

结直肠癌患者血清中可溶性P-选择素和L-选择素水平及临床意义

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[摘要] **背景与目的:** 结直肠癌是常见的消化系统恶性肿瘤, 严重威胁着人类的健康。虽然现代诊疗技术不断发展, 但近年来结直肠癌的发病率和病死率仍呈逐年上升趋势, 早期诊断和防治肝转移有助于提高结直肠癌患者的生存率, 对改善其预后具有重要意义。P-选择素和L-选择素是近年肿瘤研究领域倍受关注的分子, 其表达量及介导的黏附作用的改变在肿瘤细胞转移中起着重要作用, 但二者与结直肠癌发生及临床分期的关系鲜见报道。本研究旨在探讨结直肠癌患者手术前后血清中P-选择素和L-选择素水平高低与临床病理特征的相关性。**方法:** 选择132例结直肠癌患者及与其性别年龄相匹配的100名健康体检者。采用酶联免疫吸附试验(enzyme-linked immunosorbent assay, ELISA)检测132例结直肠癌患者手术前后血清中P-选择素和L-选择素浓度, 100名健康体检者为对照组, 结合临床病理特征对P-选择素和L-选择素水平的变化进行分析。**结果:** 结直肠癌患者术前血清P-选择素和L-选择素水平显著高于对照组(75.2 ± 13.3 vs 26.6 ± 9.6 , 89.2 ± 12.7 vs 33.9 ± 8.3 , $P < 0.05$); 术后1周P-选择素和L-选择素水平较术前没有明显下降(63.8 ± 11.1 vs 75.2 ± 13.3 , 71.5 ± 10.9 vs 89.2 ± 12.7 , $P > 0.05$); 而术后3个月则明显下降, 与术前比较差异有统计学意义(34.8 ± 10.4 vs 75.2 ± 13.3 , 40.1 ± 9.5 vs 89.2 ± 12.7 , $P < 0.01$); 本组结直肠癌患者, 临床分期越高, P-选择素和L-选择素水平越高, 其水平与肿瘤浸润深度、Dukes分期、组织学分级和淋巴结转移相关, 而与年龄、性别及肿瘤部位无明显相关($P > 0.05$); 同时, 同一结直肠癌患者血清中P-选择素和L-选择素的表达无显著相关($r = 4.114$, $P > 0.05$)。**结论:** 血清中P-选择素和L-选择素的水平在一定程度上反映了结直肠癌的侵袭、浸润和淋巴结转移的程度, 可作为预测结直肠癌发展及预后的重要指标。

[关键词] 结直肠癌; P-选择素; L-选择素

DOI: 10.3969/j.issn.1007-3969.2014.08.007

中图分类号: R735.3 文献标志码: A 文章编号: 1007-3639(2014)08-0599-05

Soluble P-selectin and L-selectin levels in serum of colorectal cancer patients and its clinical significance ZHANG Liang, LUO Gui-fei, YUAN Hui-xiong, WEI Gui-jiang (Affiliated Hospital of Youjiang Medical University for Nationalities, Baise Guangxi 533000, China)

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[Abstract] **Background and purpose:** Colorectal cancer is a kind of common digestive malignancies, which seriously threaten the human health. Although modern diagnostic and treatment technology has developed rapidly, the incidence and mortality of colorectal cancer continue to show an increasing tendency in recent years, and early diagnosis and prevention of colorectal cancer liver metastases are important to increase the survival rate of patients and to improve the prognosis. P-selectin and L-selectin is attracting much attention in cancer research field recently, and the change of their expression and mediated adhesion play an important role in tumor cell metastasis, but their relationship between the occurrence and clinical stage of colorectal cancer rarely reported. This study aimed to explore whether the serum P-selectin and L-selectin levels of colorectal cancer patients were correlated with clinical and pathological features and the situation before and after surgery. **Methods:** A total number of 132 cases of colorectal cancer patients and 100 healthy subjects with gender and age-matched were enrolled. Enzyme-linked immunosorbent assay (ELISA) was used to detect serum P-selectin and L-selectin concentrations in 132 cases before and after surgery, 100 healthy subjects were enrolled as the control group, the P-selectin and L-selectin levels were analyzed combined with the

