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血清 NSE、TSGF、FERR 及 CA125 联合检测对卵巢癌的诊断价值

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[摘　要]　**目的：**探讨血清神经元特异性烯醇化酶(neuron-specific enolase，NSE)、恶性肿瘤特异生长因子(tumor specific growth factor，TSGF)、铁蛋白(Ferritin，FERR)及糖类抗原125(carbohydrate antigen 125，CA125) 4种血清肿瘤标志物联合检测对卵巢癌的诊断价值。**方法：**选取2018年3月至2020年3月青海省第五人民医院收治的50例卵巢癌患者作为卵巢癌组，43例卵巢良性病变患者作为良性病变组，选取同期37例健康体检女性患者作为对照组。检测3组血清TSGF、CA125、NSE及FERR水平，评价各血清肿瘤标志物的敏感度和特异度；采用ROC曲线分析TSGF、CA125、NSE及FERR 4项肿瘤标志物联合检测对卵巢癌的诊断价值。**结果：**卵巢癌组患者血清肿瘤标志物TSGF、CA125、NSE及FERR水平均高于对照组及良性病变组，差异均有统计学意义(P<0.05)；卵巢癌组TSGF、CA125、NSE及FERR 4种血清肿瘤标志物单项检测阳性率均高于良性病变组及对照组，差异均有统计学意义(P<0.05)；4种血清肿瘤标志物联合检测阳性率为82.0%均高于任一单项肿瘤标志物检测阳性值，差异有统计学意义(P<0.05)；4种肿瘤标志物联合检测对卵巢癌的诊断曲线下面积为0.913，敏感度为82%，特异度为81.40%，敏感度和曲线下面积均高于4项血清肿瘤指标单独检测的诊断价值。**结论：**CA125、CEA、NSE及TSGF联合检测能明显提高卵巢癌诊断的灵敏度和准确度，其诊断价值高于单一肿瘤标志物检测。

[关键词]　卵巢癌；肿瘤标志物；联合检测；诊断价值

Diagnostic value of combined detection of serum NSE, TSGF, FERR and CA125 in ovarian cancer

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Abstract　**Objective:** To investigate the diagnostic value of combined detection of serum neuron-specific enolase (NSE), malignant tumor-specific growth factor (TSGF), ferritin (FERR) and carbohydrate antigen 125 (CA125) in ovarian cancer. **Methods:** From March 2018 to March 2020, 50 patients with ovarian cancer admitted to our hospital were selected as the ovarian cancer group, 43 patients with benign ovarian lesion as the benign lesions

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group, and 37 healthy female patients in the same period were selected as the control group. Detect three groups of serum TSGF, CA125, NSE, FERR levels to evaluate the sensitivity and specificity of each serum tumor marker; use ROC curve to analyze TSGF, CA125, NSE, FERR and the combined detection of four tumor markers for the diagnosis value of ovarian cancer. **Results:** The serum tumor markers TSGF, CA125, NSE and FERR levels in the ovarian cancer group were higher than those in the control group and the benign lesion group, and the differences were statistically significant (P<0.05); the positive rate of single detection of TSGF, CA125, NSE and FERR in the ovarian cancer group was higher than that in the benign lesion group and the control group, the difference was statistically significant (P<0.05); the positive rate of combined detection of 4 serum tumor markers was 82.0%, which was higher than that of any single tumor and the difference was statistically significant (P<0.05); the area under the curve for the diagnosis of ovarian cancer by the combined detection of four tumor markers was 0.913, with the sensitivity of 82% and the specificity of 81.40%, and the sensitivity and the area under the curve were higher than those of the four serum tumor indicators separately detected. **Conclusion:** The combined detection of CA125, CEA, NSE and TSGF can significantly improve the sensitivity and accuracy of ovarian cancer diagnosis, and its diagnostic value is higher than that of single tumor marker detection.

