

肿瘤标志物HE4在卵巢癌中的应用研究进展

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2019年06期 页码: 1095-1098 栏目: 综述 出版日期: 2019-02-08

Title: Application of tumor marker HE4 in ovarian cancer

作者: 李玮珊; 王丹波

辽宁省肿瘤医院妇科, 辽宁 沈阳 110042

Author(s): Li Weishan; Wang Danbo

Department of Gynaecology,Liaoning Cancer Hospital,Liaoning Shenyang 110042,China.

关键词: 人附睾蛋白4; 肿瘤标志物; 卵巢癌; 早期诊断

Keywords: human epididymis protein 4; tumor marker; ovarian cancer; early diagnosis

分类号: R737.31

DOI: 10.3969/j.issn.1672-4992.2019.06.047

文献标识码: A

摘要: 卵巢癌是女性生殖系统常见的一种恶性肿瘤,因早期症状不典型、进展迅速,盆腔种植转移早,其病死率一直高居妇科肿瘤之首。人附睾蛋白4(human epididymis protein 4,HE4)是一种新型肿瘤标志物,近年来研究发现其不仅对卵巢癌的早期筛查和诊断具有重要意义,而且对于评估卵巢癌的治疗效果及预后方面也有应用价值。另外,肿瘤标志物的联合检测能够提高卵巢癌诊断的灵敏度和特异度,而基于肿瘤标志物联合检测的计算模型在预测盆腔包块良恶性上更具预测价值。本文对卵巢癌肿瘤标志物HE4在卵巢癌的诊断、病情评估、治疗效果及预后方面的应用作一综述。

Abstract: Ovarian cancer is a common female genital malignancy.Because of no typical symptoms,rapid progression and early pelvic implantation,most patients are found in the late statement,the mortality rate has been the highest in gynecological tumors.HE4 is a new tumor marker.Recent studies have shown that HE4 is not only important for early screening and diagnosis of ovarian cancer,but also for the evaluation of ovarian cancer treatment efficacy and prognosis is also of application value.The combined detection of tumor markers can improve the sensitivity and specificity of ovarian cancer diagnosis,and the model based on the combination of tumor markers is more effective in predicting the benign and malignant pelvic mass.The review is about the application of HE4 in the diagnosis of ovarian cancer,disease assessment,treatment efficacy and prognosis.

参考文献/REFERENCES

- [1] Siegel R,Naishadham D,Jemal A.Cancer statistics,2013 [J] .CA Cancer J Clin,2013,63(1):11-30.
- [2] Kirchhoff C,Habben I,Ivell R,et al.A major human epididymis-specific cDNA encodes a protein with sequence homology to extracellular proteinase inhibitors [J] .Biol Reprod,1991,45(2):350-357.
- [3] Bingle L,Cross SS,High AS,et al.WFDC2 (HE4):a potential role in the innate immunity of the oral cavity and respiratory tract and the development of adenocarcinomas of the lung [J] .Respir Res,2006,7:61.
- [4] Bingle L,Singleton V,Bingle CD.The putative ovarian tumour marker gene HE4 (WFDC2),is expressed in normal tissues and undergoes complex alternative splicing to yield multiple protein isoforms [J] .Oncogene,2002,21(17):2768-2773.
- [5] Schummer M,Ng WV,Bumgarner RE,et al.Comparative hybridization of an array of 21,500 ovarian cDNAs for the discovery of genes overexpressed in ovarian carcinomas [J] .Gene,1999,238(2):375-385.
- [6] Devan SM,Pailoor J,Sthaneshwar P,et al.Pattern of tissue expression of CA-125 and HE4 in primary epithelial ovarian tumours and correlation with serum CA-125 levels [J] .Asian Pac J Cancer Prev,2013,14(8):4545-4548.
- [7] Zhu L,Zhuang H,Wang H,et al.Overexpression of HE4 (human epididymis protein 4) enhances proliferation,invasion and metastasis of ovarian cancer [J] .Oncotarget,2016,7(1):729-744.
- [8] Lu R,Sun X,Xiao R,et al.Human epididymis protein 4 (HE4) plays a key role in ovarian cancer cell adhesion and motility [J] .Biochem Biophys Res Commun,2012,419(2):274-280.
- [9] Guo YX,Neoh KH,Chang XH,et al.Diagnostic value of HE4+ circulating tumor cells in patients with suspicious ovarian cancer [J] .Oncotarget,2018,9(7):7522-7533.
- [10] Moore RG,Plante B,Hartnett E,et al.Assessment of serum HE4 levels throughout the normal menstrual cycle [J] .Am J Obstet Gynecol,2017,217(1):51-53.