clinical and pathological features. **Results:** Serum P-selectin and L-selectin levels in patients with colorectal cancer before surgery were significantly higher than those in the healthy control group (75.2 ± 13.3 vs 26.6 ± 9.6 , 89.2 ± 12.7 vs 33.9 ± 8.3 , $P < 0.05$); Compared with the patients before surgery, 1 week after surgery, the P-selectin and L-selectin levels were not significantly decreased (63.8 ± 11.1 vs 75.2 ± 13.3 , 71.5 ± 10.9 vs 89.2 ± 12.7 , $P > 0.05$); however, significantly decreased after 3 months (34.8 ± 10.4 vs 75.2 ± 13.3 , 40.1 ± 9.5 vs 89.2 ± 12.7 , $P < 0.01$); This paper studied patients with colorectal cancer, the higher clinical stage, higher P-selectin and L-selectin levels, and their expression levels with tumor invasion depth, Dukes stage, histological grade and lymph node metastasis were related, but were not correlated with age, gender and tumor site. Meanwhile, P-selectin and L-selectin levels were not significantly correlated in the same serum of patients with colorectal cancer ($r = 4.114$, $P > 0.05$). **Conclusion:** Serum P-selectin and L-selectin levels to some extent reflect the invasion of colorectal cancer, the degree of infiltration and lymph node metastasis, and which can be an important indicator in the development and prognosis of colorectal cancer.

[Key words] Colorectal cancer; P-selectin; L-selectin

结直肠癌是当代常见的消化系统恶性肿瘤, 严重威胁着人类的健康^[1]。虽然现代诊疗技术不断发展, 但近年来国内结直肠癌的发病率和病死率仍呈逐年上升趋势^[2]。早期诊断和防治肝转移有助于提高结直肠癌患者的生存率, 对改善其预后具有重要意义^[2]。而结直肠癌的浸润、转移和术后复发是预后不良的主要原因, 其发生、发展是多因素、多步骤、多分子参与的复杂过程^[3-5]。随着肿瘤因子的深入研究, 结直肠癌相关因子的定位和识别已成为研究的热点^[6]。P-选择素和L-选择素是近年来肿瘤研究领域倍受关注的分子, 其介导的黏附作用的改变在肿瘤细胞转移中起着重要作用^[7-9], 但二者与结直肠癌发生及临床分期的关系鲜见报道。2008年3月—2011年3月, 我们选择了132例结直肠癌患者及与其性别年龄相匹配的100例健康体检者。采用酶联免疫吸附试验 (enzyme-linked immunosorbent assay, ELISA) 检测132例结直肠癌患者手术前后血清中P-选择素和L-选择素浓度, 100名健康体检者为对照组, 结合临床病理特征对P-选择素和L-选择素水平的变化进行分析, 为P-选择素和L-选择素作为预测结直肠癌发生、发展及预后指标提供分子实验依据。

1 资料和方法

1.1 临床资料

选择广西右江民族医学院附属医院于2008年3月—2011年3月收治的结直肠癌患者132例,

诊断依据为临床症状、B超、X线、CT检查、肠道检查及病理学诊断。其中男性83例、女性49例; 年龄43~71岁, 平均年龄64岁; 浸润局限于浆膜内50例, 浸及浆膜外82例; 临床Dukes分期, I期19例, II期27例, III期56例, IV期30例; 组织学分级, 高分化31例, 中分化53例, 低分化48例; 无淋巴结转移53例, 有淋巴结转移79例。对照组为100名来自本院体检中心的健康体检者, 其中男性70例, 女性30例, 年龄38~75岁, 平均年龄60岁, 体温、胸片、血尿常规正常, 既往无心、肝、肺及肾等脏器疾病。所有患者术前未采用任何放化疗或生物治疗。

