

Research article

The role of neoadjuvant polychemotherapy in the treatment of patients with stage IIB cervical cancer

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ABSTRACT

Introduction and Aim: More than 85% of cervical cancer (CC) cases are reported in developing countries where access to screening is limited. With localized forms of CC, it is possible to achieve good treatment results using radical procedures compared to locally widespread processes.

Methods: This is a retrospective study of 68 patients with stage IIB CC hospitalized from 2013–2022. During the initial treatment and after a full clinical examination, all patients were diagnosed with stage IIB CC, a parametrial and vaginal involvement.

Results: Forty-six patients (74%) received two courses of chemotherapy, 14 patients (23%) received three courses, and 2 patients (3%) received four courses. The tumor became resectable after two courses in 46 patients, after 3–4 courses all patients moved on to the next surgical stage. Of the early postoperative complications, 9 patients (14.5%) had bladder atony, which was resolved by the conservative method.

Conclusion: Thus, there is a certain category of patients with CC, where it is possible to make the tumor into a resectable form, and this will increase the percentage of the surgical component of treatment, which in turn could increase the 5-year disease-free survival rates of patients with stage IIB CC.

Keywords: Cervical cancer; chemoradiotherapy; neoadjuvant polychemotherapy; 5-year disease-free survival rates; relapse-free survival rates.

INTRODUCTION

Cervical cancer (CC) is one of the most common malignant neoplasms of the female reproductive system. Despite effective screening and vaccination against human papillomavirus, according to GLOBOCAN, about 600,000 new cases of CC are registered annually worldwide, which takes up the fourth place in female cancer incidence (1).

More than 85% of CC cases are reported in developing countries where access to screening is limited, which leads to diagnosis in the later stages of the disease. If morbidity is considered, CC consistently ranks second in the female population and about 500 new cases of CC are registered annually in Kyrgyzstan (2). Considering the data available from the National Center of Oncology and Hematology, Kyrgyzstan regarding mortality then CC cases occupy the first place with 300 cases a year, i.e.,

more than half of patients with an established diagnosis die (2).

With localized forms of CC, it is possible to achieve good treatment results using radical procedures compared to locally widespread processes (a tumor >4 cm with or without spreading to the parametrium, the side walls of the pelvis, or the lower third of the vagina and /or with metastases to the lymph nodes). In locally advanced cervical cancer, the standard treatment is concurrent chemoradiotherapy (CCRT), which determines the 5-year disease-free survival, according to worldwide data for stages IB3 – 76.1%, IIB – 63.9%, and III – 40% (3–5).

Despite the improvement of CCRT, the overall survival rates are not high, which requires the study and development of new treatment tactics in patients in this group. It is well known that in the conditions of Kyrgyzstan, it is not always possible to fulfill the above standard treatment and in many cases patients

were sent to neighboring countries for an effective treatment.

The objectives of this study were to determine the criteria for the selection of patients for neoadjuvant polychemotherapy (nPCT) in patients with stage IIB CC; to conduct a retrospective analysis of the frequency and types of complications after nPCT; Determine the criteria for the effectiveness of nPCT; Assessment of 5-year disease-free and relapse-free survival rates in comparison with the control group.

MATERIALS AND METHODS

This is a retrospective study of 68 patients with stage IIB CC hospitalized from 2013–2022, the follow-up period was from 6–108 months. The age of the patients ranged from 31–74 years. More than half were middle-aged patients, and younger and older are low in number. 75% of patients are residents of the village and 25% from urban areas. In 80% of cases, patients complained of spotting from the genital tract and pain in the lumbar region. During a local examination of the pelvic organs, infiltration was determined and did not reach the pelvic walls.

During the initial treatment and after a full clinical examination, all patients were diagnosed with stage IIB CC, a parametrial and vaginal involvement. The diagnosis is histologically confirmed.