Keywords ovarian cancer; tumor markers; combined detection; diagnostic value

卵巢癌是女性生殖器官常见的恶性肿瘤之一，其发病率仅次于宫颈癌及宫体癌，可扩散至子宫、大网膜等重要器官，严重者可危及生命，致死率较高[1-2]。因卵巢位于盆腔深部、卵巢癌临床早期无症状且早期缺乏有效的诊断方法，初诊处于晚期的患者可达60%~70%，且治疗后易复发，预后不佳，因此早期明确诊断卵巢癌可极大影响患者预后[3]。目前，临床主要经病理检查确诊卵巢癌，但病理检查是有创检查，因此不适宜作为筛查手段。肿瘤标志物由肿瘤细胞基因表达或人体对肿瘤细胞反应而产生，可在血清、体液、组织及排泄物中检测到，是一类反映肿瘤存在和生长的物质，多用于肿瘤的早期诊断[4]。但检测单一肿瘤标志物的敏感度和特异度多难以满足疾病的诊断要求，漏诊及误诊率较高，因此寻求高诊断效能的肿瘤标志物或联合检测肿瘤标志物是提高卵巢癌诊断效能的关键，进而改善预后[5]。本文探讨血清神经元特异性烯醇化酶(neuron-specific enolase，NSE)、恶性肿瘤特异生长因子(tumor specific growth factor，TSGF)、铁蛋白(Ferritin，FERR)及糖类抗原125(carbohydrate antigen 125，CA125)4种血清肿瘤标志物联合检测对卵巢癌的诊断价值。

1 对象与方法

1.1 对象

选取2018年3月至2020年3月青海省第五人民医院收治的经病理确诊为卵巢癌的50例患者作为卵巢癌组，经病理确诊为卵巢良性病变的43例患者作为良性病变组，选取同期37例健康体检女性患者作为对照组。卵巢癌组：年龄38~71(51.4±9.27)岁，卵巢上皮性癌41例，输卵管癌6例，性索间质肿瘤3例；根据国际妇科联盟手术病理分期标准I~II期35例，III~IV期15例。良性病变组：年龄42~69(49.8±10.93)岁，良性畸胎瘤18例，卵巢子宫内膜异位囊肿10例，卵泡膜细胞瘤7例，黏液性囊腺瘤8例。对照组年龄34~68(52.3±11.21)岁。对照组患者无心、肝、肾等重要器官的疾病，肝肾功能正常。3组年龄比较，差异无统计学意义(P>0.05)，具有可比性。本临床研究经过青海省第五人民医院医学伦理委员会批准，患者均签署知情同意书。

1.2 方法

采集3组患者晨起空腹静脉血5 mL，3 000 r/min低温离心5 min，取上层血清，置−20 ℃冰箱保存备用。采用奥林巴斯AU5400自动生化分析仪及酶联免疫吸附试剂盒检测3组血清TSGF，DXI800贝克曼免疫分析仪及其配套试剂盒检测3组血清CA125，采用美国罗氏公司的电化学发光免疫分析仪及配套试剂盒检测3组血清NSE和FERR，具体步骤严格按照说明书进行操作。

1.3 诊断标准[6]

各项指标阳性预测值分别为：CA125≥35 U/mL，

TSGF≥65 U/mL，NSE≥13 ng/mL，FERR≥219 ng/mL。单项检测高于正常值即为阳性，联合检测中任一项高于正常值即为阳性。

1.4 统计学处理

采用SPSS 21.0软件进行统计学分析本研究数据，计量资料均符合正态分布，以均数±标准差($\bar{x}\pm s$)表示，组间比较采用等级资料的秩和检验，计数资料采用频数和率表示，构成比采用χ^2检验，建立ROC曲线，计算曲线下面积及95%CI，分析敏感度和特异度，P<0.05为差异有统计学意义。

2 结果

2.1 3组患者血清肿瘤标志物水平比较

卵巢癌组患者血清肿瘤标志物TSGF、CA125、NSE及FERR水平均高于对照组，差异均有统计学意义(P<0.05)；卵巢癌组患者血清肿瘤标志物(TSGF、CA125、NSE及FERR)水平均高于良性病变组，差异均有统计学意义(P<0.05)。

2.2 3组患者中4种血清肿瘤标志物的阳性表达情况比较

卵巢癌组TSGF、CA125、NSE及FERR 4种血清肿瘤标志物单项检测阳性率均高于良性病变组及对照组，差异有统计学意义(P<0.05)；4种血清肿瘤标志物联合检测阳性率为82.0%均高于任一单项肿瘤标志物检测阳性值，差异有统计学意义(P<0.05，表2)。

2.3 血清肿瘤标志物单独及联合检测对卵巢癌的诊断效能比较

4项肿瘤标志物联合检测对卵巢癌的诊断曲线下面积为0.913，敏感度为82%，特异度为81.40%，敏感度和曲线下面积均高于4项血清肿瘤指标单独检测的诊断价值(表3，图1)。

