发生吻合口瘘评估中的应用 *

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摘要 目的:探讨血清白蛋白(Aib)、前白蛋白(PA)、中性粒细胞与淋巴细胞比值(NLR)水平在直肠癌术后发生吻合口瘘评估中的应用。**方法:**选择 2018 年 6 月至 2019 年 12 月于我院进行直肠癌手术患者 90 例患者进行研究,其中 38 例发生术后吻合口瘘,设为研究组,52 例未发生吻合口瘘作为对照组。分析患者术后血清 Aib、PA、NLR 水平变化情况,采用受试者工作特征曲线分析血清 Aib、PA、NLR 对术后发生吻合口瘘的评估作用。**结果:**研究组血清 Aib、PA 水平显著低于对照组,NLR 水平显著高于对照组,差异显著($P<0.05$);造口组术后血清 Aib、PA 水平显著高于未造口组,NLR 水平显著低于未造口组,差异显著($P<0.05$);ROC 结果显示,血清 Aib 预测术后吻合口瘘的 AUC 为 0.967,灵敏度为 81.25%,特异度为 90.14%,截断值为 33.06 g/L;血清 PA 预测术后吻合口瘘的 AUC 为 0.772,灵敏度为 80.36%,特异度为 89.56%,截断值为 119.04 mg/L;血清 NLR 预测术后吻合口瘘的 AUC 为 0.991,灵敏度为 85.62%,特异度为 93.23%,截断值为 6.86。**结论:**监测血清 Aib、PA、NLR 水平有助早期发现直肠癌患者术后吻合口瘘。

关键词:白蛋白;前白蛋白;中性粒细胞与淋巴细胞比值;直肠癌;术后;吻合口瘘;评估

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Application of Serum AIB, PA and NLR Levels in the Assessment of Anastomotic Fistula after Rectal Cancer Operation*

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ABSTRACT Objective: To study Application of serum Albumin (AIB), prealbumin (PA), neutrophil to lymphocyte ratio (NLR) levels in the assessment of anastomotic fistula after rectal cancer operation. **Methods:** 90 patients who underwent rectal cancer surgery in our hospital from June 2018 to December 2019 were selected for this study. Among them, 38 patients with postoperative anastomotic fistula were selected as the study group, and 52 patients without anastomotic fistula were selected as the control group. The changes of serum AIB, PA and NLR levels after operation were analyzed. Receiver operating characteristic curve was used to analyze the evaluation effect of serum AIB, PA and NLR on postoperative anastomotic fistula. **Results:** Serum AIB and PA levels in the study group were significantly lower than those in the control group, and NLR levels were significantly higher than those in the control group, with significant differences($P<0.05$). After operation, the levels of AIB and PA in the stomy group were significantly higher than those in the non-stomy group, and the levels of NLR in the stomy group were significantly lower than those in the non-stomy group ($P<0.05$). ROC results showed that the AUC of serum AIB for predicting postoperative anastomotic fistula was 0.967, the sensitivity was 81.25%, the specificity was 90.14%, and the cutoff value was 33.06 g/L. The AUC of serum PA for predicting postoperative anastomotic fistula was 0.772, the sensitivity was 80.36%, the specificity was 89.56%, and the cutoff value was 119.04 mg/L. The AUC of serum NLR for predicting postoperative anastomotic fistula was 0.991, the sensitivity was 85.62%, the specificity was 93.23%, and the cutoff value was 6.86. **Conclusion:** Monitoring serum levels of AIB, PA and NLR is helpful for early detection of postoperative anastomotic fistula in patients with rectal cancer.

