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胃癌患者血清 CA125、CA724、CEA、CA199 水平的表达及与临床病理特征的关系研究 *

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摘要 目的:研究胃癌患者血清糖链抗原 125（CA125）、糖链抗原 724（CA724）、癌胚抗原（CEA）、糖链抗原 199（CA199）水平的表达及与临床病理特征的关系。**方法:**选取 2016 年 5 月 -2017 年 8 月我院收治的胃癌患者 94 例记为胃癌组，胃部良性病变患者 82 例记为良性病变组，另取同期于我院接受体检的健康志愿者 80 例记为对照组。分别测定三组受试者血清 CA125、CA724、CEA、CA199 水平，并分析上述指标与胃癌患者临床病理特征的关系，并观察胃癌患者各指标单独检测和联合检测的阳性率。**结果:**三组受试者血清 CA125、CA724、CEA、CA199 水平整体比较差异有统计学意义（P<0.05），胃癌组、良性病变组、对照组的血清 CA125、CA724、CEA、CA199 水平呈逐渐降低趋势，两两对比差异有统计学意义（P<0.05）。不同性别的胃癌患者 CA125、CA724、CEA、CA199 水平比较差异无统计学意义（P>0.05），年龄 >60 岁、TNM 分期为Ⅲ-Ⅳ期、肿瘤大小≥ 5 cm^2 的胃癌患者 CA125、CA724、CEA、CA199 水平均高于年龄≤ 60 岁、TNM 分期为Ⅰ-Ⅱ期、肿瘤大小 <5 cm^2 的胃癌患者，差异有统计学意义（P<0.05）。联合检测的胃癌阳性率高于 CA125、CA724、CEA、CA199 单独检测，且 CA724 单独检测高于 CA125、CEA、CA199 单独检测，差异有统计学意义（P<0.05）。**结论:**胃癌患者血清 CA125、CA724、CEA、CA199 水平较高，与患者的年龄、TNM 分期、肿瘤大小等因素有关，且联合检测的胃癌检出率较高，可为胃癌的早期诊断提供指导作用。

关键词:胃癌；糖链抗原 125；糖链抗原 724；癌胚抗原；糖链抗原 199；病理特征

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Expression of Serum CA125, CA724, CEA, CA199 Levels in Patients with Gastric Cancer and Its Relationship with Clinicopathological Features*

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ABSTRACT Objective: To investigate the expression of serum carbohydrate antigen 125 (CA125), carbohydrate antigen 724 (CA724), carcinoembryonic antigen (CEA) and carbohydrate antigen 199 (CA199) levels in patients with gastric cancer and its relationship with clinicopathological features. **Methods:** 94 patients with gastric cancer who were treated in our hospital from May 2016 to August 2017 were selected as gastric cancer group, and 82 patients with benign gastric lesions were selected as benign lesions group. In addition, 80 healthy volunteers who were received medical examination in our hospital at the same time were selected as the control group. The levels of serum CA125, CA724, CEA and CA199 of subjects in three groups were measured, and the relationship between the above indexes and the clinicopathological features of gastric cancer were analyzed. The positive rate of alone and combined detection of each indexes in patients with gastric cancer was observed. **Results:** There was statistically significant difference in overall comparison of serum CA125, CA724, CEA and CA199 in the three groups (P<0.05). The levels of serum CA125, CA724, CEA and CA199 in gastric cancer group, benign lesion group and control group were decreased gradually, and the difference between each groups was statistically significant (P<0.05). There was no significant difference in the levels of CA125, CA724, CEA and CA199 in patients with gastric cancer with different sex (P>0.05). The levels of serum CA125, CA724, CEA and CA199 in patients with gastric cancer with age >60 years old, TNM stage III - IV stage, tumor size ≥ 5 cm^2 were higher than that of age ≤ 60 years old, TNM stage I-II stage and tumor size <5 cm^2, the difference was statistically significant (P<0.05). The positive rate of combined detection of gastric cancer was higher than that of CA125, CA724, CEA and CA199 alone, and the positive rate of CA724 alone was higher than that of CA125, CEA and CA199 alone, the difference was statistically significant (P<0.05). **Conclusion:** The levels of serum CA125, CA724, CEA and CA199 are higher in patients with gastric cancer, which are related to the age, TNM stage and tumor size. The combined detection rate of gastric cancer is higher, which can provide guidance for early diagnosis of gastric cancer.