表1 3组血清肿瘤标志物水平比较

Table 1 Comparison of serum tumor marker levels among the three groups

组别	n	NSE/(ng·mL^{-1})	TSGF/(U·mL^{-1})	FERR/(ng·mL^{-1})	CA125/(U·mL^{-1})
卵巢癌组	50	21.37 ± 3.71*	73.24 ± 5.24*	247.88 ± 249.65*	58.26 ± 19.84*
良性病变组	43	9.24 ± 1.86$^{\#}$	56.53 ± 6.86$^{\#}$	113.61 ± 91.52$^{\#}$	39.43 ± 10.01$^{\#}$
对照组	37	5.82 ± 1.97	42.31 ± 4.87	91.84 ± 48.41	21.72 ± 8.36

与对照组相比，*P<0.05；与卵巢癌组相比，$^{\#}P$<0.05。

Compared with the control group, *P<0.05; compared with the ovarian cancer group, $^{\#}P$<0.05.

表2 3组患者中4种血清肿瘤标志物的阳性表达情况比较

Table 2 Comparison of the positive expression of 4 serum tumor markers among the three groups

组别	n	NSE/[例(%)]	TSGF/[例(%)]	FERR/[例(%)]	CA125/[例(%)]	4项联合检测/[例(%)]
卵巢癌组	50	4 (8.00)*	38 (76.00)*	16 (32.00)*	34 (68.00)*	41 (82.00)*
良性病变组	43	0 (0.00)	6 (13.9)	3 (6.98)	3 (9.30)	8 (18.60)
对照组	37	0 (0.00)	1 (2.70)	1 (2.70)	1 (2.70)	1 (2.70)

与对照组及良性病变组比较，*P<0.05。

Compared with the control group and the benign disease group, *P<0.05.

表3 血清肿瘤标志物单独检测及联合检测对卵巢癌的诊断效能比较

Table 3 Comparison of the diagnostic efficacy of single and combined detection of serum tumor markers on ovarian cancer

血清肿瘤标志物	AUC	*SE*	95%CI
NSE	0.694	0.0407	0.622~0.760
TSGF	0.780	0.0370	0.713~0.838
FERR	0.836	0.0309	0.775~0.887
CA125	0.843	0.0306	0.782~0.893
NSE+TSGF+CEA+CA125	0.913	0.0233	0.863~0.950

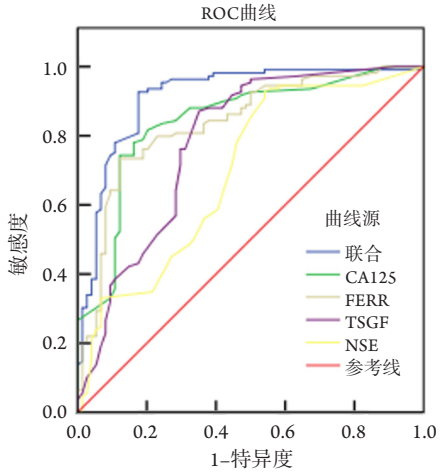

图1 TSGF、CA125、NSE及FERR 4项联合检测对卵巢癌诊断价值的ROC曲线

Figure 1 ROC curve of the diagnostic value of TSGF, CA125, NSE, FERR and the combined detection of four serum tumor markers

3 讨论

卵巢癌是一种常见的恶性肿瘤，其潜伏期较长，有2/3的患者初诊时已属于中晚期。研究[7-8]显示：卵巢癌早期确诊的患者经手术及介入治疗后，其5年生存率可达90%，而确诊为卵巢癌的晚期患者的5年生存率仅为27%，因此早期诊断及病情监测一直是妇科肿瘤的研究重点，但早期诊断有一定的困难。目前，临床采用实验室肿瘤标志物的测定来诊断患者是否患有肿瘤，TSGF、CA125、NSE及FERR作为肿瘤标志物，在卵巢癌的诊断中具有一定价值。

CA125又称黏蛋白16，由胚胎发育期体腔上皮细胞分泌，是可靠的卵巢上皮性癌肿瘤标志物，约80%卵巢癌晚期患者的血清CA125水平升高，在卵巢恶性肿瘤诊断、疗效观察及预后中的价值十分重要[9]。CA125在浆液性癌中的检测率可达70%~90%，特异度高于80%，但其在早期卵巢癌中的诊断敏感度和特异度均较差，这是因为CA125不仅是卵巢癌的特异性标志物，还存在于其他妇科良性病变及肺癌、胃癌、肝癌等患者的血清中[10]。本研究结果显示：卵巢癌组血清CA125水平均高于良性病变组及对照组，且其阳性表达情况较4种肿瘤标志物高，说明其排除肿瘤的能力较好。但有学者[11-12]认为单用CA125检测早期卵巢癌的敏感性未达40%，需联合其他肿瘤标志物进行检测才能提高早期卵巢癌的检出率。