Key words: Albumin; Prealbumin; Ratio of neutrophils to lymphocytes; Rectal cancer; Postoperative; Anastomotic fistula; Assessment

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前言

直肠癌是临床常见的恶性肿瘤,发病率及死亡率较高,对

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于具备手术的患者而言,直肠癌根治术仍是最重要的治疗方法,随着医学技术的不断提高,越来越多学者提出采用保肛方式进行手术,提高了保肛率的同时加大了术后的吻合口瘘^[1,2]。吻合口瘘是直肠癌保肛术后严重并发症之一,发生率约在3%~21%,可引起腹腔内感染、吻合口狭窄,还能提高肿瘤局部转移的风险,延长住院时间,增加患者死亡率,因此减少并预防术后吻合口瘘的发生是肛肠外科重点关注的问题之一^[3,4]。有研究显示,术后低蛋白血症是吻合口瘘发生的主要原因^[5]。Aib是血浆中含量较多的蛋白质,是术前应用状态的观察指标,参与了结直肠癌的发生;PA是一种载体蛋白,其浓度受营养状况及肝功能变化影响^[6-8]。近年来,炎症指标C反应蛋白(C-reactive protein, CRP)被证实对预测术后吻合口瘘有一定的价值,而NLR作为另一个常用的炎症反应指标,与CRP相比检测简单、费用低廉,且被证实与多种恶性肿瘤预后有关^[9]。但关于NLR水平能否用于预测直肠癌术后发生吻合口瘘还需进一步研究探索,因此,本研究通过分析血清Aib、PA、NLR水平在直肠癌术后水平变化,评估Aib、PA、NLR在直肠癌术后发生吻合口瘘的价值。

1 资料与方法

1.1 一般资料

选择2018年6月至2019年12月于我院进行直肠癌手术患者90例患者进行研究,术后随访其中38例发生术后吻合口瘘,设为研究组,男20例,女18例,年龄45~65岁,平均(53.52±4.32)岁,手术时间200.18~285.50 min,平均(252.36±20.15)min;未发生吻合口瘘作为对照组,其中男35例,女17例,年龄42~66岁,平均(54.51±4.39)岁,手术时间

205.32~282.15 min,平均(250.29±20.38)min。两组年龄比较差异无统计学意义($P>0.05$)。

参照《结直肠癌肝转移诊断和综合治疗指南》^[10], (1)便秘频繁,排便习惯改变; (2)肛门下坠感; (3)直肠镜辅助检查确诊。

纳入标准:符合上述诊断标准; (1)术前无感染者; (2)符合手术指征; (3)临床资料齐全; (4)签署知情同意书。排除标准: (1)术后感染者; (2)肿瘤远处转移者; (3)多源性直肠肿瘤; (4)直肠阴道瘘者; (5)不同意此次研究者; (6)近期其他腹部手术者; (7)出血性疾病。

1.2 方法

两组患者均给予直肠癌根治术:麻醉后,建立人工气腹,脐下切口,穿刺主操作孔,确定肿瘤情况后,游离肠段及系膜,夹闭血管,超声刀分离,游离病变肠段,清扫肿瘤病灶、淋巴结等。常规放置引流管,冲洗缝合。所有患者术后采集6 mL静脉血,采用酶联免疫分析法检测血清Aib、PA、NLR,操作均按试剂盒和相关仪器说明书进行。

1.3 统计学分析

以spss22.0软件包处理,计量资料用均数±标准差($\bar{x} \pm s$)表示,t检验,计数资料率表示, χ^2 检验,使用受试者工作特征曲线(ROC)分析血清Aib、PA、NLR的评估价值, $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组研究对象血清Aib、PA、NLR水平比较

研究组血清Aib、PA水平显著低于对照组,NLR水平显著高于对照组,差异显著($P<0.05$)见表1。

表1 两组研究对象血清Aib、PA、NLR水平比较($\bar{x} \pm s$)

Table 1 Comparison of serum AIB, PA and NLR levels between the two groups($\bar{x} \pm s$)

Groups	n	Aib(g/L)	PA(mg/L)	NLR
Research group	38	26.12±3.51	96.23±21.52	8.16±1.23
The control group	52	36.95±3.68	236.64±33.26	5.23±0.87
t value		14.059	22.757	13.243
P value		0.000	0.000	0.000

2.2 不同造口情况血清Aib、PA、NLR水平比较

造口组术后血清Aib、PA水平显著高于未造口组,NLR水

平显著低于未造口组,差异显著($P<0.05$)见表2。

表2 不同造口情况血清Aib、PA、NLR水平比较($\bar{x} \pm s$)

Table 2 Comparison of serum levels of AIB, PA and NLR under different stoma conditions($\bar{x} \pm s$)

