

Research Article

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Modern Opportunities of Stereotaxic Radiation Therapy in the Treatment of Recurrent Cervical Cancer (Cc)

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Abstract

Cervical cancer is the first in the structure of oncogynecological pathology, while in the last decade there has been a steady increase in the incidence of cervical cancer. The aim of the study was to determine the possibilities of using stereotaxic radiation therapy technologies in treatment programs for recurrent cervical cancer based on a retrospective analysis of the primary treatment of cervical cancer. A retrospective analysis of 100 cases diagnosed with recurrent cervical cancer who received radiation therapy at the Meshalkin National Medical Research Center, Novosibirsk, Russia, in the period 2011-2022. All patients received stereotactic conformal radiation therapy using the ELEKTA AXESSE device, using modern techniques: 3D conformal radiation therapy, intensity-modulated radiation therapy, rotational volume-modulated radiation. According to the results of a retrospective analysis of the localization of relapses, locoregional relapses were most often determined - 50 patients (50%), local relapses were detected in 44 cases (44%), distant relapses - 36 patients (36%), multiple (several localizations) - 43 (43%). At the same time, late relapses (more than 24 months) were most often recorded - 48 cases (65%), while early (12-24 months) only in 15 (20%) patients, progression was noted (up to 6 months) in 11 (15%). Most often, distant metastases of cervical cancer were found in the bones and lungs (35.8% each among distant metastases), in the brain and liver (14.2% each), inguinal and supraclavicular lymph nodes.

Our study showed that one of the most effective methods for treating recurrent cervical cancer is stereotactic conformal radiation therapy, in this sample it was used regardless of age, stage of the process, type of primary treatment, and results of pathomorphological examination.

Keywords: Radiotherapy; Relapse; Stereotactic radiotherapy; Combined radiotherapy; Cervical cancer.

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Relevance

Cervical cancer (CC) is the second most common cancer among women under 65 years of age and is the most common cause of death from gynecological cancer worldwide. In terms of morbidity and mortality, cervical cancer ranks fourth among all cancers. In 2020, there were 604,127 new cases of cervical cancer and 341,831 deaths worldwide. In the structure of mortality from malignant neoplasms in women under 45 years of age, cervical cancer occupies the first place [1]. Cervical cancer recurs after primary treatment in about 10-20% of patients with early disease and no evidence of lymph node metastases, and up to 64-70% of patients with lymph node metastases and/or locally advanced disease. The recurrence rate of cervical cancer correlates with the initial prevalence of the tumor process: the more advanced the stage of the tumor process, the higher the likelihood of recurrence [2]. Unfortunately, treatment strategies for this category of patients are limited to palliative management of symptoms, with most efforts to prevent disease progression and increase survival failing. One of the possible effective methods for the treatment of CC relapses is stereotactic radiation therapy [3,4], which makes it possible to deliver a radical dose of ionizing radiation non-invasively, without serious toxic complications [5]. The aim of the study was to determine the effective possibilities of using modern radiation therapy technologies in treatment programs for recurrent cervical cancer based on a retrospective analysis of the primary treatment of cervical cancer.

Material and methods

A retrospective analysis of 100 cases diagnosed with cervical cancer recurrence, who received treatment at the National Medical Research Center named after Ak. E.N. Meshalkin in the period 2011-2022. Patients were examined in accordance with international guidelines. Relapses and metastases were determined using additional research methods-MRI, CT, PET-CT, bone scintigraphy, and also confirmed by morphological examination. The age of the patients varied from 24 to 82 years, while the average age of the patients was 47.7 ± 12.5 years. Patients were included in the study group by random sequential selection. In all cases, the diagnosis of the primary tumor was morphologically confirmed: in 88 patients (88%) - squamous cell carcinoma, in 12 - adenocarcinoma (12%). Among this group, stage 0 - 2 (2%), stage I - 18 patients (18%), stage II - 36 patients (36%), stage III - 43 (43%), IV - 1 (1 %).

Concomitant pathology was detected in 41 (41%).

All patients of the study group (n=100) received stereotactic conformal radiation therapy using the ELEKTA AXESSE, using modern techniques:

1. 3D-conformal radiation therapy (3D-CRT) is a remote irradiation technology that reduces the load on healthy organs and tissues by generating an isodose that matches the volume of radiation.
2. Intensity Modulated Radiation Therapy (IMRT) is an intensity modulated dose delivery technique at static country angles.
3. Volume modulated irradiation (VMAT) is a radiotherapy technique in which irradiation is carried out with the simulta-

neous movement of the Gantry and the MLC.

