A Novel Perspective of Neoadjuvant Chemotherapy in Locally Advanced Cervical Cancer

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A high response rate of locally advanced cervical cancer in the first trials conducted in the 1980s raised high expectations from neoadjuvant chemotherapy.^{1,2} Several prospective, randomized trials were designed in different parts of the world with great enthusiasm; however, the results were unfortunately disappointing since the majority failed to prove any benefit for either local control or survival.^{2–6} In fact the Japanese trial conducted by Katsumata et al. was prematurely terminated due to inferior survival in the neoadjuvant chemotherapy arm.⁷

A study by Benedetti-Panici et al. shed new light on the indication for the exposure of patients with locally advanced cervical cancer by neoadjuvant chemotherapy. These investigators found noninferior disease-free and overall survival after radical hysterectomy, with less extensive parametrectomy in those patients who responded to neoadjuvant chemotherapy. Less radical surgery after tumor downsizing resulted in a significant reduction in late postoperative morbidity, namely bladder dysfunction. In addition, it has previously been repeatedly shown that neoadjuvant chemotherapy is effective in decreasing the size of the tumor and the prevalence of lymph node involvement, especially the presence of micrometastases,⁸ and therefore consequently diminishing the need for adjuvant treatment.^{7,9} A combination of less radical surgery, together with less need for adjuvant radiotherapy, should result in a significant improvement in long-term morbidity and quality of life.

Undoubtedly, the study has many limitations, especially the small size of the study population. If the power analysis had been calculated for a disease with a recurrence rate of 10–15 %, a noninferior trial would have required at least 700 cases. However, what is convincing is the excellent survival rate, especially local control, in both groups, taking into consideration that patients with bulky tumors before neoadjuvant chemotherapy were enrolled in the study. Isolated pelvic recurrence occurred in only 6 of 72 patients from both groups.

A lack of standardization of different types of radical hysterectomy is a key limitation in many surgical trials, especially in a multicenter setting.^{10,11} In many institutions, only one type of procedure is performed that fits all patients irrespective of tumor size or other prognostic factors. However, the quality of surgery at the authors' institution was one of the important strengths of the study. The institution has had a long tradition in high-quality radical surgery and conducting surgical trials in gynecological oncology. The substantial difference between the two types of radical hysterectomy in their hands is reflected in significantly different morbidity, especially bladder dysfunction. It has been repeatedly shown that spontaneous voiding recovery, loss of bladder sensation, and urinary incontinence are closely related to the extent of parametrial resection, which is the principle difference between type B and C radical hysterectomy.

No final conclusions can be made from the Benedetti-Panici study due to its retrospective design, historical cohort as a control group and, most importantly, the small cohort size. In addition, it should be emphasized that only selected patients with negative lymph nodes and clinical response to neoadjuvant chemotherapy were enrolled in the study. Nevertheless, the results stimulate interest in the implementation of neoadjuvant chemotherapy in the management of patients with locally advanced cervical cancer

with the primary intent of improving their quality of life after treatment.

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