The tumor staging of the disease was determined according to the Tumour-Node-Metastasis classification (6), based on the data of bimanual, rectovaginal, morphological studies, rectoscopy, cystoscopy, ultrasound, and magnetic resonance imaging of the pelvic organs. Of 62 patients, 95% of patients had histologically verified squamous cell non-cancerous cancer and 5% of patients had adenocarcinoma. According to the degree of differentiation in 90% of patients, a moderate degree of differentiation is G2, a high degree of differentiation is G1 in 8% of patients, and a low degree of differentiation is G3 in 2% of patients.

The selection criteria for nPCT were

- Histologically confirmed diagnosis of CC
- The presence of infiltration beyond the vaginal arches (<1/3)
- The absence of regional and distant metastases
- Absence of decompensated concomitant pathology

Patients received the first stage of nPCT treatment, the second stage was surgical treatment, and the final stage was radiation therapy. Chemotherapy regimens

consisted of paclitaxel, carboplatin, cisplatin, bleomycin, 5 fluorouracil, and cyclophosphane. 80% of patients had side effects of chemotherapy in the form of nausea, vomiting, diarrhea, stomatitis, hair loss, leukopenia, and anemia, which did not affect the course of the treatment.

The criteria for the effectiveness of nPCT were

- Reduction of the size of the cervical tumor
- Decrease in the intensity of bleeding from the tumor
- Reduction of the size of infiltration beyond the vaginal arches
- Decrease in cervical density
- Mobility of the cervix

RESULTS

The study of the rate and completeness of tumor regression under the influence of nPCT revealed their dependence on sensitivity to chemotherapy, the initial size of the tumor, and the number of chemotherapy courses.

46 patients (74%) received two courses of chemotherapy, 14 patients (23%) received three courses, and 2 patients (3%) received four courses. The tumor became resectable after two courses in 46 patients, after 3–4 courses all patients moved on to the next surgical stage. As a result, out of 68 patients, 62 patients had extended uterine extirpation with lymphadenectomy. Infiltration in the parameters persisted in 6 patients after chemotherapy courses, which was a contraindication to surgical intervention, and the patients were transferred to radiation therapy. All patients who moved to the surgical stage underwent radical surgery. In 12 patients (19%) of cases, in the postoperative histological report, there were data for the presence of metastasis in the lymph nodes and invasion of more than 0.5 mm, in some cases with a transition to the cervical canal, and therefore, these patients received postoperative chemotherapy from 2–4 courses.

The duration of the operation varied from 2–4 hours. The average blood loss is 600 ml. Of the intraoperative complications, bleeding up to 1500 ml was noted in two cases. Of the early postoperative complications, 9 patients (14.5%) had bladder atony, which was resolved by the conservative method, vaginitis was observed in 5 patients (8%). Lymphocysts in 6 (9.6%) patients, the maximum size of cysts was up to 12 cm, which was eliminated by conservative methods of treatment.

