Does any serum marker predict the ovarian endometrioma accompanied with or without deep infiltrative endometriosis?

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Endometriosis is a multifactorial and chronic inflammatory disease, involving more than 10% of women of reproductive age, contributing to a heavy burden of socioeconomic health problems, such as pelvic adhesion, chronic pelvic pain, infertility and other comorbidities, including malignant transformation and an inability or psychosomatic stress.[1–5] The management of women with endometriosis is still controversial, because it often involves the hormone maneuver and may deteriorate the reproductive function. The use of noninvasive procedures is often considered the first-line therapy, such as physical therapy and medication.[6] However, some of them may not respond to conservative treatment well or some of them might be complicated with endometriosis-related severe complications, such as ureter stricture and reduced capacity of reproductive performance, contributing to the need of more invasive procedures, such as operations.[7,8] Ovarian endometrioma might be one of the most diagnosed endometrioses, which can be successfully managed by surgical approach with a relatively low risk of surgery-related complications.[7]

However, a certain-type endometriosis, such as deep infiltrative endometriosis (DIE) might be the biggest challenge during the operation. It is very difficult to finish complete resection without organ injury or the need of repairing process.[9] An accurate preoperative diagnosis of ovarian endometrioma accompanied with DIE women is of paramount importance. The more extensive surgical preparation and more detailed surgical plan can significantly decrease the surgery-related morbidity. We are happy to learn a recent publication to address this.[10] In the June issue of the *Journal of the Chinese Medical Association*, an impressive article entitles "The relationship between C-reactive protein, carbohydrate antigen 125, and hematological parameters to endometriotic nodule localization in pelvis" has been published.[10] The authors used the three common serum markers, including C-reactive protein (CRP), carbohydrate antigen 125 (CA 125), and hematological parameters to predict the coexistence of DIE in women with ovarian endometrioma.[10] The authors found that women with DIE had a statistically significant higher serum level of CRP and CA 125 than women without DIE did.[10] In addition, higher levels of CRP and CA 125 were also associated with severity of DIE (a bigger number of nodularity).[10] The hemoglobin level was statistically significantly lower in women with DIE than that without DIE.[10] Finally, the authors found that only serum level of CA 125 was an independent predictor for women with ovarian endometrioma accompanied with DIE.[10] The study is interesting and worthy of discussion.

At first, we would like to discuss the simple parameters obtained from the peripheral hematological parameters in their study. In our previous comment,[11] we had criticized the value of using the peripheral hematological parameters in the prediction of prognosis of cancers, although some evidence has supported that these systemic inflammatory response markers, such as subgroup of white cell counts, and platelet counts and their ratios obtained from the simple peripheral blood test.[10–12] Since the behaviors of endometriosis are similar to those of cancer with either invasion or metastasis, we believed that the similar strategy might fail to provide an effective role in the prediction of patients with DIE. As predicted above and shown by authors, results not only showed the absence of any correlation of peripheral hematological parameters in the prediction of the presence of DIE, but also failed to be associated with severity of DIE, although the authors still believed that their findings were accidental and may be incorrect, because the authors favored a large cohort to clarify the aforementioned results.[10] Like our comment before, it may be relatively difficult to follow the cut-off value of these simple hematological parameters if physicians would like to apply these into their clinical routine practice without their own standard reference.[11] In addition, if the authors are so worrisome about their reports, the other two parameters, including the stronger parameter as CA 125 should be tested in the large number of studied subjected to validate their findings. That is why the authors still hesitated to comment the value of these serum biomarkers in the clinical practice.[10]

Second, the similar challenge is also present in the use of CRP or CA 125 in the prediction of DIE. CRP is a nonspecific inflammatory serum marker, which is widely used in various kinds of

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diseases, including infections, autoimmune diseases, and cancers.[13,14] CA 125 is also widely used in routine clinical practice, especially for those patients with malignant peritoneal carcinomatosis during the follow-up or the monitoring response.[15] Since the serum level of CA 125 is dramatically elevated in variant forms of endometriosis, such as adenomyosis.[6] In the Topdagi Yilmaz's study, the authors did not provide the detailed information of these patients. It is still uncertain that the relationship between adenomyosis and DIE. Without evaluation of this or comprehensive review of these variant types of endometriosis, these confounding factors might significantly bias the results.

Taken together, although systematic inflammatory response biomarkers can be easily measured, the validation for the specific purpose, such as the prediction of disease severity, or concealed catastrophic situations may need further confirmation. These uncertainties may require more and more studies to test.

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