doi: 10.13241/j.cnki.pmb.2017.10.025

CRP 联合 CA72-4, CEA, CA19-9 检测对胃癌早期诊断的临床价值

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摘要 目的:探究 C 反应蛋白(CRP)联合胃癌抗原(CA72-4)、癌胚抗原(CEA)、糖类抗原(CA19-9)检测对胃癌早期诊断的临床价值。**方法:**选择 2014 年 3 月～2016 年 6 月我院收治的胃癌患者(103 例)为胃癌组,包括早期胃癌患者 30 例,中晚期患者 73 例;同期就诊于我院的良性胃病患者为良性胃病组(61 例),另选择 20 例年龄、性别相匹配的健康体检人群为健康对照组。比较三组人群血清 C 反应蛋白(CRP)、CA72-4、CEA、CA19-9 水平,并探讨其表达与胃癌患者临床病理特征之间的关系。**结果:**早期胃癌组、良性胃病组患者的血清 CRP、肿瘤标志物 CA72-4、CEA、CA19-9 的表达水平及阳性检测率均显著高于健康对照组(P＜0.05);早期胃癌组的上述指标显著高于良性胃病组(P＜0.05)。肿瘤分化程度低、发生转移、临床分期为Ⅲ,Ⅳ期胃癌患者的血清 CRP、CA72-4、CEA、CA19-9 阳性检测率显著高于肿瘤高分化、未发生转移、临床分期为Ⅰ、Ⅱ期的胃癌患者(p＜0.05)。血清 CRP、CA72-4、CEA、CA19-9 联合检测胃癌的敏感度 92.23%，特异度为 90.85%，联合检测敏感度显著高于 CRP (68.93%)、CA72-4 (71.84%)、CEA (77.67%)、CA19-9(59.22%)单项检测(p＜0.05)。**结论:**血清 CRP、CA72-4、CEA、CA19-9 水平与胃癌的临床病理特征密切相关,联合检测能显著提高检测灵敏度,有利于胃癌早期诊断。

关键词:胃癌;诊断;C 反应蛋白;胃癌抗原;癌胚抗原;糖类抗原
中图分类号:R735.2 **文献标识码:**A **文章编号:**1673-6273(2017)10-1896-04

Clinical Value of CRP combined with CA72-4, CEA, CA19-9 Detection in the Early Diagnosis of Gastric Cancer

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ABSTRACT Objective: To explore the clinical value of CRP combined with tumor marker detection in early diagnosis of gastric cancer. **Methods:** 103 patients treated and diagnosed as early gastric cancer in our hospital from March, 2014 to June, 2016 were enrolled in gastric cancer group, including early gastric cancer 30 cases, middle and advanced gastric cancer 73 cases; other 61 patients with benign gastric disease was enrolled in benign gastric disease group; another 20 health people was control group. The level of serum CRP, tumor markers were compared among three groups, and its relevance to clinical pathology of gastric cancer patients was also discussed. **Results:** The level and positive rate of serum CRP, CA72-4, CEA, CA19-9 of gastric cancer group and benign gastric disease group were significantly higher than control group, and those of gastric cancer group were obviously higher than benign gastric disease group (p＜0.05); gastric cancer patients with lower tumor differentiation, metastasis, Ⅲ, Ⅳ stages presented higher serum CRP, CA72-4, CEA, CA19-9 level (p＜0.05); the sensitivity and specificity of combined detection of serum CRP and CA72-4, CEA, CA19-9was 92.23% and 90.85%, respectively, which were significantly higher than single detection (p＜0.05). **Conclusion:** The level of serum CRP, CA72-4, CEA, CA19-9was closely related to clinical pathology, combined detection of serum CRP and CA72-4, CEA, CA19-9 could effective improve the sensitivity, which will benefit the early diagnosis of gastric cancer.