Groups	n	Aib(g/L)	PA(mg/L)	NLR
Colostomy group	13	29.58±3.65	105.36±20.96	7.53±1.15
Non stoma group	25	24.32±3.43	91.48±21.33	8.49±1.21
t value		6.994	3.071	3.796
P value		0.000	0.003	0.000

2.3 血清Aib、PA、NLR在直肠癌术后发生吻合口瘘的预测价值

ROC结果显示,血清Aib预测术后吻合口瘘的AUC为0.967,灵敏度为81.25%,特异度为90.14%,截断值为33.06 g/L;

血清 PA 预测术后吻合口瘘的 AUC 为 0.772, 灵敏度为 80.36%, 特异度为 89.56%, 截断值为 119.04 mg/L; 血清 NLR 预测术后吻合口瘘的 AUC 为 0.991, 灵敏度为 85.62%, 特异度为 93.23%, 截断值为 6.86, 见图 1、表 3。

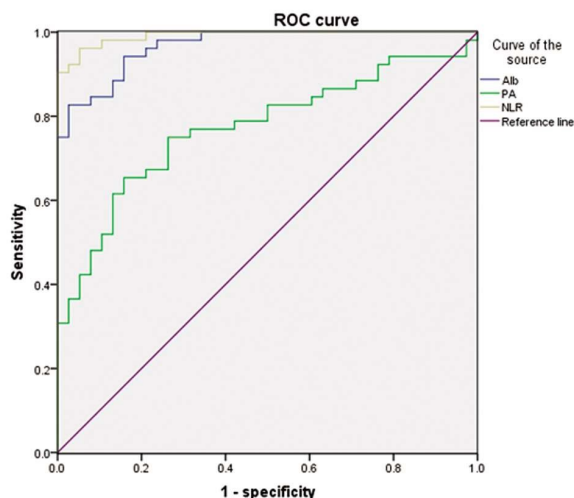


图 1 血清 Alb、PA、NLR 预测术后发生吻合口瘘的 ROC 曲线

Fig.1 ROC curve of serum AIB, PA and NLR in predicting postoperative anastomotic leakage

表 3 血清 Alb、PA、NLR 预测术后发生吻合口瘘的预测价值分析

Table 3 The predictive value of serum AIB, PA and NLR in predicting postoperative anastomotic leakage

Index	AUC(95 %CI)	Standard error	P	Sensitivity	Specificity	Cut off value
Alb	0.967(0.938~0.996)	0.015	0.000	81.25	90.14	33.06 g/L
PA	0.772(0.675~0.869)	0.049	0.00	80.36	89.56	119.04 mg/L
NLR	0.991(0.980~1.000)	0.006	0.000	85.62	93.23	6.86

-60%, 受食物蛋白含量影响, 在维持血液胶体渗透压机营养等方面起重要作用, 当肝脏病或营养不良等情况下其水平降低^[23-25]。有研究显示, 当发生恶性肿瘤时可消耗大量蛋白质, 减弱蛋白质分解代谢增强合成代谢, 导致患者营养状况逐步恶化, 最终导致 Alb 水平降低^[26]。Wang Y^[27]等研究显示, 食管癌术后 Alb 明显降低, 且在静脉营养支持下其水平逐步上升。PA 由肝细胞合成, 是一种负性急性时相蛋白, 在电泳分离时, 常显示 Alb 前方, 在炎症感染后 6-8 h 升高, 其半衰期约 12 h-1.9 d, 当机体在应激期时, PA 启动免疫系统, 杀伤病原体, 当疾病好转时, 合成 PA, 因此, PA 在炎性疾病中表达较高, 且随着炎症反应的加重而下降^[28,29]。有研究显示, ALB、PA 在肝脏受损时合成减少, 在多种疾病中表达异常^[30]。本研究结果显示, 直肠癌术后发生吻合口瘘的患者血清 ALB、PA 水平低于术后未发生吻合口瘘的患者, 且造口组术后血清 Alb、PA 水平显著高于未造口组, 提示, ALB、PA 在直肠癌术后发生吻合口瘘中表达较高, 代表患者体内感染控制不佳, 是术后吻合口瘘发生的重要影响因素。Kim C H^[31]等研究也显示, 直肠癌保肛术后 Alb、PA 降低, 则提示患者发生吻合口瘘的可能, 与本研究结果相似。分析其原因可能是因为直肠癌患者行保肛术后可刺激患者机体应激状态, 释放大量炎症因子, 损伤毛细血管的内皮细胞, 导致

