

Correspondence

## Differing prognosis of cervical cancer patients with high risk of treatment failure after radical hysterectomy

**To the editor:** In the article of Kim et al.,<sup>1</sup> the authors suggested that there was a subgroup of patients with increased risk of treatment failure after adjuvant concurrent chemoradiation therapy (CCRT) within high-risk group of patients with early-stage cervical cancer. And, they advocated new strategies, such as consolidation chemotherapy after CCRT, in these very high-risk patients.

This study may be informative in that it proposed the selection criteria for more aggressive therapy including consolidation chemotherapy among high-risk cervical cancer patients. However, there are some limitations to be overcome in this study. First, the criteria of dividing patients into two groups were not supported sufficiently. In the present study, high-risk patients who were candidates for adjuvant CCRT were arbitrarily divided into two groups; group A with negative parametrium, negative resection margins, and unilateral pelvic lymph node metastasis (involved lymph nodes  $\leq 2$ ), and group B with either bilateral pelvic lymph node involvement or more than 2 lymph node involvement or positive parametrium with lymph node involvement. The selection criteria were based on the results of previous retrospective studies identifying risk factors for recurrence in early-stage cervical cancer after radical hysterectomy and/or postoperative radiation therapy.<sup>2-4</sup> These include number of positive lymph nodes (2 or more in most studies), parametrial invasion, tumor size, lymphovascular tumor emboli, and histologic types. Among these, the number of positive lymph nodes, bilaterality of lymph node involvement, and parametrial involvement were selected in this study. Even though a significant difference in survival between the two groups was demonstrated, assessment of potential risk factors, including stage, invasion depth of cervix, and above mentioned variables, for correlation with treatment failure after CCRT using univariate/multivariate analysis is required before developing the selection criteria.

Secondly, there has not been any definite evidence of survival benefit of consolidation chemotherapy after adjuvant CCRT so far. There has been only one prospective study, which showed no survival benefit of consolidation chemotherapy after adjuvant CCRT.<sup>5</sup> However, there have been several

studies suggesting that the number of chemotherapy cycles may affect survival.<sup>6,7</sup> Recently, a phase III randomized study of CCRT with or without adjuvant chemotherapy in high-risk patients with early-stage cervical carcinoma following radical hysterectomy is under development (RTOG-0724). We have to wait for the results of this prospective study and other phase II studies to validate the hypothesis of this study, and to determine which subgroup of patients with early-stage cervical cancer can benefit from more aggressive therapy.

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DOI:10.3802/jgo.2009.20.2.132

**In reply:** We are grateful to Dr. Kim for interest and advice in our article. We admit that the criteria of dividing patients into two groups in this study were somewhat arbitrary.

Generally the major prognostic factors for patients having radical hysterectomy and pelvic lymphadenectomy for stages IB to IIA cervical cancer are as follows:

Lymph node status, size of primary tumor, depth of stromal invasion, lymph-vascular space invasion, parametrial extension, histologic type, and resection margin status.

We know that univariate and multivariate analysis is required before subgrouping the each criteria in this study. However, the number of patients was too small for such analysis in this study, and these criteria are already known to have poorer prognosis in other studies.<sup>1-6</sup> So, we subgrouped the three criteria based on the previous report.

We also know that there is not any definite evidence of survival nor disease free benefit of consolidation chemotherapy after adjuvant concurrent chemoradiation therapy (CCRT). The only report about the consolidation chemotherapy after CCRT by Lee et al.<sup>7</sup> dealt with small number of patients (25 vs. 15) but is not enough for disregarding the trial of consolidation treatment. I also agree with you that we cannot say there is any beneficial role in consolidation chemotherapy after CCRT until the result of other prospective study is published.

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DOI:10.3802/jgo.2009.20.2.133