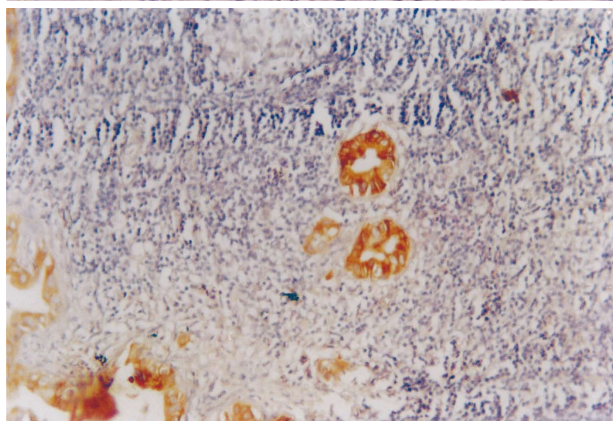
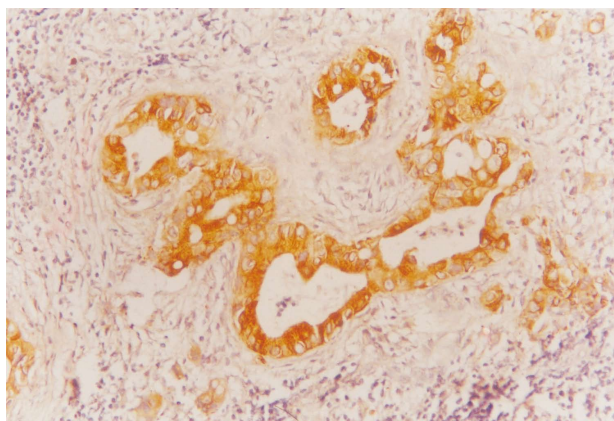
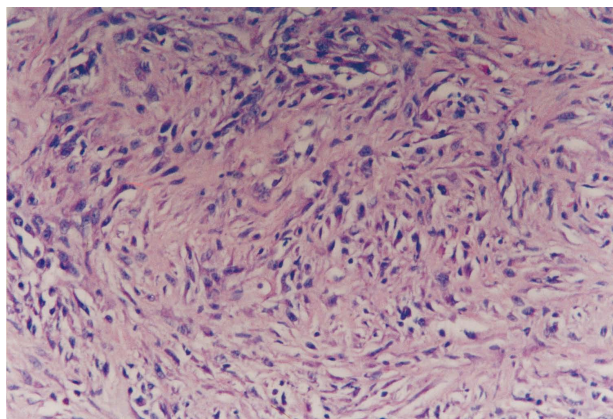
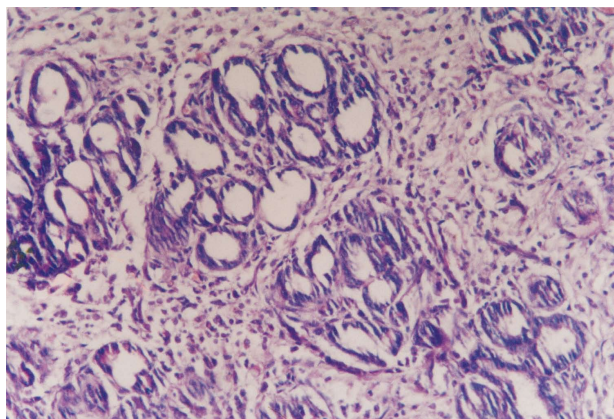


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全直肠系膜切除术切缘血管内皮生长因子检测的临床意义

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Clinical significance of detection for vascular endothelial growth factor in resection margin following total mesorectal excision

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Abstract

AIM: To investigate the expression and its significance of vascular endothelial growth factor (VEGF) in the resection margin following total mesorectal excision (TME) for human rectal cancer.

METHODS: VEGF was detected in the tissue specimens of cancer, distal mesorectal margin (DMM), circumferential resection margin (CRM) and outer pelvic fascia from 60 rectal cancer patients received TME. The pathological data were retrospectively analyzed.

RESULTS: VEGF expression was significantly higher in the tissues of rectal cancer than that in the normal tissues (54/60 vs 2/20, $P < 0.001$). VEGF was also expressed in tissues of CRM (9/60). However, no VEGF expression was detected in the tissues of DMM and outer pelvic fascia. VEGF expression was closely related with the differentiation degree, Dukes staging and lymph node metastasis ($P < 0.05$ or $P < 0.01$).