Key words: Gastric cancer; Sugar chain antigen 125; Sugar chain antigen 724; Carcinoembryonic antigen; Sugar chain antigen 199; Pathological features

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前言

胃癌属于临床上最为常见的消化系统恶性肿瘤之一，由于该病发病早期具有较强的隐匿性，因此绝大部分患者属于中晚期，无法耐受手术根治，故预后较差[1-3]。而早期有效的诊断并给予针对性治疗可以抑制肿瘤进展，从而提高患者的生存率[4]。由此，寻找一种有效的临床诊断方式显得尤为重要。血清肿瘤标志物是目前临床上研究的热点，其属于肿瘤相关抗原，一般存在于肿瘤患者的排泄物、体液、组织中，可反映肿瘤的发生、发展[5-7]。通过监测血清肿瘤标志物水平以诊断肿瘤发展情况的方式具有简便、实用、可重复性较高等优势，已在临床上开始被广泛应用[8,9]。鉴于此，本文通过研究胃癌患者血清糖链抗原 125（CA125）、糖链抗原 724（CA724）、糖链抗原 199（CA199）、癌胚抗原（CEA）水平的表达及与临床病理特征的关系，旨在为临床诊治提供数据支持，现作以下报道。

1 资料与方法

1.1 一般资料

将 2016 年 5 月到 2017 年 8 月于我院住院治疗的胃癌患者 94 例纳入胃癌组。纳入标准[10]：（1）所有患者均经病理诊断确诊为胃癌；（2）入组前未行抗肿瘤治疗者；（3）年龄均 >20 岁；（4）患者的病历资料基本完整；（5）患者已签署知情同意书。排除标准：（1）伴有自身免疫性疾病者；（2）存在精神疾病或交流沟通障碍者；（3）合并其他恶性肿瘤疾病者。其中男性 50 例，女性 44 例，年龄 32-78 岁，平均年龄（61.25± 10.16）岁；TNM 分期：Ⅰ-Ⅱ期 32 例，Ⅲ-Ⅳ期 62 例；肿瘤大小：<5 cm^2 有 45 例，≥ 5 cm^2 有 49 例。另取同期我院收治的胃部良性病变患者 82 例记为良性病变组，其中男性患者 46 例，女性患者 36 例，年龄 33-75 岁，平均年龄（60.53± 10.72）岁。再取同期于我院接受体检的健康志愿者 80 例记为对照组，其中男性 42 例，女性 38 例，年龄 30-76 岁，平均年龄（62.19± 10.83）岁。三组性别、年龄比较，差异无统计学意义（P>0.05），均衡可比。本研究已获我院伦理委员会授权。

1.2 研究方法

两组患者在入组后均为其采集晨间的空腹静脉血约 5 mL，对照组则于体检时采集清晨空腹静脉血 5 mL，以 3000 r/min 离心 10 min，取上层血清保存于 -80℃冰箱中待检。采用全自动电化学发光免疫分析仪（罗氏公司，型号 cobas e601）分别测定三组受试者血清 CA125、CA724、CEA、CA199 水平，相关试剂盒均购自上海酶联科技有限公司，具体操作严格按照试剂盒说明书进行。阳性检测标准如下：CA125>35 U/ml，CA724>9.8 U/mL，CEA>3.4 ng/mL，CA199>39 U/mL，联合检测中若有一项指标为阳性，即判断为阳性。

1.3 观察指标

对比三组受试者血清 CA125、CA724、CEA、CA199 水平，分析上述血清 CA125、CA724、CEA、CA199 与胃癌患者临床病理特征的关系，并观察胃癌患者各指标单独检测和联合检测的阳性率。

1.4 统计学方法

本文数据均以 SPSS20.0 软件统一进行统计分析，计量资料以（$\bar{x}$± s）表示，实施 t 检验，多组间对比予以单因素方差分析，计数资料以[n(%)]表示，实施 x^2 检验，检验水准设置为 α=0.05。