1.2 检测方法

实验所需血清样本均为清晨空腹静脉血 (3 mL), 3 000 r/min离心10 min, 收集上层血清, 采用ELISA法检测血清中P-选择素和L-选择素水平, 试剂盒为美国Gene May公司产品, 实验步骤严格按照说明书进行。术后1周及术后3个月采血及检测方法相同。

1.3 统计学处理

采用SPSS 17.0统计软件进行数据分析, 计量资料数据采用 $\bar{x} \pm s$ 记录, 用 t 检验, 组间分析采用列变量为有序变量的行 \times 列表的 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 结直肠癌组和正常对照组血清P-选择素和L-选择素水平检测结果比较

132例结直肠癌患者血清P-选择素和L-选

择素水平显著高于正常对照组($P<0.05$); 术后1周与术前血清水平变化差异不大($P>0.05$), 而与正常组比较差异有统计学意义($P<0.05$); 术后3个月与术前血清水平变化差异有统计学意义($P<0.05$), 与正常组比较差异无统计学意义($P>0.05$, 表1)。

2.2 P-选择素和L-选择素水平与结直肠癌临床病理特征的关系

以年龄、性别、肿瘤部位、浸润深度、

Dukes分期、组织学分级及淋巴结转移为指标, 对132例结直肠癌患者分别独立进行分类, 研究P-选择素和L-选择素在各个分类组间的表达差异, 发现P-选择素和L-选择素水平在结直肠癌患者血清中的表达与患者的年龄、性别、肿瘤部位差异无统计学意义($P>0.05$), 而与浸润深度、Dukes分期、组织学分级及淋巴结转移差异有统计学意义($P<0.05$, 表2)。

表1 结直肠癌组与正常对照组血清P-选择素和L-选择素水平检测结果比较

Tab. 1 The test results of serum P-selectin and L-selectin levels in colorectal cancer and normal control group

Group	n	P-selectin		L-selectin	
		Level	P value	Level	P value
Control group	100	25.6±9.6		33.9±8.3	
Cancer group	132	75.2±13.3	< 0.05	89.2±12.7	< 0.05
After 1 week	132	63.8±11.1	< 0.05	71.5±10.9	< 0.05
After 3 months	132	34.8±10.4	> 0.05	40.1±9.5	> 0.05

P value: Comparison of each experimental group and the control group in the table.

表2 结直肠癌患者血清中P-选择素和L-选择素的表达与临床病理特征的关系

Tab. 2 The relationship between the P-selectin and L-selectin expression of colorectal cancer patients and the clinical and pathological features

Analysis index	n	P-selectin		L-selectin	
		$\bar{x}\pm s$	P value	$\bar{x}\pm s$	P value
Age/year					
≤55	76	75.29±10.7	> 0.05	81.25±13.0	> 0.05
>55	56	69.54±11.2		78.46±10.8	
Gender					
Male	83	77.88±9.0	> 0.05	75.58±12.6	> 0.05
Female	49	70.89±12.6		74.32±10.7	
Tumor location					
Colon	87	68.19±9.5	> 0.05	78.50±11.4	> 0.05
Rectum	45	72.56±11.4		80.16±9.4	
Invasion					
Intraserosal	50	76.32±11.6	< 0.05	83.89±13.7	< 0.05
Extraserosal	82	49.68±8.7		51.82±10.5	
Classification					
Highly	31	79.21±12.4	< 0.05	88.20±13.0	< 0.05
Moderate	53	70.69±11.1		76.35±12.1	
Low	48	42.25±10.8		50.36±12.9	
Dukes					
I	19	45.81±11.5	< 0.05	48.66±10.7	< 0.05
II	27	57.90±10.2		63.25±13.5	
III	56	75.43±12.7		80.64±12.8	
IV	30	79.32±11.5		86.92±11.5	
Metastasis					
Yes	79	76.66±11.4	< 0.05	89.52±11.6	< 0.05
No	53	43.38±10.2		51.55±10.3	

2.3 结直肠癌患者血清中P-选择素和L-选择素表达的相关性

将132例患者P-选择素和L-选择素有无表达进行计数分类, 采用列变量为有序变量的行×列表的 χ^2 检验, 检验P-选择素和L-选择素表达有无关联。相关分析显示P-选择素和L-选择素表达无显著相关($\chi^2=4.114$, $P>0.05$, 表3)。