- [11] Hallamaa M,Huhtinen K,Suvitie P,et al.Serum concentrations of HE4 change little during in vitro fertilization [J] .Acta Obstet Gynecol Scand,2014,93(7):640-646.
- [12] Tian Y,Wang C,Cheng L,et al.Determination of reference intervals of serum levels of human epididymis protein 4 (HE4) in Chinese women [J] .J Ovarian Res,2015,8:72.
- [13] Yu S,Yang HJ,Xie SQ,et al.Diagnostic value of HE4 for ovarian cancer:a meta-analysis [J] .Clin Chem Lab Med,2012,50(8):1439-1446.
- [14] Al Musalhi K,Al Kindi M,Al Aisary F,et al.Evaluation of HE4,CA-125,risk of ovarian malignancy algorithm (ROMA) and risk of malignancy index (RMI) in the preoperative assessment of patients with adnexal mass [J] .Oman Med J,2016,31(5):336-344.
- [15] Xu Y,Zhong R,He J,et al.Modification of cut-off values for HE4,CA125 and the ROMA algorithm for early-stage epithelial ovarian cancer detection:Results from 1021 cases in South China [J] .Clin Biochem,2016,49(1-2):32-40.
- [16] Ortiz-Munoz B,Aznar-Oroval E,Garcia GA,et al.HE4,Ca125 and ROMA algorithm for differential diagnosis between benign gynaecological diseases and ovarian cancer [J] .Tumour Biol,2014,35(7):7249-7258.
- [17] Terlikowska KM,Dobrzycka B,Witkowska AM,et al.Preoperative HE4,CA125 and ROMA in the differential diagnosis of benign and malignant adnexal masses [J] .J Ovarian Res,2016,9(1):43.
- [18] Gasiorowska E,Michalak M,Warchol W,et al.Clinical application of HE4 and CA125 in ovarian cancer type I and type II detection and differential diagnosis [J] .Ginekol Pol,2015,86(2):88-93.
- [19] Jiang J,Bo D,Chang X,et al.Discrepant clinicopathologic characteristics and HE4 performance in type I and type II epithelial ovarian cancer [J] .Int J Clin Exp Med,2015,8(11):21303-21310.
- [20] Xu XR,Wang X,Zhang H,et al.The clinical significance of the combined detection of serum Smac,HE4 and CA125 in endometriosis-associated ovarian cancer [J] .Cancer Biomark,2018,21(2):471-477.
- [21] Stiekema A,Boldingh QJ,Korse CM,et al.Serum human epididymal protein 4 (HE4) as biomarker for the differentiation between epithelial ovarian cancer and ovarian metastases of gastrointestinal origin [J] .Gynecol Oncol,2015,136(3):562-566.
- [22] Delic R,Stefanovic M,Krivec S,et al.Comparison of HE4 and CA125 levels in women with benign gynecologic disorders:Does age or menopausal status matter [J] ?Wien Klin Wochenschr,2016,128(Suppl 7):543-547.
- [23] Huhtinen K,Suvitie P,Hiissa J,et al.Serum HE4 concentration differentiates malignant ovarian tumours from ovarian endometriotic cysts [J] .Br J Cancer,2009,100(8):1315-1319.
- [24] Moore RG,Brown AK,Miller MC,et al.The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass [J] .Gynecol Oncol,2008,108(2):402-408.
- [25] Hamed EO,Ahmed H,Sedeek OB,et al.Significance of HE4 estimation in comparison with CA125 in diagnosis of ovarian cancer and assessment of treatment response [J] .Diagn Pathol,2013,8:11.
- [26] Zapardiel I,Gorostidi M,Ravaggi A,et al.Utility serum marker HE4 for the differential diagnosis between endometriosis and adnexal malignancy [J] .Int J Gynecol Cancer,2016,26(1):52-55.
- [27] Diavatis S,Papanikolaou A.Level of HE4 is correlated with diagnosis of struma ovarii:A case report [J] .Am J Case Rep,2016,17:459-461.
- [28] Zhang L,Chen Y,Liu W,et al.Evaluating the clinical significances of serum HE4 with CA125 in peritoneal tuberculosis and epithelial ovarian cancer [J] .Biomarkers,2016,21(2):168-172.
- [29] Jia MM,Deng J,Cheng XL,et al.Diagnostic accuracy of urine HE4 in patients with ovarian cancer:a meta-analysis [J] .Oncotarget,2017,8(6):9660-9671.
- [30] Macuks R,Baidekalna I,Donina S.Urinary concentrations of human epididymis secretory protein 4 (HE4) in the diagnosis of ovarian cancer:a case-control study [J] .Asian Pac J Cancer Prev,2012,13(9):4695-4698.
- [31] Elsammak MY,Attia A,Hassan HA,et al.Evaluation of pleural fluid human epididymis 4 (HE4) as a marker of malignant pleural effusion [J] .Tumour Biol,2012,33(5):1701-1707.
- [32] Chudecka-Glaz A,Cymbaluk-Ploska A,Menkiszak J,et al.HE4 tumor marker concentration in neoplastic peritoneal effusion and in peritoneal fluid associated with benign gynecological diseases [J] .J Ovarian Res,2014,7:22.
- [33] Kalapotharakos G,Asciutto C,Henic E,et al.High preoperative blood levels of HE4 predicts poor prognosis in patients with ovarian cancer [J] .J Ovarian Res,2012,5(1):20.
- [34] Nassir M,Guan J,Luketina H,et al.The role of HE4 for prediction of recurrence in epithelial ovarian cancer patients-results from the OVCAD study [J] .Tumour Biol,2016,37(3):3009-3016.
- [35] Braicu EI,Fotopoulou C,Van Gorp T,et al.Preoperative HE4 expression in plasma predicts surgical outcome in primary ovarian cancer patients:results from the OVCAD study [J] .Gynecol Oncol,2013,128(2):245-251.
- [36] Angioli R,Plotti F,Capriglione S,et al.Can the preoperative HE4 level predict optimal cytoreduction in patients with advanced ovarian carcinoma [J] ?Gynecol Oncol,2013,128(3):579-583.
- [37] Shen Y,Li L.Serum HE4 superior to CA125 in predicting poorer surgical outcome of epithelial ovarian cancer [J] .Tumour Biol,2016,37(11):14765-14772.
- [38] Pelissier A,Roulot A,Guery B,et al.Serum CA125 and HE4 levels as predictors for optimal interval surgery and platinum sensitivity after neoadjuvant platinum-based chemotherapy in patients with advanced epithelial ovarian cancer [J] .J Ovarian Res,2016,9(1):61.
- [39] Innao P,Pothisuwan M,Pengsa P.Does human epididymis protein 4 (HE4) have a role in prediction of recurrent epithelial ovarian cancer [J] .Asian Pac J Cancer Prev,2016,17(9):4483-4486.
- [40] Manganaro L,Michienzi S,Vinci V,et al.Serum HE4 levels combined with CE CT imaging improve the management of monitoring women affected by epithelial ovarian cancer [J] .Oncol Rep,2013,30(5):2481-2487.

