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Editorial

Adjuvant hysterectomy in patients with locally advanced cervical cancer treated with concurrent chemoradiotherapy

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Since the publication of 5 randomized controlled trials, concurrent chemoradiation therapy (CCRT) is accepted as treatment for locally advanced cervical cancer (LACC), including stages IB2 to IVA according to the 2014 International Federation of Gynecology and Obstetrics staging system [1]. Although CCRT improves survival outcomes in these patients compared with radiotherapy alone, the 5-year overall survival rate remains approximately 70%. Moreover, 24%–48% of patients harbor residual tumors after definitive CCRT [2], and those with residual tumors ≥2 cm have even poorer prognosis than those who achieve complete response after CCRT [3,4]. To extirpate the residual tumor and improve local control and overall survival, some investigators have administered adjuvant hysterectomy (AH) after radiotherapy. Before the era of CCRT, the Gynecologic Oncology Group-71 trial had evaluated the role of AH in 256 patients with bulky stage IB cervical cancer who were treated with radiation without concomitant chemotherapy. Patients were randomly assigned to the AH arm after radiation (n=132) or radiation only (n=124) [5]. There was no difference in overall survival between the 2 arms, although the 5-year local recurrence rate was lower in the AH arm (14% vs. 27%). In the era of CCRT, there are few studies with high-quality data regarding the therapeutic effect of AH after definitive CCRT. One randomized controlled trial by a French group evaluated this issue in patients who achieved clinical and radiological complete response after definitive CCRT [6]. In this trial, there was no significant difference in 3-year event-free survival (72% vs. 89%) and overall survival (86% vs. 97%) rates between the AH and no-AH arms. However, the trial was discontinued prematurely due to insufficient accrual (n=61) and thus had suboptimal power to draw concrete results [7].

Albert et al. performed a large, nationwide population-based study using the National Cancer Database to determine the treatment pattern and survival impact of AH in patients with stage IB2 to IIA2 cervical cancer diagnosed between 2010 and 2014 who received CCRT [8]. In this study, the authors identified a total of 1,546 patients, of whom 1,407 (91.0%) received CCRT alone and 139 (9.0%) received AH after CCRT. For patients without nodal metastases, there was no significant difference in 4-year overall survival rates between the AH group and CCRT alone group (84.9% vs. 77.8%, p=0.072). On multivariable Cox regression adjusted by prognostic factors (including age, stage, tumor size, comorbidity, histology, node metastasis, chemotherapy regimen, and insurance), there was no difference in survival between two groups. This result suggests that AH is used infrequently in the modern era and does not

contribute to improving survival after adjusting for other prognostic factors. Considering that it is very challenging to perform clinical trials related to surgery, this study provides further evidence and may answer the conflicting question about the uncertain benefit of AH using large-scale population-based data. Nonetheless, the results of this study should be interpreted with caution. As the authors acknowledged, this study did not provide information regarding residual tumors, which is one of the most important prognostic factors in patients with LACC after definitive CCRT. Thus, the true therapeutic effect of AH could not be assessed in patients with residual tumors. A recent prospective study demonstrated promising results of AH in this population. Forty patients with residual tumors received AH 14 to 18 weeks after CCRT, and 10% (4 out of 40) recurred between 5 and 9 years of follow-up [9]. Future studies should focus on the issue regarding whether AH is effective in patients with residual tumors after definitive CCRT.

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