



doi:10.3978/j.issn.1005-6947.2015.08.023
http://dx.doi.org/10.3978/j.issn.1005-6947.2015.08.023
Chinese Journal of General Surgery, 2015, 24(8):1170-1174.

· 临床研究 ·

术前血清 CEA 和 CA19-9 水平检测对结肠癌术后 早期复发转移的预测价值

朱磊, 赵阳, 韩仕峰, 姜艳辉, 阚丽丽

(辽河油田总医院 普通外科, 辽宁 盘锦 124010)

摘要

目的: 探讨术前血清 CEA 与 CA19-9 水平在结肠癌根治术后早期复发转移的预测价值。
方法: 收集 2012 年 1 月—2015 年 1 月收治的 129 例术后发生复发转移结肠癌患者的临床资料, 分析术前静脉血清 CEA 和 CA19-9 水平与患者术后早期复发转移及其他临床病理学参数的关系。
结果: 129 例结肠癌患者中术后早期复发转移(术后 12 个月内) 82 例, 晚期复发转移(超过 12 个月) 47 例; 术前 CEA 阳性者 74 例中, 早期复发转移 56 例(75.8%), 术前 CA19-9 阳性者 68 例中, 早期复发转移 51 例(75.0%)。统计分析显示, 结肠癌术后早期复发转移与术前 CEA 与 CA19-9 阳性密切相关; 术前 CEA 和 CA19-9 阳性患者与 T 分期与 TNM 分期升高及淋巴结转移及脉管浸润比例增加; 术前 CEA 与 CA19-9 阳性患者术后早期复发转移率分别高于各自阴性患者, 且两者均阳性患者早期复发转移率高于单一阳性或双阴性患者, 差异均有统计学意义(均 $P < 0.05$)。
结论: 术前血清 CEA 与 CA19-9 水平检测在结肠癌术后早期复发转移和预后判断中具有重要价值, 术前两者均阳性患者预后差。

关键词

结肠肿瘤; 肿瘤标记, 生物学; 预后
中图分类号: R735.3

Predictive significance of preoperative serum CEA and CA19-9 determination in early recurrence/metastasis of colon cancer after operation

ZHU Lei, ZHAO Yang, HAN Shifeng, JIANG Yanhui, KAN Lili

(Department of General Surgery, Liaohe Oil Center Hospital, Panjin, Liaoning 124010, China)

Abstract

Objective: To investigate the value of serum CEA and CA19-9 in predicting early recurrence/metastasis of colon cancer after radical surgery.
Methods: The clinical data of 129 patients with postoperative recurrence and metastasis of colon cancer and treated from January 2012 to January 2015 were collected. The relations of preoperative CEA and CA19-9 levels with early postoperative recurrence/metastasis and other clinicopathologic variables were analyzed.
Results: Of the 129 patients, early recurrence/metastasis (within 12 months after surgery) occurred in 82 cases and another 47 cases had late recurrence/metastasis (over 12 months after surgery); early recurrence/

收稿日期: 2015-02-24; 修订日期: 2015-05-15。

作者简介: 朱磊, 辽河油田总医院主治医师, 主要从事普外科疾病方面的研究。

通信作者: 朱磊, Email: zhulei19862012@126.com

metastasis occurred in 56 of the 74 patients with positive preoperative CEA and 51 of the 68 patients with positive preoperative CA19-9. Statistical analyses showed that there was a close relationship between early postoperative recurrence/metastasis of colon cancer and preoperative CEA or CA19-9 level; the ratios of cases with advanced T or TNM stage, lymph node metastasis or vascular invasion was increased in patients with positive preoperative CEA or CA19-9. The rate of early postoperative recurrence/metastasis in patients with positive preoperative CEA or CA19-9 was significantly higher than that in corresponding negative ones, and in patients with both positive CEA and CA19-9 was significantly higher than that in either single positive or double negative ones, and all differences had statistical significance (all $P < 0.05$).

Conclusion: Preoperative determination of serum CEA and CA19-9 levels has important significance in predicting early postoperative recurrence/metastasis of colon cancer, and patients with both positive CEA and CA19-9 may face a poor prognosis.

