Editorial

Management of patients with intermediate-risk early stage cervical cancer

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Conflict of Interest

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► See the article “Chemoradiotherapy is not superior to radiotherapy alone after radical surgery for cervical cancer patients with intermediate-risk factor” in volume 31, e35.

Kim et al. [1] retrospectively compared the outcome of 2 types of adjuvant treatment, radiotherapy versus chemoradiation, in patients with intermediate-risk (IR) early stage cervical cancers. Criteria for the IR group were adopted from the Gynecologic Oncology Group (GOG) 92 study published in 1999 [2]. While a combination of risk factors was required in the GOG trial, all cases with at least 1 risk factor were eligible in the current study. The authors did not find difference in a 5-year recurrence-free survival (RFS) or overall survival and concluded that chemoradiation is not superior to adjuvant radiotherapy alone. In addition to the lack of survival benefit, a combined treatment was associated with a significantly higher risk of grade 3 toxicity.

The choice of treatment for the IR group of patients is indeed one of the most controversial topics in the current management of cervical cancer. While in patients with high risk factors, such as positive lymph nodes (LNs), parametrial involvement, or positive surgical margins, there is an evidence from several randomized trials about a benefit from a combined chemoradiation, in the IR group no such prospective study has been conducted.

The paper from Kim et al. undoubtedly represents an important contribution to the current discussion about the management of the IR group. The authors should be acknowledged for including a large number of cases from one institution and for the long follow-up. At the same time, we should be aware of the limitations of the results. The authors themselves point out that the choice between the 2 types of adjuvant treatment was up to the preference of the attending physician. Risk factors were more frequently represented in the chemoradiation group (+10% tumors ≥ 4 cm; +30% lymphovascular space invasion; +20% combination of 3 risk factors). Radical hysterectomy and pelvic lymphadenectomy were the only enrollment criteria, irrespective of the type of procedure or its quality. This is also a major limitation of the original GOG 92 study. Surgical treatment was, after all, the main treatment modality and its quality influences the risk of recurrence, mainly the local control, and, hence, can modify a benefit of adjuvant therapy. Another limitation, which the publication has in common with GOG 92, is an inaccurate assessment of risk factors. Most importantly, the tumor size, which is the main risk factor, did not require a measurement using imaging or pathology.

As far as the management of the IR group is concerned, we should discuss one more approach, which was not addressed in the study. That is: Can these patients be spared adjuvant treatment at all?

The evidence for the improved RFS after adjuvant radiotherapy comes from only 1 randomized study which was conducted three decades ago [2]. Several other publications supported a better outcome after adjuvant radiotherapy; however, all were retrospective and they suffered from limitations such as a small sample size, heterogeneity of patient population, or lack of control groups [3]. Recently, 2 institutions which traditionally have not used the GOG criteria for adjuvant treatment indication, showed an excellent local control after more extensive (type C2) radical hysterectomy without any adjuvant treatment [3,4].

We should take into consideration that the selection of patients with IR factors is currently much more accurate than 30 years ago. Sentinel LN detection and their ultrastaging enables detection of an additional 10%–15% of cases with small macrometastases or micrometastases, which means these cases are then moved to the high-risk category. Modern imaging technology accurately detects any parametrial involvement and those patients are referred for definitive chemoradiation. Undoubtedly, the cohort of IR patients in 2020 would be different than the one in 1980. Even the results of Kim et al. [1] paper can be used to illustrate the evolution of the outcome in time. Comparing identical groups of IR patients treated by radical surgery and adjuvant radiotherapy, in the Kim et al. [1] study the 5-year RFS was 91% and a local RFS was better than 99%, whereas in the GOG study the 2-year recurrence rate reached 15%, from which the majority of events were in the pelvis (18/21).

One of the important tasks of our discipline is to define the optimal management for the IR group defined by current standards of clinical and pathological staging. In the new European clinical practice guidelines, primary chemoradiation is suggested in patients in whom a need for a combined treatment is known before the surgery [5]. If this applied to all patients with IR factors, the role of radical hysterectomy would disappear in the future. New prospective evidence is needed to compare several approaches, including an increased radicality of surgery without any additional treatment, a standard radicality of parametrectomy combined with adjuvant radiotherapy/chemoradiation or a primary definitive chemoradiation. In the era of decreasing incidence of cervical cancer, such study will require the widest international collaboration.

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