Key words: Gastric cancer; Diagnosis; CRP; Tumor marker; Clinical pathology
Chinese Library Classification(CLC): R735.2 Document code:A
Article ID:1673-6273(2017)10-1896-04

前言

胃癌是世界范围内高发的恶性肿瘤,中、韩、日三国是胃癌发病较为集中国家,占全球胃癌总数的 67%左右。我国胃癌发病率占全球 42%,每年新发病例 40 万左右,其中超 2/3 的患者死亡[1,2]。临床数据表明不同临床分期胃癌患者的 5 年生存率差异较大，胃癌早期经手术治疗的 5 年存活率可达 95%左右,进展期为 50%左右,晚期仅为 6%左右,由此可见胃癌早期治疗的重要性[3,4]。然而,我国胃癌患者早期诊断率较低,大部分患者就诊时病情已发展到进展期或晚期,这也是导致我国胃癌患者整

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(收稿日期:2016-12-07 接受日期:2016-12-30)

体生存率不高的重要因素。胃癌发病隐匿,早期症状与一般胃病无异,未能引起患者重视,加之侵入性检查手段(胃镜、病理、X 线等)对患者身心带来损伤,患者接受度普遍较低可能是胃癌早期诊断率低的重要原因[5,6]。因此,探寻检测方法简便、特异性强、灵敏度高的胃癌早期诊断方法势在必行。肿瘤标志物是恶性肿瘤基因的表达产物,已被用于多种肿瘤的检测。研究表明 C 反应蛋白(CRP)参与肿瘤病理发展过程,与肿瘤风险,预后密切相关[7,8]。本研究旨在探究 CRP 与肿瘤标志物联合检测在胃癌早期诊断中的临床价值。

1 资料与方法

1.1 一般资料

选择 2014 年 3 月～2016 年 6 月我院收治的胃癌患者 103 例为胃癌组,包括男性 60 例,女性 43 例,平均年龄(47.32± 5.03)岁,其中包括早期胃癌患者 30 例,中晚期患者 73 例,其他临床病理指征见表 3;同时选择同期就诊于我院的良性胃病患者 61 例为良性胃病组(包括胃溃疡 26 例、慢性浅表性胃炎 22 例、慢性萎缩性胃炎 8 例、急性胃炎 3 例、胃息肉 2 例),男性 36 例、女性 25 例,平均年龄(46.93± 4.65)岁;另外选择 20 例年龄、性别相匹配的健康体检人群为健康对照组。三组人群基线资料比较,差异无统计学意义(P＞0.05)。纳入标准:① 胃癌及良性胃部疾病均经胃镜或经组织病理确诊;② 所有受试人群的病历资料完整;③ 均与患者签署知情同意书,该研究获得我院伦理委员会批准。排除标准:① 合并其他恶性肿瘤;② 伴有免疫系统疾病;③ 合并内分泌、血液疾病。对 56 例胃癌患者术后 3 个月进行复诊,检查有无转移或复发。

1.2 检测方法

采集所有入组人员清晨空腹静脉血 5.0 mL，抗凝处理后,经离心获得血清标本。血清 CRP 采用全自动生化分析仪(罗氏 cobas8000)进行检测。采用化学发光法(罗氏 cobas e 602)检测血清肿瘤标志物 CEA、CA72-4、CA19-9 水平。

1.3 评定标准

各指标正常值参考范围界定如下:CRP≤ 10 mg/L,CA72-4≤ 6.9 U/mL,CEA≤ 5.0 ng/mL,CA19-9≤ 39 U/mL。每项指标检测值超过正常值均视为阳性。联合检测时,其中一项阳性则判定为联合检测阳性;每一项均为阴性时,联合检测才判定为阴性。敏感度定义为:胃癌组阳性病例数与胃癌组患者总例数的比值;特异度定义为:对照组与良性胃病组阴性病例数之和与该两组总病例数的比值。

1.4 统计学分析

使用 SPSS18.0 软件,计数资料采用卡方检验、计量资料以 " 均数± 标准差 " 表示,多组间比较采用方差分析检验,两两比较采用 SNK-q 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 三组血清 CRP、CA72-4、CEA、CA19-9 水平的比较