CONCLUSION: VEGF is highly expressed in tissues of rectal cancer, and negatively or weakly positively expressed in DMM and CRM.

Key Words: Rectal cancer; Distal mesorectal margin; Circumferential resection margin; Outer pelvic fascia;

Total mesorectal excision; Vascular endothelial growth factor

Zhan XL, Tian SL. Clinical significance of detection for vascular endothelial growth factor in resection margin following total mesorectal excision. *Shijie Huaren Xiaohua Zazhi* 2005;(18):2278-2281

摘要

目的: 探讨血管内皮生长因子(VEGF)在直肠癌及其切缘的表达及其临床意义。

方法: 取实施TME的60例直肠癌患者直肠癌组织(I)、直肠系膜远端切缘(II)、直肠系膜周围切缘(III)、盆筋膜壁层(IV)病理标本, 采用免疫组化SP法对标本进行VEGF检测, 并回顾性分析临床病理学资料。

结果: 直肠癌组织中VEGF高度表达(54/60), 肿瘤相对的盆筋膜脏层(直肠系膜周围切缘)中有VEGF存在(9/60), 在直肠系膜远端切缘及盆筋膜壁层标本中未见VEGF表达。VEGF在直肠癌组织中的表达有高度特异性。VEGF表达与直肠癌分化程度、Dukes分期及淋巴结转移密切相关($P < 0.05$ 或 $P < 0.01$)。

结论: VEGF在直肠癌组织中高度表达, 直肠远端系膜切缘及直肠系膜周围切缘不表达或表达为弱阳性。

关键词: 直肠癌; 直肠系膜远端切缘; 直肠系膜周围切缘; 盆筋膜壁层; 全直肠系膜切除术; 血管内皮生长因子

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0 引言

包括直肠癌在内的实体肿瘤的生长与转移依赖血管新生的理论已被大量实验和临床研究证实, 血管内皮生长因子(vascular endothelial growth factor, VEGF)作为最重要的促血管生成因子, 在肿瘤发生、发展中起重要作用^[1-4]。全直肠系膜切除术(total mesorectal excision, TME)已成为一种标准的直肠癌根治技术, 已被越来越多的外科医生应用于临床^[5-7]。国外学者的研究表明, VEGF在直肠癌组织中、癌组织侵袭前缘以及微小转移灶中的表达比率可以作为直肠癌预后的一种独立、敏感和有效的标志物^[8-12]。我们拟通过免疫组化方法对TME手术后系膜切缘VEGF的检测, 为证实TME技

术在直肠癌治疗中的价值提供分子水平的依据。

1 材料和方法

1.1 材料 收集本院2004-01/2005-03行TME的60例直肠癌患者的病理标本,术前未接受过抗肿瘤治疗。男22例,女38例,平均年龄34—78岁。所有病例均经病理诊断证实。其中溃疡型33例(55.0%),肿块型4例(6.7%),浸润型26例(38.3%);腺瘤癌变3例(5.0%),高分化腺癌18例(30.0%),中、低分化腺癌23例(38.3%),黏液腺癌13例(21.7%),印戒细胞癌3例(5.0%)。Dukes A期3例(5.0%),B期27例(45.0%),C期28例(46.7%),D期2例(3.3%);每例分别于直肠癌组织(I)、直肠系膜远端切缘(II)、直肠系膜周围切缘(III)、盆筋膜壁层(IV)取病理标本(大小约1 cm×1 cm×1 cm)作为试验组;另选取20例直肠腺瘤病例的正常肠组织(I')及正常结肠系膜(II')作阴性对照组。标本置于40 g/L甲醛固定液,常规石蜡包埋,连续切片2张,4 μm厚连续切片。抗VEGF和UltraSensitiveTM S-P超敏试剂盒购于福州迈新生物技术开发有限公司。