2 结果

2.1 三组受试者血清 CA125、CA724、CEA、CA199 水平对比

三组受试者血清 CA125、CA724、CEA、CA199 水平整体比较差异有统计学意义（P<0.05），胃癌组、良性病变组、对照组的血清 CA125、CA724、CEA、CA199 水平呈逐渐降低趋势，两两对比差异有统计学意义（P<0.05），见表 1。

表 1 三组受试者血清 CA125、CA724、CEA、CA199 水平对比（$\bar{x}$± s）

Table 1 Comparison of serum CA125, CA724, CEA, and CA199 levels of subjects in the three groups ($\bar{x}$± s)

Groups	n	CA125（U/mL）	CA724（U/mL）	CEA（ng/mL）	CA199（U/mL）
Gastric cancer group	94	48.56± 8.13^{ab}	43.81± 6.78^{ab}	24.79± 5.09^{ab}	52.98± 8.17^{ab}
Benign lesion group	82	14.62± 3.15^{a}	7.02± 2.12^{a}	3.88± 2.45^{a}	18.56± 4.24^{a}
Control group	80	10.85± 2.63	4.73± 1.36	2.64± 1.43	4.39± 1.65
F	-	32.922	29.503	20.842	41.285
P	-	0.000	0.000	0.000	0.000

Note: compared with the control group, ^{a}P<0.05, compared with the benign lesion group, ^{b}P<0.05.

2.2 血清 CA125、CA724、CEA、CA199 水平与胃癌患者临床病理特征关系分析

不同性别的胃癌患者 CA125、CA724、CEA、CA199 水平比较差异无统计学意义（P>0.05），年龄 >60 岁、TNM 分期为Ⅲ-Ⅳ期、肿瘤大小≥ 5 cm^2 的胃癌患者 CA125、CA724、CEA、CA199 水平均高于年龄≤ 60 岁、TNM 分期为Ⅰ-Ⅱ期、肿瘤大小 <5 cm^2 的胃癌患者，差异有统计学意义（P<0.05），见表 2。

2.3 胃癌患者各指标单独检测和联合检测的阳性率对比

联合检测的胃癌阳性率高于 CA125、CA724、CEA、CA199 单独检测，且 CA724 单独检测高于 CA125、CEA、CA199 单独检测，差异有统计学意义（P<0.05），见表 3。

3 讨论

相关研究报道显示，随着近年来人们生活水平的不断提高以及饮食习惯的逐渐改变，我国的胃癌发病率不仅逐年升高，而且更趋年轻化，对人们生命健康影响巨大[11]。临床上首次就

表 2 血清 CA125、CA724、CEA、CA199 水平与胃癌患者临床病理特征关系分析[n(%)]

Table 2 Analysis of the relationship between serum CA125, CA724, CEA, CA199 levels and the clinicopathological features of patients with gastric cancer[n (%)]

Features		n	CA125(U/mL)	CA724(U/mL)	CEA(ng/mL)	CA199(U/mL)
Gender	Male	50	48.32± 8.25	44.28± 7.52	24.26± 5.50	51.43± 8.22
	Female	44	49.21± 8.43	43.69± 6.47	25.31± 5.11	53.01± 8.05
Age (years)	≤ 60	41	40.69± 7.52	40.52± 6.21	20.55± 4.32	40.35± 7.52
	>60	53	58.23± 9.05[a]	51.85± 8.02[a]	29.55± 5.51[a]	61.72± 8.51[a]
TNM stage	Ⅰ-Ⅱstage	32	41.32± 7.64	41.71± 7.15	19.83± 4.92	42.83± 6.56
	Ⅲ-Ⅳstage	62	54.45± 8.66[b]	50.62± 7.96[b]	26.51± 6.16[b]	60.15± 8.33[b]
Tumor size(cm^2)	<5	45	42.76± 7.52	39.55± 7.02	21.72± 4.73	43.22± 7.06
	≥ 5	49	55.11± 8.65[c]	50.72± 8.20[c]	28.26± 6.02[c]	59.14± 8.62[c]

Note: compared with ≤ 60 years old, [a]P<0.05; compared with TNM stage I-II stage, [b]P<0.05; compared with tumor size <5 cm^2, [c]P<0.05.