早期胃癌组、良性胃病组患者的血清 CRP、CA72-4、CEA、CA19-9 水平均显著高于健康对照组 (P＜0.05)，早期胃癌组 CA72-4、CEA、CA19-9 水平显著高于良性胃病组(P＜0.05)。

表 1 三组血清 CRP、CA72-4、CEA、CA19-9 水平比较($\bar{x}$± s)

Table 1 Comparison of the levels of serum CRP, CA72-4, CEA, CA19-9 among three groups ($\bar{x}$± s)

Groups	Number	CRP (mg/L)	CA72-4(U/mL)	CEA (ng/mL)	CA19-9 (U/mL)
Early gastric cancer group	30	19.77± 3.21[a]	23.71± 2.53[ab]	25.42± 1.37[ab]	51.94± 2.46[ab]
Benign gastric disease group	61	16.92± 5.26[a]	5.27± 3.29[a]	4.07± 0.80[a]	27.32± 3.29[a]
Health control group	20	1.8± 0.3	4.6± 1.2	3.61± 0.29	23.33± 3.21

Note: compared with health control group, [a]P<0.05; compared with benign gastric disease group, [b]P<0.05.

2.2 三组血清 CRP、CA72-4、CEA、CA19-9 检测阳性率比较

早期胃癌组、良性胃病组患者的血清 CRP、CA72-4、CEA、CA19-9 阳性检出率显著高于健康对照组(P＜0.05),早期胃癌组 CA72-4、CEA、CA19-9 阳性检出率显著高于良性胃病组(P＜0.05)。

表 2 三组血清 CRP、CA72-4、CEA、CA19-9 的阳性检出率比较[例(%)]

Table 2 Comparison of the positive rate of serum CRP, CA72-4, CEA, CA19-9 among three groups[n(%)]

Groups	Number	CRP	CA72-4	CEA	CA19-9
Early gastric cancer group	30	13(43.33)[a]	12(40.00)[ab]	14(46.67)[ab]	11(36.67)[ab]
Benign gastric disease group	61	29(47.54)[a]	13(21.31)[a]	11(18.33)[a]	8(13.11)[a]
Health control	20	3(15)	2(10)	1(5)	0(0)

Note: compared with health control group, [a]P<0.05; compared with benign gastric disease group, [b]P<0.05.

2.3 血清 CRP、CA72-4、CEA、CA19-9 水平与胃癌患者临床病理特征的相关性

肿瘤分化程度低、发生转移、临床分期为Ⅲ、Ⅳ期胃癌患者的血清 CRP、CA72-4、CEA、CA19-9 阳性检出率显著高于肿瘤高分化、未发生转移、临床分期为Ⅰ、Ⅱ期的胃癌患者 (p＜0.05)。

表 3 不同临床病理胃癌患者血清 CRP、CA72-4、CEA、CA19-9 检测阳性率比较[例(%)]

Table 3 Comparison of the positive rate of serum CRP, CA72-4, CEA, CA19-9 between gastric cancer patients with different clinicopathological charateristics[n(%)]

Pathological characteristics	Number 103	CRP 71	CA72-4 74	CEA 80	CA19-9 61
Tumor differentiation					
Medium, High	45	21(46.67)	22(48.89)	25(55.56)	16(35.56)
Low	58	50(86.21)[a]	52(89.66)[a]	55(94.83)[a]	45(77.58)a
Metastasis					
Yes	70	58(82.86)[b]	62(88.57)[b]	67(95.71)[b]	54(77.14)[b]
No	31	13(41.94)	12(38.71)	13(41.94)	7(22.58)
TNM Stages					
Ⅰ,Ⅱ	30	13(43.33)c	12(40.00)[c]	14(46.67)[c]	11(36.67)c
Ⅲ	34	26(76.47)	28(82.35)	30(88.23)	23(67.65)
Ⅳ	39	32(82.05)	34(87.18)	36(92.30)	27(69.23)

Note: compared with medium, high tumor differentiation, [a]P<0.05; compared with nometastasis, [b]P<0.05; compared with Ⅲ, Ⅳclinical stages, [c]P<0.05.