- [41] Capriglione S, Luvero D, Plotti F, et al. Ovarian cancer recurrence and early detection: may HE4 play a key role in this open challenge? A systematic review of literature [J]. *Med Oncol*, 2017, 34(9):164.
- [42] Scaletta G, Plotti F, Luvero D, et al. The role of novel biomarker HE4 in the diagnosis, prognosis and follow-up of ovarian cancer: A systematic review [J]. *Expert Rev Anticancer Ther*, 2017, 17(9):827-839.
- [43] Moore RG, McMeekin DS, Brown AK, et al. A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass [J]. *Gynecol Oncol*, 2009, 112(1):40-46.
- [44] Dayyani F, Uhlig S, Colson B, et al. Diagnostic performance of risk of ovarian malignancy algorithm against CA125 and HE4 in connection with ovarian cancer: A meta-analysis [J]. *Int J Gynecol Cancer*, 2016, 26(9):1586-1593.
- [45] Karlsen MA, Sandhu N, Hogdall C, et al. Evaluation of HE4, CA125, risk of ovarian malignancy algorithm (ROMA) and risk of malignancy index (RMI) as diagnostic tools of epithelial ovarian cancer in patients with a pelvic mass [J]. *Gynecol Oncol*, 2012, 127(2):379-383.
- [46] Escudero JM, Auge JM, Filella X, et al. Comparison of serum human epididymis protein 4 with cancer antigen 125 as a tumor marker in patients with malignant and nonmalignant diseases [J]. *Clin Chem*, 2011, 57(11):1534-1544.
- [47] Molina R, Escudero JM, Auge JM, et al. HE4 a novel tumour marker for ovarian cancer: Comparison with CA125 and ROMA algorithm in patients with gynaecological diseases [J]. *Tumour Biol*, 2011, 32(6):1087-1095.
- [48] Chudecka-Glaz A, Cymbaluk-Ploska A, Luterek-Puszynska K, et al. Diagnostic usefulness of the risk of ovarian malignancy algorithm using the electrochemiluminescence immunoassay for HE4 and the chemiluminescence microparticle immunoassay for CA125 [J]. *Oncol Lett*, 2016, 12(5):3101-3114.
- [49] Van Gorp T, Cadron I, Despierre E, et al. HE4 and CA125 as a diagnostic test in ovarian cancer: prospective validation of the Risk of Ovarian Malignancy Algorithm [J]. *Br J Cancer*, 2011, 104(5):863-870.
- [50] Goff BA, Agnew K, Neradilek MB, et al. Combining a symptom index, CA125 and HE4 (triple screen) to detect ovarian cancer in women with a pelvic mass [J]. *Gynecol Oncol*, 2017, 147(2):291-295.
- [51] Pitta DR, Sarian LO, Barreta A, et al. Symptoms, CA125 and HE4 for the preoperative prediction of ovarian malignancy in Brazilian women with ovarian masses [J]. *BMC Cancer*, 2013, 13:423.
- [52] Karlsen MA, Hogdall EV, Christensen IJ, et al. A novel diagnostic index combining HE4, CA125 and age may improve triage of women with suspected ovarian cancer - An international multicenter study in women with an ovarian mass [J]. *Gynecol Oncol*, 2015, 138(3):640-646.
- [53] Gong SP, Chen YN, Zhang YD, et al. Diagnostic value of CA125, HE4 and Copenhagen Index in differentiating benign from malignant epithelial ovarian tumors [J]. *J Southern Med Univ*, 2017, 37(5):628-632.

备注/Memo: 2017年辽宁省肿瘤医院人才引进科研启动基金

更新日期/Last Update: 1900-01-01