Editorial

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Coexisting carcinoma in endometrial hyperplasia: does more risk factor mean better discrimination?

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Few gynecologists would argue against that nuclear atypicality and glandular complexity in endometrial hyperplasia are associated with an increased risk of endometrial cancer [1,2]. Moreover, the possible existence of occult endometrial carcinoma or the risk of progression to carcinoma in complex or atypical endometrial hyperplasia has been a rationale to offer invasive surgery when a patient was found to have these histologic features [1]. Interestingly, a recent long-term observational study reported that the progression to carcinoma was observed in only 1.9% for non-atypical endometrial hyperplasia after 4 years follow-up [3]. The data reassure us that the risk of progression to carcinoma including coexistence of carcinoma may be negligible when no atypia was found. Also this low rate supports nonsurgical management of non-atypical endometrial hyperplasia. However, in cases with atypia, things go different. For atypical hyperplasia, the 4-year cumulative risk increased to 8.2%. After 9 years, the cumulative progression risk further increased to 12.4%. Should we offer decisive hysterectomy in all patients with atypia? Is there any room for individualized management in patients with atypical endometrial hyperplasia?

In this issue of Journal of Gynecologic Oncology, an observational study from the Taiwanese Gynecologic Oncology Group (TGOG) provided several risk factors that we should take into consideration in planning treatment of endometrial hyperplasia. First, the authors confirmed that several clinical variables, such as older age, menopausal status, history of diabetes, history of abnormal uterine bleeding, and high body mass index (BMI) were independent risk factors. Second, they tried to improve the accuracy in the prediction of coexisting carcinoma using these clinical risk factors. Did they success in improving the accuracy of the model? Unfortunately, it seems not. When the authors integrated atypia with other clinical risk factors, the discrimination performance did not increased significantly. Thus, it may not be surprising that the authors emphasized no risk factors but only atypia in the conclusion. Then, what would be the scientific merit of this multi-center study?

First, in the authors' data, positive likelihood ratios were high when a patient with atypical endometrial hyperplasia had high BMI or in her menopause. Especially, when a patient with atypical hyperplasia was in her menopause, a positive likelihood ratio was increased to more than 5.0. This indicates the presence of risk factors other than atypia, such as high BMI or menopause, may represent high likelihood of coexisting carcinoma. Therefore, if we find that a patient with atypical hyperplasia has other risk factors, especially menopause, a pathologist should examine the specimen more carefully, and a surgeon should offer adequate information to a patient and allow her to choose decisive treatment. Because the authors used logistic modeling, it is evident that the probability of coexisting carcinoma would increase further if a patient has additional risk factors.

Second, it is surprising that 25 out of 191 patients (13%) with non-atypical endometrial hyperplasia were found to have coexisting carcinoma. In general, it has been believed that the risk of progression to carcinoma is less than 4% in non-atypical hyperplasia [2]. Correspondingly, a recent large-

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scale study showed that cumulative progression risk was only 1.9% through 9 years of observation in patients with non-atypical hyperplasia [3]. In contrast to previous knowledge, the TGOG report alerts that substantial proportion of patients with non-atypical hyperplasia has coexisting carcinoma. If the results from TGOG were not affected from serious selection bias, the results suggest that coexisting carcinoma may not have a significant role in the clinical progression to carcinoma in non-atypical hyperplasia. However, we should remember that the natural history of endometrial hyperplasia is difficult to define because of the unstable reproducibility of pathologic examination or the diversity in sampling methods. Therefore, it may be immature to interpret the TGOG data as a recommendation for aggressive treatment in non-atypical hyperplasia. Rather, despite the incidence rate of coexisting carcinoma, hormone treatment should be recommended first based on its excellent outcome in the patients with non-atypical hyperplasia [4,5].

Although the TGOG data did not provide a decisive prediction model to help an individualized treatment in atypical endometrial hyperplasia, I believe that gynecologic oncologists should keep trying to find an efficient risk model for these patients. Above all, more effort should be directed toward the estimation of clinical effectiveness of hormone treatment in atypical endometrial hyperplasia, because majority of these patients are subjected to aggressive surgical treatment. Considering its low progression rate and good response rate to hormonal therapy, the role of hormonal treatment should be explored as an ideal treatment option regardless of women's desire for fertility. To establish an individualized treatment in these patients, Asian society should continue to communicate and collaborate further.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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