Cervical adenocarcinoma *in situ* with negative conization margin: negligible or not?

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Frequently, clinicians confront situations that a pile of cumulated data about a disease does not help them to make clear decision. Cervical adenocarcinoma *in situ* (AIS) is one of them. It has been commonly believed that the disease has multifocal location and this raised the concern for the safety of conservative management in treatment of cervical AIS. Thus, even with negative conization margins, many recommend further surgery in fear of a risk of residual or recurrent disease. However, due to its relatively lower incidence than its counterpart, many studies regarding of outcome of AIS are small-sized and retrospective, which limited their usefulness as an evidence for decision-making evidence.

In this issue of Journal of Gynecologic Oncology, Kim et al. [1] reported the retrospective observational data of 99 women with AIS in single institution. Despite its retrospective nature, the study provides helpful insight of the disease and is one of the large-scale observational sets currently available. The most intriguing data in the study were the incidence of residual margin and recurrence data of AIS with negative margin. The authors found the residual disease only in 4.4% of patients who underwent further surgery. On the other hand, they also found the 3.6% of recurrence rate in the AIS patients who received conservative management, which was corresponds well to the pathologic outcome of surgically managed cases. The good correspondence between incidence rate of residual lesion and the recurrence rate is very interesting, especially in light of recent systemic review by Salani et al. [2]. In the report,

the authors estimated the recurrence rate as 2.6% in the conservatively-managed patients, which is well corresponds to the study by Kim et al.

However, the estimated incidence of residual disease in the hysterectomy specimen was as much as 20.3%, which is evidently higher than that of data presented by Kim et al. This discrepancy is not surprising. First, in the systemic review, the authors included many case reports. Many case reports reported the disastrous outcome of conservative expectation after conization when the margin was negative. Therefore, it can be serious source of bias exaggerating the incidence of failure in margin-negative patients. Indeed, simple application of random-effect model in the previous systemic review, we can easily found that the incidence decreased to 15%. On the other hand, in the Kim's data, selection bias might have influenced and decreased the incidence of conization failure in margin-negative patients because clinicians would advise hysterectomy more frequently in the patient with higher risk. Despite the discrepancy of rate of residual disease, the good correspondence of recurrence rate of margin-negative patients between two studies (2.6% and 3.6%, respectively) gave us important insight for selecting treatment strategy because the known recurrence rate of cervical carcinoma *in situ* is about 2% [3,4].

For the patients with margin-negative AIS, what treatment strategy can be drawn from these data? First, it is evident that margin-negative young patients who want to preserve their fertility can be treated with conservative expectation. Second, the collective evidences suggests that margin-negative patients should be given with the choice to select between decisive hysterectomy and conservative expectation with careful follow-up, even they do not wish to retain fertility. Adequate information including warning for the chance

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of residual disease and low incidence of recurrence rate should be provided through patient counseling. However, considering subsequent rate of residual disease and limited accuracy in surveillance technique, definite hysterectomy still should be regarded as the gold standard in margin-negative patients.

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