1.2 方法 进行常规HE染色组织学分析和VEGF免疫组化S-P法检测。VEGF采用0.01 mol/L(pH6.0)柠檬酸盐缓冲液高温、高压抗原修复,检测时每批染色均设阴性对照(以PBS代替一抗)。VEGF阳性为细胞质或细胞膜染色呈棕黄色,在显微镜下(×400)计数至少5个随机视野,取平均值。阳性细胞数<10%为(-),11-25%为(+),26-50%为(++),≥51%为(+++)。同时,收集该组患者的临床病理资料,包括患者的年龄、性别、肿瘤的部位、类型、分化程度、分期、有无淋巴结转移以及远处转移等进行回顾性分析。

统计学处理 采用SPSS10.0统计分析软件包处理,数据统计采用 χ^2 检验, $P<0.05$ 有统计学意义。

2 结果

2.1 VEGF在不同组织中的表达情况 试验组直肠癌组织(I)标本VEGF染色为阳性,其余标本染色为阴性或弱阳性;对照组各个标本染色均为阴性或弱阳性。VEGF在癌组织中的表达与对照组组织中的表达存在显著差异($P<0.05$,表1)

2.2 VEGF与临床病理指标的关系 经 χ^2 检验VEGF表达与

直肠癌分化程度、Dukes分期及淋巴结转移密切相关($P<0.05$ 或 $P<0.01$)。低分化腺癌VEGF阳性率高于高分化腺癌($P<0.01$);Dukes分期的C和D期VEGF阳性率(93.3%)明显高于A和B期(43.3%);有淋巴结转移的病例VEGF阳性率(93.8%)显著高于无淋巴结转移病例(85.7%)。但是VEGF表达与患者年龄、性别、浸润深度以及远处器官转移不相关($P>0.05$,表2)。

表2 直肠癌组织VEGF表达与临床病理指标的关系

	n	VEGF表达强度	
		-	≥ +
性别			
男	22	2	20
女	38	4	34
年龄(岁)			
<50	16	1	15
≥50	44	5	39
肿瘤大小			
<5cm	23	3	20
≥5cm	37	3	24
肿瘤类型			
肿块型	4	0	4
溃疡型	33	4	29
浸润型	26	2	24
分化程度			
腺瘤癌变	3	3	0
高分化腺癌	18	2	16
中、低分化腺癌	23	1	22
黏液腺癌	13	0	13
印戒细胞癌	3	0	3
浸润深度			
肌层	27	3	24
全层	33	3	30
淋巴结转移			
无	28	4	24
有	32	2	30
远处转移			
无	59	6	53
有	1	0	1
Dukes分期			
A+B	30	4	26
C+D	30	2	28

3 讨论

直肠癌是消化道最常见的恶性肿瘤之一,约占大肠癌的60%,近年来发病率呈明显上升的趋势^[13]。手术根治性切除仍是直肠癌的主要治疗方法。Heald *et al*^[14-16]提出切除标本的直肠系膜完整无撕裂,在肉眼及镜下无切缘累及(circumference margin involvement, CMI)是判断根治手术是否成功的重要因素。TME的彻底与否须经病理医生严格检查后判定。“彻底的”TME须做到直肠远端系膜边缘(distal mesorectal margin, DMM)和直肠系膜周围切除边缘(circumferential resection margin, CRM)阴性。直肠系膜切除不足,CRM(+)常导致局部复发。DMM(+)及CRM(+)是肿瘤进展的预后因素。目前病理的“R”分级已取代传统的外科医生根据手

表1 VEGF的表达情况

分组		VEGF表达强度			
		-	+	++	+++
试验组	I	6	15	31	8
	II	60	0	0	0
	III	51	9	0	0
	IV	60	0	0	0
对照组	I'	53	7	0	0
	II'	60	0	0	0