Key words Colonic Neoplasms; Tumor Markers, Biological; Prognosis

CLC number: R735.3

结肠癌发病率位于西方国家中常见恶性肿瘤的第三位^[1],近年来在中国,结肠癌的发病率明显增加。目前,根治性手术仍然是结肠癌的主要治疗方法^[2-3]。虽然过去几十年来结肠癌的外科手术和药物治疗手段不断改善,但其预后仍然很差^[4-5],这主要归因于缺乏可靠的远处转移和局部复发的预测指标。选择具有高度敏感性和特异性的肿瘤学标记物识别远处转移和局部复发的高风险患者,从而为这类患者提供最佳的个体化化疗是今后的研究重点。血清CEA、CA19-9等肿瘤标志物在结肠癌诊断价值方面的研究较多,但关于其对结肠癌患者术后复发转移的影响报道较少。本研究通过回顾性分析结肠癌术前血清CEA和CA19-9水平,探讨其与结肠癌术后早期复发转移和预后的关系。

1 资料与方法

1.1 一般资料

2012年1月—2015年1月共收治129例术后发生复发转移的结肠癌患者,其中男68例,女61例;年龄 ≥ 65 岁65例, < 65 岁64例;依据国际抗癌联盟(UICC)TNM分期标准:I期22例,II期37例,III期41例,IV期29例。全部临床资料依靠患者术后定期返院复查获得,检查项目主要包括入院后次日晨血常规及血清肿瘤标志物检查,肺部CT、腹部增强CT及肠镜检查;129例复发患者中局部复发共39例,腹膜种植转移22例,局部复发+腹膜种植转移37例,远处转移31例;其中术后12个月内出现复发转移82例(早期组),超过

12个月后复发转移47例(晚期组)。

1.2 纳入标准和排除标准

纳入标准:年龄18~80岁;术前影像学检查未发现远处转移,择期行结肠癌根治术,术中证实腹腔内无转移或肝转移,术后病理学检查确诊为结肠癌;术前循环和呼吸系统无重大疾病,可耐受手术者;术前未行放化疗。

排除标准:年龄 < 18 岁或 > 80 岁以上者;术中探查有腹腔内多发转移或肝脏转移者;无法完成根治性切除者;围手术期相关研究指标未能完成检测者;合并其它脏器存在严重基础疾病者;随访不足3个月者。

1.3 方法

比较129例患者术前CEA和CA19-9两种肿瘤标志物数值,其中CEA ≥ 9.7 mg/mL定为阳性,CA19-9 ≥ 39 U/mL定为阳性。

1.4 统计学处理

用SPSS 13.0软件进行统计分析,计数资料应用 χ^2 检验。检验水准 $\alpha = 0.05$ 。

2 结果

2.1 结肠癌术后早期出现复发转移患者术前血清CEA、CA19-9水平

82例结肠癌术后早期出现复发转移患者术前血清CEA水平为5.7~920 mg/mL,中位水平为87.6 mg/mL,阳性率为68.3% (56/82);术前血清CA19-9水平为21~2 068 U/mL,中位水平为153.3 U/mL,阳性率为62.2% (51/82)。

2.2 结肠癌患者临床病理学参数与复发时间的关系

单因素分析结果显示, 结肠癌患者早期复发转移与术前血清 CEA 与 CA19-9 阳性有关 ($P=0.001$ 、 0.004), 而与其他病理参数关系不明显 (均 $P>0.05$) (表 1)。

表 1 129 例结肠癌术后复发转移患者的临床资料 [n (%)]

Table 1 Clinical data of the 129 colon cancer patients with postoperative recurrence/metastasis [n (%)]

因素	早期组 (n=82)	晚期组 (n=47)	P
性别			
男	43 (52.4)	25 (53.2)	0.934
女	39 (47.6)	22 (46.8)	
年龄 (岁)			
< 65	46 (56.1)	21 (44.7)	0.212
≥ 65	36 (43.9)	26 (55.3)	
术前 CEA			
(+)	56 (68.3)	18 (38.3)	0.001
(-)	26 (31.7)	29 (61.7)	
术前 CA19-9			
(+)	51 (62.2)	17 (36.2)	0.004
(-)	31 (37.8)	30 (63.8)	
肿瘤大小 (cm)			
< 5	37 (45.1)	20 (42.6)	0.777
≥ 5	45 (54.9)	27 (57.4)	
分化程度			
中高分化	38 (46.3)	20 (42.6)	0.677
低分化	44 (53.6)	27 (57.4)	
淋巴结转移			
有	49 (59.8)	24 (51.1)	0.338
无	33 (40.2)	23 (48.9)	
脉管浸润			
有	47 (57.3)	21 (44.7)	0.167
无	35 (42.7)	26 (55.3)	
T 分期			
T ₁ +T ₂	36 (43.9)	27 (57.4)	0.139
T ₃ +T ₄	46 (56.1)	20 (42.6)	
TNM 分期			
I+II	40 (48.8)	19 (40.4)	0.359
III+IV	42 (51.2)	28 (59.6)	
病理类型			
腺癌	24 (29.3)	15 (31.9)	0.229
黏液癌	31 (37.8)	20 (42.6)	
未分化癌	27 (32.9)	12 (25.5)	