TSGF是一种肿瘤血管增殖因子，特异度较高，可随恶性肿瘤的形成、增长而缓慢释放到外周血中，在恶性肿瘤形成之初即可检出，多应用于卵巢癌的早期辅助诊断、疗效监测、初筛[13]。有学者[14]指出：血清CA125联合TSGF检测卵巢癌相较于两项单一检测的准确性变化不大，特异性略低，但敏感度有较大提高。本研究结果显示，卵巢癌组血清TSGF水平均高于良性病变组及对照组，且其阳性表达情况稍高于CA125，但其特异性略低，与之前研究结果相似。

NSE是一种糖酵解酶，也是神经细胞的蛋白质标志物，可大量存在于神经细胞肿瘤及正常神经组织，无性细胞瘤及卵巢未成熟畸形胎瘤患者血清NSE水平升高[15]。FERR是机体内一种贮存铁的可溶性组织蛋白质，正常人血清FERR含量较少，可作为原发性肝癌诊断的第2指标，在淋巴癌、卵巢癌、乳腺癌、结肠癌患者血清中铁蛋白水平均有增高[16]。本研究结果显示：卵巢癌组患者血清肿瘤标志物NSEFE和RR水平均高于良性病变组及对照组；CA125、FERR、NSE及TSGF的ROC曲线

下面积分别为0.843、0.836、0.694及0.780，4种肿瘤标志物联合检测的曲线下面积为0.913，敏感度为82%，特异度为81.40%，曲线下面积及敏感度均高于4项指标单独检测的诊断价值，特异性有所降低，与以往研究数据相似。因恶性肿瘤的复杂生物学特性及多样性的基因表达，同种肿瘤可有多种肿瘤标志物，不同肿瘤或同种肿瘤的不同组织的肿瘤标志物可能相同，也可能不同。多数肿瘤标志物单一检测的敏感度和特异度较差，而多种肿瘤标志物联合检测虽可提高诊断敏感度，但也可能降低其特异度，因此合理联合多种肿瘤标志物进行检测可提高肿瘤诊断的敏感度和特异度[17]。本研究中TSGF可增加CA125单独检测的敏感度，但未能提高特异度，NSE在早期卵巢癌中的特异度较高，FERR亦可用于辅助诊断，4项联合检测可提高早期卵巢癌的诊断效能。

综上所述，CA125、CEA、NSE及TSGF是临床价值较高的卵巢癌肿瘤标志物，有较高的辅助诊断作用，4项联合检测能明显提高卵巢癌诊断的灵敏度和准确度，其诊断价值高于单项肿瘤标志物的检测。