表3 结直肠癌患者血清中P-选择素和L-选择素表达的关系
Tab. 3 Relations P-selectin and L-selectin in serum of patients with colorectal cancer

P-selectin	L-selectin		χ^2	P value
	+	-		
+	78	24	4.114	<0.05
-	11	19		

3 讨 论

可溶性P-选择素和L-选择素属于选择素家族的功能性细胞黏附分子, 仅存于活化内皮细胞表面^[9]。正常组织中的内皮细胞一般不表达P-选择素和L-选择素, 只有当内皮细胞受到某些炎性因子如细菌脂多糖、白细胞介素、肿瘤坏死因子等刺激被激活时才表达, 是炎性反应过程中最早出现的黏附分子^[10]。P-选择素和L-选择素介导活化的内皮细胞与中性粒细胞的黏附作用, 有助于白细胞稳定地黏附于内皮细胞, 继而迁移至血管外组织, 从而促进肿瘤细胞的侵袭转移^[11-12]。

肿瘤的侵袭转移是一个多步骤、多环节、多因素、多分子参与的复杂过程, 在这一过程中, 多种分子各自发挥不同作用, 并在时间和空间上相互配合, 协同促进细胞的癌变。近年来, 随着分子生物学发展, 对P-选择素和L-选择素的结构、功能、调控及病理生理作用进行了较为深入的研究。查阅文献发现^[13], P-选择素和L-选择素的表达受体内外许多调节因子的影响, 静息时, 内皮细胞上的P-选择素和L-选择素含量甚微, 当受到炎性反应因子刺激后, P-选择素和L-选择素表达显著增加。有研究证实^[14-15], P-选择素和L-选择素与肺癌、胶质瘤、胃癌、卵巢癌和肾癌等的浸润转移的

有关。Zheng等^[16]发现P-选择素的表达水平与肝癌患者的预后关系十分密切, P-选择素的表达水平越低, 其5年生存率越高; Cooney等^[17]发现乳腺癌淋巴转移患者中, P-选择素在原位灶、转移灶的血管内皮和淋巴细胞中的高表达与肿瘤的高转移有关; Radhakrishnan等^[18]还发现前列腺癌患者血清中L-选择素水平异常升高。我们的研究显示, 结直肠癌患者血清P-选择素和L-选择素水平明显高于正常对照组, 且与肿瘤的浸润、Dukes分期、有无淋巴结转移相关, 患者术后3个月血清P-选择素和L-选择素水平比术前明显降低, 可能提示P-选择素和L-选择素参与了结直肠癌的发展、侵袭和转移。本研究还发现, 术后1周血清P-选择素和L-选择素水平与术前相比无明显变化, 可能是患者仍处于应激期, 机体内炎性反应过程尚未消退, 手术创伤刺激大量炎性因子分泌, 使得血清中P-选择素和L-选择素仍维持在高水平。进一步分析P-选择素和L-选择素表达与肿瘤临床病理因素的相关性发现, P-选择素和L-选择素水平与患者的年龄、性别、肿瘤部位无关。但与癌细胞浸润的深度及Dukes分期、组织学分级、临床分级及有无淋巴结转移相关。提示密切观察病情, 动态检测患者血清P-选择素和L-选择素水平变化对预测结直肠癌转移, 观察病情、判断疗效及评估预后具有重要意义。研究结果还显示, P-选择素和L-选择素表达在结直肠癌患者中无相关关系, 是2个各自发挥独立作用的调控因子。

总之, P-选择素和L-选择素在结直肠癌的发生、发展、浸润转移过程中均发挥着各自重要的作用, 其表达水平能够反映结直肠癌患者的预后状况, 也可能成为1项新的肿瘤标志物, 深入研究和监测P-选择素和L-选择素将有助于判断结直肠癌的发展趋势和预后评估。

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(收稿日期: 2013-12-02 修回日期: 2014-05-17)