3 讨论

近年来, 直肠癌发病率逐步增加, 且在中青年中发病率增长更为明显, 调查显示, 按目前的增长趋势, 至 2030 年直肠癌发病率可增加 124.2%, 严重威胁人们的生命^[1]。手术是直肠癌的主要治疗方法, 随着保肛手术的推广, 直肠癌保肛术后吻合口瘘的发生明显升高, 吻合口瘘是直肠癌术后常见并发症, 多发生在术后 5-7 d^[12,13]。国外研究显示, 直肠癌术后吻合口瘘的发生率超过 10%, 其中中低位直肠癌可高达 20%, 死亡率高达 7.5%^[14]。吻合口瘘的发生能增加肿瘤复发率, 加重因瘘口大量肠液引流所致内环境紊乱状况, 严重者可合并器官功能障碍而死亡, 同时吻合口瘘症状无明显特征, 仅根据症状难以明确诊断, 给患者带来的极大困扰, 因此, 早期发现吻合口瘘, 并采取有效的治疗措施对改善患者预后具有重要意义^[15-18]。有研究显示, 分析患者早期血清水平变化可对术后发生吻合口瘘进行早期诊断, 为预测吻合口瘘的发生提供新思路^[19,20]。

有研究显示, 直肠癌术前均存在不同程度营养状态下降, 同时术后患者特征是以高分解代谢为主, 可引起急性蛋白性营养不良, 加大术后肿瘤复发的风险^[21]。相关研究显示, 直肠癌患者营养风险发生率高达 25%-53%^[22]。Alb 由 585 个氨基酸残基组成, 是血清总蛋白的主要蛋白质成分, 占总蛋白的 40%

Alb、PA 经损伤的毛细血管内皮渗漏, 降低其水平。

有研究显示, 肿瘤的发生与肿瘤预后有关, 炎症能抑制肿瘤细胞增殖, 同时也可通过分泌肿瘤生长刺激因子等促进肿瘤细胞增殖^[32]。NLR 是反应炎症的重要指标, 检测更为简单、方便, 能反映体内中性粒细胞和淋巴细胞的平衡, 当机体发生炎症反应时可被激活, 并迁移至肿瘤细胞周围, 释放大量能诱导细胞 DNA, 产生适合肿瘤生存的微环境, 其水平升高也促进癌症的发展, 导致多种肿瘤患者预后不良^[33,34]。Jeon Y^[35]等研究也显示, NLR 是循环血管内皮生长因子的主要来源之一, 而血管内皮生长因子是促进肿瘤新血管生成, 的必备条件之一, 高 NLR 是直肠癌患者预后独立危险因素。有研究显示, NLR 可用于预测结直肠癌手术患者的围手术期并发症, 但很少被用于早期预测吻合口瘘的发生^[36]。本研究结果显示, 直肠癌术后发生吻合口瘘的患者血清 NLR 水平显著高于术后未发生吻合口瘘的患者, 且造口组术后血清 NLR 水平显著低于未造口组, 提示, 吻合口瘘可出现炎症反应, 导致 NLR 大量生成, 可作为预测吻合口瘘发生的标志物。本研究进一步深入分析发现, 血清 Alb 预测术后吻合口瘘的 AUC 为 0.967, 截断值为 33.06 g/L; 血清 PA 预测术后吻合口瘘的 AUC 为 0.772, 截断值为 119.04 mg/L; 血清 NLR 预测术后吻合口瘘的 AUC 为 0.991, 截断值为

6.86,提示,血清 AIb、PA、NLR 对预测直肠癌患者术后吻合口瘘的发生具有良好的应用价值。但本研究样本量较少,时间较短,为观察治疗前后各指标变化,今后应扩大样本量深入研究。综上所述,监测血清 AIb、PA、NLR 水平有助早期发现直肠癌患者术后吻合口瘘,对改善患者预后具有重要意义。

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