参考文献

1. 倪军, 郭子健, 张力. 单独与联合检测四项肺癌血清肿瘤标志物在肺癌诊断中的价值[J]. 中华内科杂志, 2016, 55(1): 25-30.
   NI Jun, GUO Zijian, ZHANG Li. The value of detecting four lung cancer serum tumor markers alone and in combination in the diagnosis of lung cancer[J]. Chinese Journal of Internal Medicine, 2016, 55(1): 25-30.
2. 谭雯, 胡彩萍, 薛莎莎, 等. 多种肿瘤标志物检测对卵巢癌诊断及复发的临床价值[J]. 中国肿瘤临床与康复, 2018, 25(7): 826-828.
   TAN Wen, HU Caiping, XUE Shasha, et al. The clinical value of multiple tumor markers in the diagnosis and recurrence of ovarian cancer[J]. Chinese Journal of Clinical Oncology and Rehabilitation, 2018, 25(7): 826-828.
3. 李洪英, 王兰. 子宫内膜异位症不孕患者血清CA125 水平与术后妊娠结局的关系[J]. 河北医学, 2014, 20(2): 195-197.
   LI Hongying, WANG Lan. The relationship between the serum CA125 level and the pregnant outcome in patients with endometriosis[J]. Hebei Medicine, 2014, 20(2): 195-197.
4. Man YN, Wang YN, Hao J, et al. Pretreatment plasma D-dimer, fibrinogen, and platelet levels significantly impact prognosis in patients with epithelial ovarian cancer independently of venous thromboembolism[J]. Int J Gynecol, 2015, 25(1): 24-32.
5. 赵瑞珩. ROC曲线评价血清CA125、CA199和CEA对卵巢癌的诊断价值[J]. 中国实验诊断学, 2015, 19(11): 1954-1955.
   ZHAO Ruiheng. ROC curve to evaluate the diagnostic value of serum CA125, CA199 and CEA for ovarian cancer[J]. Chinese Journal of Laboratory Diagnosis, 2015, 19(11): 1954-1955.
6. Hu Y, Zhu Y, Zhang W, et al. Utility of plasma circBNC2 as a diagnostic biomarker in epithelial ovarian cancer[J]. Onco Targets Ther, 2019, 14(12): 9715-9723.
7. 张爽爽, 夏庆民, 郑荣寿, 等. 中国2010年卵巢癌发病与死亡分析[J]. 中国肿瘤, 2016, 25(3): 169-173.
   ZHANG Shuangshuang, XIA Qingmin, ZHENG Rongshou, et al. Analysis of the incidence and mortality of ovarian cancer in China in 2010[J]. Chinese Cancer, 2016, 25(3): 169-173.
8. Sie ń ko J, Teliga-Czajkowska J, Przytula E, et al. Peroxiredoxin-1 as a prognostic factor in patients with ovarian cancer[J]. Ann Agric Environ Med, 2019, 26(3): 415-419.
9. Falcão FJA, Oliveira FRA, Cantarelli F, et al. Carbohydrate antigen 125 predicts pulmonary congestion in patients with ST-segment elevation myocardial infarction[J]. Braz J Med Biol Res, 2019, 52(12): e9124.
10. 熊雯, 周新娥, 黄娟, 等. 血清 CA125、HE4及IL-17检测对上皮性卵巢癌的早期诊断价值分析[J]. 中国计划生育和妇产科, 2016, 8(3): 69-73.
    XIONG Wen, ZHOU Xin'e, HUANG Juan, et al. The value analysis of serum CA125, HE4 and IL-17 detection in the early diagnosis of epithelial ovarian cancer[J]. Chinese Family Planning and Obstetrics and Gynecology, 2016, 8(3): 69-73.
11. Li Y, Wang ZC, Luo L, et al. The clinical value of the combined detection of sEGFR, CA125 and HE4 for epithelial ovarian cancer diagnosis[J]. Eur Rev Med Pharmacol Sci, 2020, 24(2): 604-610.
12. Jin C, Yang M, Han X, et al. Evaluation of the value of preoperative CYFRA21-1 in the diagnosis and prognosis of epithelial ovarian cancer in conjunction with CA125[J]. J Ovarian Res, 2019, 12(1): 114.
13. 宋斌斌, 潘柏申. 卵巢癌血清标志物的临床应用[J]. 检验医学, 2015, 30(8): 866-870.
    SONG Binbin, PAN Baishen. Clinical application of serum markers for ovarian cancer[J]. Laboratory Medicine, 2015, 30(8): 866-870.
14. 李梅. 白细胞介素-6、糖类抗原72-4、血清癌抗原125联合人附睾蛋白4对卵巢癌的诊断价值[J]. 安徽医药, 2016, 20(6): 1138-1139.
    LI MEI. The diagnostic value of interleukin-6, carbohydrate antigen 72-4, serum cancer antigen 125 combined with human epididymal protein 4 in ovarian cancer[J]. Anhui Medicine, 2016, 20(6): 1138-1139.
15. Chen L, Wang X, Shu J, et al. Diagnostic value of serum D-dimer, CA125, and neutrophil-to-lymphocyte ratio in differentiating ovarian cancer and endometriosis[J]. Int J Gynaecol Obstet, 2019, 147(2):

212-218.

16. 张涛, 程晓军, 张波. CA199、CA125及CEA联合检测诊断卵巢癌的临床价值[J]. 贵州医药, 2016, 40(9): 973-975.
ZHANG Tao, CHENG Xiaojun, ZHANG Bo. The clinical value of combined detection of CA199, CA125 and CEA in the diagnosis of ovarian cancer[J]. Guizhou Medical Journal, 2016, 40(9): 973-975.

17. 徐仁根, 王君. 7种血清肿瘤标志物对原发性卵巢癌患者的临床诊断研究[J]. 检验医学与临床, 2016, 13(4): 480-481.
XU Rengen, WANG Jun. Clinical diagnosis of 7 serum tumor markers in patients with primary ovarian cancer[J]. Laboratory Medicine and Clinics, 2016, 13(4): 480-481.

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