2.4 血清 CRP、CA72-4、CEA、CA19-9 联合检测在胃癌诊断中的作用

血清 CRP、CA72-4、CEA、CA19-9 联合检测胃癌的敏感度 92.23%，特异度为 90.85%，联合检测敏感度显著高于 CRP(68.93%)、CA72-4(71.84%)、CEA(77.67%)、CA19-9(59.22%)单项检测(p＜0.05)。

表 4 血清 CRP、CA72-4、CEA、CA19-9 联合检测在胃癌诊断中的作用(%)

Table 4 Effect of CRP combined with CA72-4, CEA, CA19-9detection in gastric cancer diagnosis (%)

Items	Sensitivity	Specificity
CRP	68.93	60.49
CA72-4	71.84	81.48
CEA	77.67	85.19
CA19-9	59.22	90.12
CRP+CA72-4+CEA+CA19-9	92.23[a]	90.85

Note: compared with single detection, [a]P<0.05.

3 讨论

肿瘤标志物是肿瘤细胞分泌的代谢产物的总称，分布在患者的肿瘤组织或体液中，在正常成人组织中表达极低，仅在胚胎组织中存在[9]。糖蛋白癌胚抗原(CEA)是一种广谱肿瘤标志物，临床检测发现其在多种癌症组织中均有较高的表达水平，在胃癌中其初检阳性率在 20%～79%左右，且伴随肿瘤转移，晚期患者的 CEA 水平更高[10,11]。胃癌抗原(CA72-4)是高分子黏蛋白，对胃肠道肿瘤、卵巢粘液性腺癌、非小细胞肺癌较为敏感，对胃癌的检测特异性较高，与 CA19-9 联合检测，阳性率显著升高，并且对肿瘤复发、淋巴结受累具有提示作用[12-14]。与 CA72-4 类似，CA19-9 亦是一种糖蛋白，在胰腺癌、肝胆系癌、胃癌、结直肠癌组织中其表达量明显升高，临床研究显示，其表达水平与肿瘤临床分期密切相关，可对 CA19-9 水平小于 1000 U/mL 的胰腺癌患者中约 55%可通过手术切除肿瘤，超过 88%的 CA19-9 水平大于 1000 U/mL 的胰腺癌患者无法切除肿瘤[15-17]。C 反应蛋白(CRP)是由肝细胞合成的急性蛋白在机体处于炎症状态时表达量升高。近年来，在肿瘤患者血清中发现 CRP 的合成量加大，推测与肿瘤细胞坏死、浸润正常组织造成局部组织损伤而导致炎症反应有关，有研究表明 CRP 水平与胃癌腹腔转移、晚期胃癌预后不良密切相关[18-20]。

本研究结果显示胃癌患者的血清肿瘤标志物 CA72-4、CEA、CA19-9 阳性检测率显著高于健康对照组，且与其临床病理特征密切相关，肿瘤分化程度低、发生转移、临床分期为Ⅲ，Ⅳ期胃癌患者的上述指标阳性检测率明显较高，提示其对于诊断和预测胃癌预后具有重要的临床意义。现阶段针对肿瘤的血清学检测主要还是倾向于肿瘤标志物检测，CRP 检测较少。采用 CRP 与肿瘤标志物联合检测胃癌，结果显示血清肿瘤标志物联合 CRP 检测胃癌的敏感度 92.23%，特异度为 90.85%，联合检测敏感度显著高于单项检测。

综上所述，血清 CRP、CA72-4、CEA、CA19-9 水平与胃癌的临床病理密切相关，联合检测能显著提高检测灵敏度，有利于胃癌早期诊断。

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