表 3 胃癌患者各指标单独检测和联合检测的阳性率对比

Table 3 Comparison of the positive rates of alone and combined detection of patients with gastric cancer

Detection indexes	Positive detection number(n)	Positive rate(%)
CA125	46	48.94ab
CA724	67	71.28a
CEA	49	52.13ab
CA199	51	54.26ab
Combined detection	82	87.23

Note: compared with combined detection, [a]P<0.05; compared with CA724, [b]P<0.05.

诊的胃癌患者中,早期诊断率低于 10%,其中有 85%以上患者均为中晚期[12,13]。而导致这一结果发生的原因较多,其中最主要的原因是临床上迄今为止缺乏特异性与敏感性较高的诊断手段。有报道显示[14-16],血清肿瘤标志物水平会随肿瘤的进展而发生变化,其可被用于恶性肿瘤的临床诊断、鉴别中。血清肿瘤标志物水平的检测具有操作简便、可重复性较高、对患者造成的创伤较小等优势,并且肿瘤标志物可在一定程度上反映胃癌的发生、发展过程,有研究发现,联合检测肿瘤标志物可提高胃癌的检查率,可为早期诊断以及早期治疗提供指导依据[17-19]。

本研究结果显示，胃癌组、良性病变组、对照组的血清 CA125、CA724、CEA、CA199 水平呈逐渐降低趋势(P<0.05),提示了胃癌患者血清 CA125、CA724、CEA、CA199 水平存在明显高表达。究其原因,CA125 属于非特异性肿瘤标志物,是一种主要存在于卵巢癌细胞系中的抗原,同时其含量在多种妇科恶性肿瘤以及消化道肿瘤中均异常升高[20-22]。CA724 属于具有高分子量的一种糖蛋白,亦是近年来临床上所开展的一种新型肿瘤标志物,具有较佳的检测特异性,且在消化道肿瘤的检测中具有较高的价值[23,24]。CEA 是一种具有人类胚胎抗原特性的酸性糖蛋白,是细胞膜的结构蛋白,主要存在于消化道与胚胎肝、肠、胰腺组织中，是临床上应用最为广泛的肿瘤标志物[25-27]。CA199 则是一种糖抗原,在多种消化道恶性肿瘤中具有较多的合成,一般以黏蛋白的形式存在于血清中,同时其水平变化受肿瘤的大小、转移以及浸润的影响,是具有高度特异性的消化道肿瘤标记物之一[28-30]。此外,年龄 >60 岁、TNM 分期为Ⅲ-Ⅳ期、肿瘤大小≥ 5 cm^2 的胃癌患者 CA125、CA724、CEA、CA199 水平均高于年龄≤ 60 岁、TNM 分期为Ⅰ-Ⅱ期、肿瘤大小 <5 cm^2 的胃癌患者,差异有统计学意义(P<0.05)。这提示了上述四项血清学指标与胃癌患者的年龄、肿瘤临床分期、肿瘤大小均存在密切相关,且随着年龄的不断增长、病情的逐渐加重,上述四项血清学指标水平显著升高。因此,在临床工作中我们可能通过对上述指标水平进行检测,从而有效诊断胃癌,并判断胃癌患者的病情严重程度,进一步为临床治疗方案的制定提供参考依据。本研究结果还显示，联合检测的胃癌阳性率高于 CA125、CA724、CEA、CA199 单独检测,且 CA724 单独检测高于 CA125、CEA、CA199 单独检测(P<0.05)。这表明了联合检测可有效提高临床检出率,具有较高的临床应用价值,这也为今后胃癌诊断方向的研究提供了新思路。

综上所述，胃癌患者血清 CA125、CA724、CEA、CA199 水平存在明显高表达,且与临床病理特征有密切关系,临床上可通过联合检测上述四项指标水平,从而判断胃癌患者的病情严重程度,亦为临床胃癌的治疗以及预后评估提供了新的靶点与思路。

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