术判定所谓的“治愈切除”的概念。直肠癌手术 R_0 代表直肠系膜完整切除, 且 CRM(-) 及 DMM(-); R_1 为镜下播散, 有癌残留; R_2 为肉眼播散, 有癌残留。理想的 TME 应做到 R_0 , 即直肠系膜的完整切除并且 CRM(-) 及 DMM(-)。但是“肉眼及镜下”的观察毕竟在一定程度上对发现微小转移灶有相当局限性^[17, 18]。肿瘤的浸润和转移是肿瘤细胞与细胞外基质 (ECM) 相互作用的结果^[19, 20], 此过程远远早于肉眼和常规病理切片检查所见^[21, 22]。肿瘤及其微小转移癌巢基质所分泌的 VEGF 不仅具有血管相和淋巴相作用, 还可以通过降低同质性黏附作用使肿瘤细胞容易从瘤体脱落, 并与基质的胶原纤维黏附, 有利于肿瘤细胞的运动和转移灶形成^[23-25]。而业已证实, VEGF 可以通过简单、廉价的免疫组化法检出^[26]。本试验显示, VEGF 在肿瘤及其累及区域表达为阳性或强阳性, 在正常组织中不表达或为弱阳性; VEGF 表达强度与直肠癌的分化程度、Dukes 分期及淋巴结转移密切相关, 但与患者的年龄、性别、肿瘤大小、部位、浸润深度以及远处器官转移没有明显相关性。我们通过对直肠癌组织及其周围组织的 VEGF 检测, 证明直肠癌存在着局部的累及^[27, 28]。直肠系膜远端切缘和直肠系膜周围切缘不仅在镜下未见癌细胞, 实现了 R_0 ^[29], 而且在分子水平上通过 VEGF 的表达证明了 CRM(-) 及 DMM(-)。由此在分子水平论证了 TME 在直肠癌治疗中的价值。与既往的方法相比, 本试验快捷、检出率高, 更能说明直肠癌存在局部病变, TME 彻底切除了直肠癌的局部病变。通过精确取材、减少试验步骤, 降低了假阴性和假阳性的发生几率, 提高了试验的准确性。

然而, 在本试验中, 我们观察到, 有 9 例标本直肠系膜周围切缘常规病理检查为阴性, 而采用免疫组化 S-P 法检测 VEGF 时结果却为阳性。这 9 例病例究竟是假阳性还是癌巢残留或仅表明其恶性程度更高, 尚需要更进一步的研究。

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• 临床经验 •

善宁对急性胰腺炎患者血小板参数变化的影响

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Effects of octreotide on platelet parameters in patients with acute pancreatitis

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Abstract

AIM: To investigate the changes of platelet parameters in patients with mild and severe acute pancreatitis (MAP and SAP) after treated with octreotide.

METHODS: The full-automatic blood cell counter was used to obtain the platelet count (PLT), mean platelet volume (MPV), and platelet distribution width (PDW) in the patients with MAP and SAP before and 1 wk after treatment with octreotide.

RESULTS: The platelet parameters of the patients with MAP were not significantly different from that of the normal controls. One week after treatment, there was still no significant change in the PLT. However, the

MPV and PDW were increased markedly (10.88 ± 2.40 vs 10.11 ± 1.66 , $P < 0.05$; 17.98 ± 4.41 vs 16.62 ± 1.38 , $P < 0.05$). In patients with SAP, the PLT was decreased markedly (161.61 ± 68.30 vs 191.60 ± 31.98 , $P < 0.05$), and the MPV and PDW were increased markedly (11.82 ± 2.33 vs 9.81 ± 0.79 , $P < 0.01$; 19.33 ± 7.07 vs 16.36 ± 0.51 , $P < 0.05$) as compared with those in the normal controls. One week after treatment, the PLT was notably elevated (251.61 ± 84.07 vs 161.61 ± 68.30 , $P < 0.01$), while the MPV and PDW were not changed ($P > 0.05$) as compared with those before treatment. For SAP, the PLT increased more (112.53 ± 89.31 vs 57.81 ± 68.24 , $P < 0.05$), and the MPV and PDW decreased more (1.29 ± 2.79 vs -0.17 ± 2.04 , $P < 0.01$; 2.75 ± 8.81 vs -0.89 ± 3.44 , $P < 0.01$) at 1 wk in the octreotide treatment patients as compared with those of general treatment ones.

CONCLUSION: The platelet parameters can reflect the severeness of acute pancreatitis. Octreotide can improve the microcirculation by decreasing MPV and PDW, increasing PLT.

Key Words: Acute pancreatitis; Octreotide; Platelet count; Mean platelet volume; Platelet distribution width

Huang J, Lu SQ, Chen JR. Effects of octreotide on platelet parameters in patients with acute pancreatitis. *Shijie Huaren Xiaohua Zazhi* 2005;13(18):2281-2283

摘要

目的: 研究血小板参数在轻症急性胰腺炎(MAP)与重症急性胰腺炎(SAP)中的变化特点及善宁治疗后对其的影响。