SHORT REPORT
UDC: 618.146-006:616-085

Arch Oncol 2005;13(2):89-90.
DOI: 10.2298/AOO0502089M

Neoadjuvant chemotherapy in treatment of cervical cancer - controversies

Aljoša Mandić

KEY WORDS: *Cervix Neoplasms; Neoadjuvant Therapy; Treatment Outcome*

Institute of Oncology Sremska Kamenica, Serbia & Montenegro; Address correspondence to: Dr. Aljoša Mandić, Institute of Oncology Sremska Kamenica, Institutski put 4, 21204 Sremska Kamenica, Serbia & Montenegro, E-mail: aljosa.m@eunet.yu; The manuscript was received: 08.07.2005, Provisionally acepted: 11.07.2005, Accepted for publication: 15.07.2005

INTRODUCTION

Cervical cancer is still one of the main problems in female populations of developing countries. Early diagnosis and screening programs are still the best solution for decreasing of disease incidence. Despite improved screening techniques for preinvasive disease, approximately 13,000 new invasive cervical cancer cases are diagnosed, and 4000 patients die each year (1). Also early diagnosis of cervical cancer is opened to the different modalities of treatment having in mind the volume of tumor, stromal invasion, lymphvascular status, histopathological type, lymph nodes metastasis, age of patients, and their general health conditions. Patients with stages IB and IIA cervical cancer can be treated either with radical hysterectomy plus pelvic lymphadenectomy or with the irradiation of whole pelvis with equivalence in survival outcome (2).

Nowadays, the standard management of cervical cancer depends on clinical stage and tumor volume. Stage IB1 patients are submitted to radical hysterectomy and those with stage IB2 or higher stage disease are treated with radiotherapy. Controversies about the selection of surgical versus nonsurgical cases are still current such as are the controversial thoughts for bulky cervical cancer treatment. Controversies also exist regarding the indications for adjuvant radiotherapy after radical surgery and about the indications for the adjuvant hysterectomy, which can be considered after radiotherapy.

Many studies offer different therapeutic approach for the early stage of the cervical cancer and the standard management of this disease is changing. After years of studying multimodality treatments as an alternative to radiation alone in randomized phase III trials, the standard treatment has changed to chemoradiotherapy based on cisplatin. The addition of cisplatin-based chemotherapy to concurrent radiotherapy has improved survival in patients with bulky disease or patients with positive lymph nodes (3-6).

Neoadjuvant chemotherapy (NACT) is used to shrink the tumor before radical hysterectomy or radiotherapy. Tumor size is an important prognostic factor in patients with stage IB cervical cancer. Treatment of stage IB2 cervical cancer remains controversial because of that. Questions about the best treatment approach are still opened. Data from randomized trials suggest that neoadjuvant platinum based chemotherapy prior to definitive surgery is associated with better results than primary radiation (7,8). NACT prior to surgery or radiation therapy has been studied as a means to reduce tumor bulk, thereby rendering subsequent therapy more effective.

Hwang YY et al. presented a ten-year follow-up of 80 patients with locally advanced stage IB-IIB cervical cancer with tumor diameter of = 4 cm, after NACT by cisplatin, bleomycin, and vincristine, and radical hysterectomy. The study showed a reduction in tumor size after NACT in 75 cases. Overall, 5- and 10-year disease-free actual survival rates were 82% and 79.4%, respectively. Clinical stage, initial tumor size, clinical response, and residual tumor size were not risk factors for recurrence after this therapy, but pelvic lymph node metastasis was a significant risk factor for recurrence (9).

One prospective randomized study was performed in which 295 patients in stage IIB were randomly allocated to three groups: only surgery, only radiation, and both combined with NACT. After 84-month follow-up (mean), the survival rate for surgery and NACT was 65%, for radiation and chemotherapy was 54%, for radiation alone was 48%, and for surgery alone was 41%. The best survival rate was in patients who received chemotherapy followed by surgery and radiation. Resectability was significantly better in NACT plus surgery group (80%) compared with only-surgery group (56%) ($P \leq 0.001$)(10). In Kim's et al. study cisplatin, vinblastine, and bleomycin were used before radical hysterectomy in stage I and IIA tumors larger than 4 cm; complete response rate was reported in 44% and partial response rate in 50% patients (11). According to these results NACT could be a good modality that can decrease the size of tumors.

