Editorial

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Preoperative CA-125 in low-grade endometrial cancer: risk stratification and implications for treatment

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> ▶ See the article "Improved preoperative risk stratification with CA-125 in low-grade endometrial cancer: a multicenter prospective cohort study" in volume 30, e70.

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Although the majority of women with endometrial cancer are diagnosed with early stage low-risk disease and have an excellent prognosis, a small proportion of them have a poor outcome. Because of the global obesity epidemic, the incidence of endometrial cancer is increasing every year [1]. This will translate into more women who will recur and die of endometrial cancer. Identifying those at highest risk of recurrence is important in planning treatment.

In this issue, Reijnen et al. [2] report the outcomes of the PIpelle Prospective ENDOmetrial carcinoma (PIPENDO) study, a prospective cohort study including women with endometrial cancer diagnosed at 9 hospitals in the Netherlands. All had preoperative cancer antigen 125 (CA-125) testing. CA-125 was elevated in 26.2% of women with low-grade (grade 1 or 2 endometrioid) endometrial cancer (EC), and almost 1 in 5 (19.4%) had a recurrence. The majority of these recurrences (73.7%) were distant. Elevated CA-125 was significantly associated with advanced International Federation of Gynecology and Obstetrics stage and deep myometrial invasion, and in the multivariable analysis adjusting for covariates, CA-125 was independently associated with both disease-free survival (DFS; hazard ratio [HR]=3.62; 95% confidence interval [CI]=2.15–6.09) and disease-specific survival (DSS; HR=4.18; 95% CI=2.26–7.72).

The majority of women with low-grade EC in this study did not have lymphadenectomy or lymph node sampling, including 92.7% and 77.8% with normal and elevated CA-125 levels, respectively. Preoperative elevated CA-125 is known to be associated with lymph node metastases [3-7]. Therefore, an elevated preoperative CA-125 in the context of low-grade EC might justify referral to a gynecologic oncologist for comprehensive surgical staging, including lymph node assessment. Preoperative computed tomography scan is insufficiently sensitive to detect occult nodal disease [8,9].

L1 cell adhesion molecule expression (L1CAM) [10,11] and p53 mutations or high-copy number alterations according to TCGA [12] are recognized for their association with adverse outcomes in endometrial cancer. It remains to be determined if these biomarkers can tailor treatment. Until then, CA-125 can be obtained on anyone diagnosed with endometrial cancer. Reijnen et al. [2] have demonstrated that CA-125 can identify those with low-grade endometrial cancer who are at high risk of recurrence, including distant metastases.

Consideration should be given to surgical staging (which could include sentinel node biopsy rather than complete lymphadenectomy [13,14]) for those with an elevated CA-125, irrespective of preoperative grade.

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