2.3 血清 CEA 与 CA19-9 阳性与临床病理参数的关系

CEA 与 CA19-9 阳性均分别与 T 分期 ($P=0.028$ 、 0.013)、TNM 分期 ($P=0.021$ 、 0.026)、淋巴结转移 ($P=0.007$ 、 0.010) 及脉管浸润密切相关 ($P=0.019$ 、 0.028), 而均与性别、年龄、肿瘤大小、病理类型和分化程度无关 (均 $P>0.05$) (表 2)。

表 2 术后早期复发转移患者术前 CEA、CA19-9 阳性与相关因素关系分析 [n (%)]

Table 2 Analysis of the relations of positive preoperative CEA and CA19-9 with other clinicopathologic factors [n (%)]

因素	n	CEA 阳性组 (n=56)	P	CA19-9 阳性组 (n=51)	P
T 分期					
T ₁ +T ₂	36	19 (52.8)	0.028	17 (47.2)	0.013
T ₃ +T ₄	46	37 (80.4)		34 (73.9)	
TNM 分期					
I+II	40	22 (55.0)	0.021	20 (50.0)	0.026
III+IV	42	34 (81.0)		31 (73.8)	
淋巴结转移					
有	49	39 (79.6)	0.007	36 (73.5)	0.010
无	33	17 (51.5)		15 (45.5)	
脉管浸润					
有	47	37 (78.7)	0.019	32 (68.1)	0.028
无	35	19 (54.3)		19 (54.3)	

2.4 血清 CEA 和 CA19-9 阳性与结肠癌术后早期复发转移的关系

术前 CEA 阳性者 74 例, 其中早期复发转移者共 56 例 (75.7%); 术前 CA19-9 阳性者 68 例, 其中早期复发转移者共 51 例 (75.0%)。本研究显示, CEA 阳性组和 CA19-9 阳性组术后早期复发转移率分别高于 CEA 阴性组 ($P=0.001$) 和 CA19-9 阴性组 ($P=0.004$); 而 CEA/CA19-9 双阳性组术后早期复发转移率明显高于两者单一阳性及两者均阴性组 (均 $P<0.05$) (表 3)。

表 3 术前血清 CEA 和 CA19-9 阳性与结肠癌术后早期 (12 个月内) 复发转移的关系 [n (%)]

Table 3 Relationship between positive preoperative CEA and CA19-9 with early postoperative recurrence/metastasis (with 12 months after surgery) in colon cancer patients [n (%)]

指标	n	复发或转移	P
CEA			
(+)	74	56 (75.8)	0.001
(-)	55	26 (47.3)	
CA19-9			
(+)	68	51 (75.0)	0.004
(-)	61	31 (50.8)	
CEA/CA19-9			
(+)/(+)	43	36 (83.7)	0.035
(+)(-)	23	10 (43.5)	
(-)(+)	27	16 (59.3)	
(-)(-)	36	13 (36.1)	

3 讨论

结肠癌术后复发转移是影响其预后的重要因素,由于对于术后早期复发概念的定义不同,导致制定合理有效的治疗方案仍然存在一定困难,有学者^[6-7]将术后早期复发时间设定为术后2年,也有学者^[8-9]认为时间设定为术后3年以内更为合理,考虑到国内结肠癌确诊时间及手术时机等因素,本研究设定术后12个月以内发现的再发肿瘤病灶为术后早期复发转移。对于此类患者,若能够及时予以合理的治疗干预手段,可明显提升此类患者远期生存率。由此选取合适的预测指标成为结肠癌术后治疗的关键因素,CEA和CA19-9是目前用于胃肠道恶性肿瘤研究最多的血清肿瘤标志物。

CEA是一个相对分子质量为 1.8×10^5 的糖蛋白,是结肠癌患者最常用的血清肿瘤标志物之一。目前认为CEA与结肠癌的发生及其生物学行为存在密切关联,其敏感性与结肠癌的肿瘤分期呈密切相关^[10-11],进而认为血清CEA是术前检测结肠癌及预测术后复发转移的重要肿瘤标志物^[10]。CA19-9是糖类相关抗原之一,也是消化道肿瘤常用的血清肿瘤标志物之一,既往研究证实其在胰腺癌中表达异常增高,是胰腺癌早期诊断及判断预后的重要肿瘤标志物^[12-13]。近年来相关研究报道^[14-16],CA19-9在结肠癌中可明显增高,是影响其预后的重要因素之一。