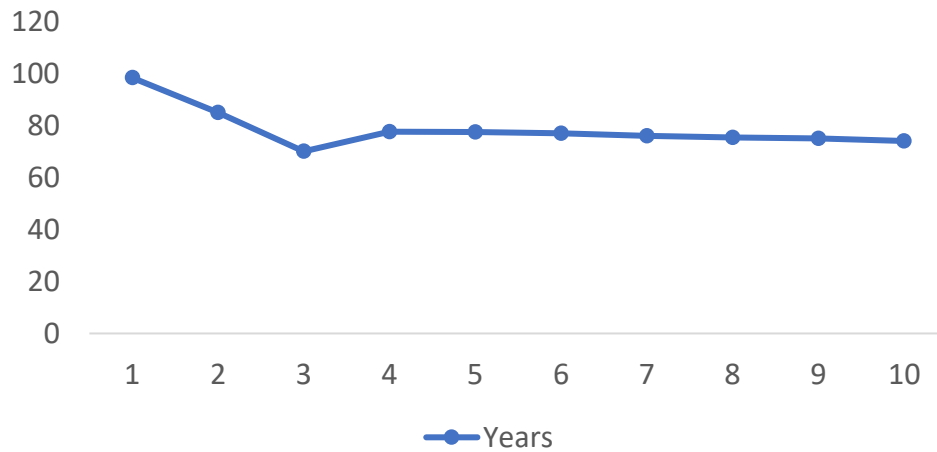


Fig. 1. The 5-year disease-free survival rates in the patients with stage IIB CC

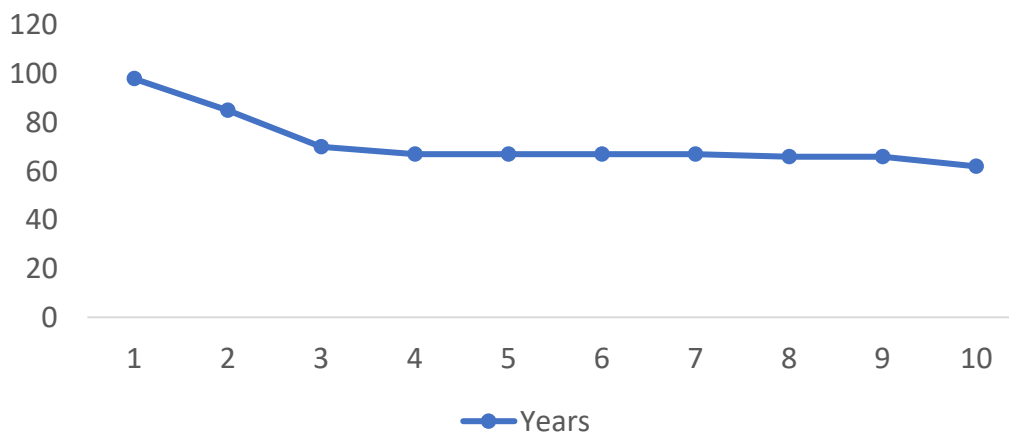


Fig. 2. The relapse-free survival rates in the patients with stage IIB CC

DISCUSSION

As a result of our study, out of 68 patients with stage IIB CC included in the study, 62, after the nPCT, showed lysis of tumor infiltration, and the transition of the tumor to a resectable form. After that, it became possible to perform the 2-stage surgical treatment in the volume of expanded extirpation of the uterus with appendages with pelvic lymph dissection. Then the patients underwent combined chemoradiotherapy. The use of nPCT made it possible to transfer patients with stage IIB CC to a resectable form in 92% of cases, this, in turn, allowed radical surgical intervention to be performed, thereby increasing the 5-year disease-free and relapse-free survival rates by 10% after complex treatment compared with the results of combined treatment of patients with stage IIB CC according to the literature.

Stage IIB in the group of locally advanced cervical cancer requires special attention, since transitional forms between stages IIA and IIB, when there was widespread infiltration, where there are chances of performing radical surgical procedure, which can lead to better survival rates. The use of nPCT to achieve the

conditions of resectability of the process in the world has been studied since the 1960s. According to many studies, an improvement in the overall survival results was noted after nPCT before radical surgery or before CCRT (7). This was achieved due to the systemic effect of cytostatics, which led to a decrease in the size of the primary tumor focus, an increase in the ablaticity of the surgical field and the effect on micrometastases. According to González et al., nPCT gives a tumor reduction of up to 40% of cases (8). The above factors prompted us to start scientific work in order to evaluate the effectiveness of the use of nPCT in the complex treatment of patients with stage IIB CC.

CONCLUSION

However, the results of the treatment of patients in this category are ambiguous and of further great scientific and practical interest. Thus, there is a certain category of patients with CC, where it is possible to make the tumor to a resectable form, and this will increase the percentage of the surgical component of treatment, which in turn could increase the 5-year disease-free survival rates of patients with stage IIB CC.

But the use of radiation therapy after surgical treatment increases the number of complications. Therefore, the combination of chemotherapy and surgical treatment seems more promising and requires continued scientific research in this direction.

CONFLICTS OF INTEREST

None.

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