M. Modarress et al. compared the efficacy of preoperative combined chemoradiation and NACT programs followed by radical surgery in stages IB-IIB bulky cervical cancer (12). Sixty patients with stage IB-IIB bulky cervical cancer were treated with preoperative external-beam radiotherapy to 45 Gy plus weekly cisplatin 50 mg/m^2 or preoperative NAIC by cisplatin 50 mg/m^2 and vincristine 1 mg/m^2 every 7 to 10 days, for three courses. Surgery was performed in 4 to 6 weeks after the completion of the preoperative treatment. There were no significant differences between age, stage, tumor size, and histopathologic type in two groups. In chemoradiotherapy group, 23.7% of patients had complete clinical response and in NACT group 16.7% without statistical significance. Partial clinical response to treatment in NACT and chemoradiotherapy groups was detected in 25 (83.3%) and 23 (67.7%)

patients, respectively without statistically significance. There were no other significant differences between NACT and chemoradiotherapy in treatment efficacy and survival prognostic factors. After treatment, there were more complications in the chemoradiotherapy group than in NACT group.

These results could point to both NACT and chemoradiotherapy methods as a reasonable treatment modality for improving the operability in patients with stage IB-IIB bulky cervical cancer by decreasing the size of tumor. Of course these studies included small number of patients so it is very difficult to compare effects of these methods. Further prospective randomization studies will be able to distinguish which treatment option will be better for these patients or we will get the similar effects. Also the effects of NACT are needed to investigate in higher stages of cervical cancer.

REFERENCE

1. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics. CA Cancer J Clin 2002;52:23-47.
2. Landoni F, Maneo A, Colombo A. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. Lancet 1997;350:535-40.
3. Jurado M, Martinez-Monge R, Garcia-Foncillas J, Azinovic I, Aristu J, Lopez-Garcia G, et al. Pilot study of concurrent cisplatin, 5-fluorouracil, and external beam radiotherapy prior to radical surgery +/- intraoperative electron beam radiotherapy in locally advanced cervical cancer. Gynecol Oncol 1999;74:30-7.
4. Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL III, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 1999;340:1154-61.
5. Peters WA III, Liu PY, Barrett RJ II, Stock RJ, Monk BJ, Berek JS, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol 2000;18:1606-13.
6. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, et al. Concurrent cisplatin-based chemoradiation in locally advanced cervical cancer. N Engl J Med 1999;340:1144-53.
7. Sardi J, Sananes C, Giaroli A, Bayo J, Gomez Rueda N, Vighi S, et al. Results of a prospective randomized trial with neoadjuvant chemotherapy in stage IB, bulky, squamous carcinoma of the cervix. Gynecol Oncol 1993;49:156-65.
8. Stewart LA, Tiernay JF. Neoadjuvant chemotherapy and surgery versus standard radiotherapy for locally advanced cervical cancer: a meta-analysis using individual patient data from randomised controlled trials [abstract]. Proc ASCO 2002;21:207a. Abstract 825.
9. Hwang YY, Moon H, Cho SH. Ten-year survival of patients with locally advanced, stage Ib-IIb cervical cancer after neoadjuvant chemotherapy and radical hysterectomy. Gynecol Oncol 2001;82:88-93.
10. Disaia PJ, Creasman WT. Invasive cervical cancer. In: Disaia PJ, Creasman WT, eds. Clinical gynecology oncology. St. Louis, MO: Mosby; 2002. p. 53-80.
11. Kim DS, Moon H, Kim KT, et al. Two-year survival: preoperative adjuvant chemotherapy in the treatment of cervical cancer stages Ib and II with bulky tumor. Gynecol Oncol 1989;33:225-30.
12. Modarress M, Maghami FQ, Golnavaz M, Behtash N, Mousavi A, Khalil GR. Comparative study of chemoradiation and neoadjuvant chemotherapy effects before radical hysterectomy in stage IB-IIB bulky cervical cancer and with tumor diameter greater than 4 cm. J Gynecol Cancer 2005;15:483-488.