



## Reply to “The differential diagnostic value of serum HE4 in ovarian disease with elevated CA125; Importance of diagnostic added value in clinical practice”

Weishan Li<sup>1</sup>

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The diagnostic value is estimated by two parameters: the reliability and the accuracy. The reliability of the tumor markers CA125 and HE4 in diagnosis has been confirmed in a large number of researches. Actually, CA125 and HE4 are not new indicators and have been widely used in the screening and diagnosis of ovarian diseases in clinical diagnosis and treatment. I am a doctor and find that the elevation of serum CA125 levels in many kinds of benign ovarian diseases can lead to an increasing risk of misdiagnosis. Its specificity is low. The significance of our study is mainly to propose the diagnostic added value of HE4 in screening and diagnosis of ovarian diseases with elevated CA125. In our study, HE4 levels in benign and malignant ovarian disease with elevated CA125 levels were analyzed using ROC curve. The AUC values for HE4 before and after menopause were 0.912 and 0.894. The cutoff values calculate in our study in both premenopausal and postmenopausal patients showed improved diagnostic accuracy and efficiency compared with those recommended by the HE4 detection kit that was used (Table 5 and Table 6). The premenopausal HE4 cutoff value was 78.03 pmol/L, which was higher than the cutoff value recommended by the diagnostic kit (70 pmol/L). In patients with elevated serum CA125, the increase in premenopausal HE4 cut-off value compared to the standard value can improve the specificity and positive predictive value of diagnosis. There are several benign factors, such as endometriosis and pelvic inflammatory disease, causing elevation of serum CA125 in premenopausal patients. That is, in clinic diagnosis, a little bit elevation of CA125 should not let premenopausal patients be panic. The HE4 cutoff value in postmenopausal patients was 119.70 pmol/L,

which was lower than that recommended by the diagnostic kit (140 pmol/L). In patients with elevated serum CA125, the decrease in postmenopausal HE4 cut-off value compared to the standard value can improve the sensitivity and negative predictive value of diagnosis. The risk of malignant disease was higher than benign disease for patients with elevated serum CA125 after menopause. We also recommend reducing the HE4 diagnostic cutoff level from 140 to 119.70 pmol/L for differential diagnosis of postmenopausal patients with elevated CA125. That is the significant guidance for clinic diagnosis of ovarian disease. It is worth mentioning that the tumor marker cannot be used alone to diagnose the disease. The diagnostic model of ovarian diseases includes the patient's medical history, symptoms, laboratory tests and imaging examinations, etc. There is no doubt that the pathology is the gold standard for diagnosis. Our study discusses one aspect of combined detection of HE4 and CA125 for early screening and diagnosis of ovarian diseases.

### Compliance with ethical standards

**Conflict of interest** The author declares no conflict of interest.

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✉ Weishan Li  
961675507@qq.com

<sup>1</sup> Cancer Hospital of China Medical University, No. 44, Xiaohe Road, Dadong District, Shenyang 110042, Liaoning, China