有文献^[17-19]报道,血清CEA与结肠癌的T分期、TNM分期、淋巴结转移具有重要关联。本研究结果发现,术前血清CEA水平与结肠癌T分期、TNM分期、淋巴结转移和脉管浸润有关,同时 T_3+T_4 期、III+IV期和存在脉管浸润、淋巴结转移的结肠癌患者CEA阳性率明显高于 T_1+T_2 期、I+II期和无淋巴结转移及脉管浸润的结肠癌患者($P<0.05$)。本研究结果显示,血清CEA与结肠癌组织分化无关。有文献^[14-16]报道,CA19-9与结肠癌T分期、TNM分期和淋巴结转移有关,但也有研究^[20]认为术前CA19-9水平是否增高与结肠癌术后早期复发转移之间并无关联。本研究结果显示,CA19-9水平与结肠癌T分期、TNM分期和淋巴结转移有关, T_3+T_4 期、III+IV期和有淋巴结转移的患者CA19-9阳性率明显高于 T_1+T_2 期、I+II期和无淋巴结转移的结肠癌患者,与文献报道的基本一致。

有研究^[21-24]发现,CEA和CA19-9是结肠癌术后复发转移和预后的重要指标,术前血清CEA和CA19-9成倍增高的结肠癌患者预后更差。本研究结果发现,血清CEA和CA19-9水平与结肠癌术后复发转移和预后有关,CEA阳性组和CA19-9阳性组患者术后早期复发转移率均分别明显高于CEA阴性组和CA19-9阴性组患者;本研究同时还发现,CEA和CA19-9均为阳性的结肠癌患者术后早期复发转移率明显高于CEA阳性/CA19-9阴性、CEA阴性/CA19-9阳性和CEA和CA19-9均为阴性的结肠癌患者。本研究结果提示,术前联合检测血清CEA和CA19-9水平可能作为判定结肠癌术后早期复发转移和预后的指标。

近期有学者^[25]提出从外周静脉血中检测肿瘤标记物来判断肿瘤预后的方法并不可取,原因在于受到肿瘤细胞类型、肝脏代谢状态、外周血中肿瘤标记物浓度较低等因素影响,可导致其敏感性及其特异性受限,进而提出应在肿瘤附近的肠系膜静脉抽取测定,但尚需进一步研究论证。

综上所述,本研究结果提示,术前血清CEA和CA19-9水平检测在结肠癌术后早期复发转移和预后判断中具有重要价值,术前联合检测血清CEA和CA19-9水平有助于预测结肠癌术后早期复发转移及其预后^[26]。

参考文献

- [1] Siegel R, Ward E, Brawley O, et al. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths[J]. *CA Cancer J Clin*, 2011, 61(4):212-236.
- [2] Smith JA, King PM, Lane RH, et al. Evidence of the effect of 'specialization' on the management, surgical outcome and survival from colorectal cancer in Wessex[J]. *Br J Surg*, 2003, 90(5):583-592.
- [3] West NP, Hohenberger W, Weber K, et al. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon[J]. *J Clin Oncol*, 2010, 28(2):272-278.
- [4] Heinemann V, von Weikersthal LF, Decker T, et al. FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial[J]. *Lancet Oncol*, 2014, 15(10):1065-1075.
- [5] Saltz LB, Clarke S, Díaz-Rubio E, et al. Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line

- therapy in metastatic colorectal cancer: a randomized phase III study[J]. *J Clin Oncol*, 2008, 26(12):2013-2019.
- [6] Cho YB, Chun HK, Yun HR, et al. Clinical and pathologic evaluation of patients with recurrence of colorectal cancer five or more years after curative resection[J]. *Dis Colon Rectum*, 2007, 50(8):1204-1210.
- [7] Kobayashi H, Mochizuki H, Sugihara K, et al. Characteristics of recurrence and surveillance tools after curative resection for colorectal cancer: a multicenter study[J]. *Surgery*, 2007, 141(1):67-75.
- [8] Tsai HL, Chu KS, Huang YH, et al. Predictive factors of early relapse in UICC stage I-III colorectal cancer patients after curative resection[J]. *J Surg Oncol*, 2009, 100(8):736-743.
- [9] Aghili M, Izadi S, Madani H, et al. Clinical and pathological evaluation of patients with early and late recurrence of colorectal cancer[J]. *Asia Pac J Clin Oncol*, 2010, 6(1):35-41.
- [10] Polat E, Duman U, Duman M, et al. Diagnostic value of preoperative serum carcinoembryonic antigen and carbohydrate antigen 19-9 in colorectal cancer[J]. *Curr Oncol*, 2014, 21(1):e1-7.
- [11] Goldstein MJ and Mitchell EP. Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer[J]. *Cancer Invest*, 2005, 23(4):338-351.
- [12] Zhou G, Niu L, Chiu D, et al. Changes in the expression of serum markers CA242, CA199, CA125, CEA, TNF- α and TSGF after cryosurgery in pancreatic cancer patients[J]. *Biotechnol Lett*, 2012, 34(7):1235-1241.
- [13] Nakai Y, Isayama H, Sasaki T, et al. A retrospective analysis of early CA19-9 change in salvage chemotherapy for refractory pancreatic cancer[J]. *Cancer Chemother Pharmacol*, 2013, 72(6):1291-1297.
- [14] Lin PC, Lin JK, Lin CC, et al. Carbohydrate antigen 19-9 is a valuable prognostic factor in colorectal cancer patients with normal levels of carcinoembryonic antigen and may help predict lung metastasis[J]. *Int J Colorectal Dis*, 2012, 27(10):1333-1338.
- [15] Basbug M, Arikanoglu Z, Bulbuller N, et al. Prognostic value of preoperative CEA and CA 19-9 levels in patients with colorectal cancer [J]. *Hepatogastroenterology*, 2011, 58(106):400-405.
- [16] Shibutani M, Maeda K, Nagahara H, et al. Significance of CEA and CA19-9 combination as a prognostic indicator and for recurrence monitoring in patients with stage II colorectal cancer[J]. *Anticancer Res*, 2014, 34(7):3753-3758.
- [17] Jung TD, Yoo JH, Lee MJ, et al. Prognostic significance of the decreased rate of perioperative serum carcinoembryonic antigen level in the patients with colon cancer after a curative resection[J]. *Ann Coloproctol*, 2013, 29(3):115-122.
- [18] Lee WS, Baek JH, Kim KK, et al. The prognostic significant of percentage drop in serum CEA post curative resection for colon cancer[J]. *Surg Oncol*, 2012, 21(1):45-51.
- [19] Michl M, Koch J, Laubender RP, et al. Tumor markers CEA and CA 19-9 correlate with radiological imaging in metastatic colorectal cancer patients receiving first-line chemotherapy[J]. *Tumour Biol*, 2014, 35(10):10121-10127.
- [20] Morita S, Nomura T, Fukushima Y, et al. Does serum CA19-9 play a practical role in the management of patients with colorectal cancer?[J]. *Dis Colon Rectum*, 2004, 47(2):227-32.
- [21] Tsai HL, Cheng KI, Lu CY, et al. Prognostic significance of depth of invasion, vascular invasion and numbers of lymph node retrievals in combination for patients with stage II colorectal cancer undergoing radical resection[J]. *J Surg Oncol*, 2008, 97(5):383-387.
- [22] Yakabe T, Nakafusa Y, Sumi K, et al. Clinical significance of CEA and CA19-9 in postoperative follow-up of colorectal cancer[J]. *Ann Surg Oncol*, 2010, 17(9):2349-2356.
- [23] Holubec L Jr, Topolcan O, Pikner R, et al. Criteria for the selection of referential groups in tumor marker statistical evaluation on the basis of a retrospective study[J]. *Anticancer Res*, 2003, 23(2A):865-870.
- [24] Ryuk JP, Choi GS, Park JS, et al. Predictive factors and the prognosis of recurrence of colorectal cancer within 2 years after curative resection[J]. *Ann Surg Treat Res*, 2014, 86(3):143-151.
- [25] Peng Y, Zhai Z, Li Z, et al. Role of blood tumor markers in predicting metastasis and local recurrence after curative resection of colon cancer[J]. *Int J Clin Exp Med*, 2015, 8(1):982-990.
- [26] Yu H, Son GM, Joh YG. The clinical significance of preoperative serum levels of carbohydrate antigen 19-9 in colorectal cancer[J]. *J Korean Surg Soc*, 2013, 84(4):231-237.

(本文编辑 宋涛)

本文引用格式：朱磊，赵阳，韩仕峰，等. 术前血清CEA和CA19-9水平检测对结肠癌术后早期复发转移的预测价值[J]. 中国普通外科杂志, 2015, 24(8):1170-1174. doi:10.3978/j.issn.1005-6947.2015.08.023

Cite this article as: ZHU L, ZHAO Y, HAN SF, et al. Predictive significance of preoperative serum CEA and CA19-9 determination in early recurrence/metastasis of colon cancer after operation[J]. *Chin J Gen Surg*, 2015, 24(8):1170-1174. doi:10.3978/j.issn.1005-6947.2015.08.023