Using the active breathing control system (ABC - Active Breathing Coordinator) - a type of radiation treatment that is used to irradiate tumors of organs that are mobile during breathing. (lungs, liver, pancreas, etc.)

Different dose limits were used for critical organs, corresponding to the following hypofractionation regimens: ROD 4-8 Gy for 3-10 fractions. ROD and SOD were determined taking into account the tolerance of the surrounding structures. In patients with lung metastases, radiosurgery (SRS) was used, ROD 18 Gy per 1 fraction.

All patients received topometric CT and MRI scans, followed by image fusion; if necessary, PET-CT data were used. Clinical tumor volume (CTV) was the same as for GTV. For PTV, an offset of 2-4 mm was used depending on local mobility. With metastases to the lungs, mobility was assessed depending on the position of the focus during maximum inspiration and expiration.

Response to treatment was assessed by clinical examination, ultrasound and MRI of CT at 3, 6, and 12 months in the first year, and every 6 months thereafter.

Results

We analyzed the primary methods of treatment received by the patients of the study group. As a result, it was revealed that the main methods of treatment were surgical (used up to stage IIa inclusive), radiation therapy (in combination with chemotherapy), combined methods. The most common method of treatment was combined radiation therapy, which was used in 38 patients (38%), only surgical treatment was received by 23 (23%), chemoradiation therapy was performed in 19 (19%), surgery in combination with adjuvant radiation therapy was performed in 19 (19%), chemotherapy (with palliative purpose) - in 1 patient (1%). An analysis of the primary treatments and the time to recurrence for each of them showed that in the case of the surgical method of treatment (including 4 cases in combination with adjuvant chemotherapy, in 3 cases with neoadjuvant chemotherapy), relapses occurred on average after 37, 6 months. In the case of a combination of the surgical method with adjuvant radiation therapy, the occurrence of relapse was noted after an average of 31.4 months, with the use of chemoradiotherapy - after 23 months. Most likely, earlier periods of recurrence in patients treated with combined methods of treatment are explained by the initial neglect of the disease. Analysis of the distribution of patients by stages showed that among patients with recurrent cervical cancer in this sample, stage III was the most common - 43 patients (43%), II - 36 patients (36%), I - 18 (18%), IV - 1 (1%). In our study, it was found that locoregional recurrences were most often determined - 50 patients (50%), local relapses were detected - 44 patients (44%), distant - 36 patients (36%), multiple (several localizations) - 43 (43%).

CC relapses were classified according to the time of occurrence into 3 groups: progression (up to 6 months), early relapses (from 6 to 12 months), late relapses (more than 12 months). The most frequent were late relapses - 65 patients (65%), early - 20 (20%), progression - 15 (15%). Locoregional relapses of cervical cancer occurred in early forms of relapses, and more often in late ones (65.6% of all locoregional relapses). CC metastases most often occurred in the late follow-up period (more than 12 months) -

68.2%. Local relapses were also observed in longer periods (60%). The analysis of radiation reactions and complications in patients with recurrent CC was carried out. In general, it should be noted that stereotactic radiation therapy was tolerated satisfactorily and was carried out in all patients in the planned volume. In all cases, radiation reactions and complications corresponded to I-II severity, did not lead to a break in the combined treatment, and were stopped by the appointment of symptomatic drug therapy. Acute toxicity grade 3-4 and complications after stereotactic radiation therapy were not observed.

One-year mortality for patients with recurrent CC was 9% (Figure 1). Three-year survival was 74%. The five-year survival rate was 52% (Figure 2). Depending on the location of the recurrence, five-year survival was 55% for the local recurrence group, 55% for the loregional recurrence, 64% for the distant relapses, and 47% for the multiple relapses group (Figure 3). Depending on the method of recurrence treatment, the five-year survival rate for the stereotaxic radiotherapy group was 62%, for the chemoradiotherapy group, 68%, for the drug therapy group, 34%, and for the surgical treatment group, 44% (Figure 4).

Clinical example

Patient D., 44 years old. In 2012 applied to the hospital at the place of residence, where a separate diagnostic curettage, a knife biopsy of the cervix was carried out, according to the result of a histological examination of 06/04/2012, squamous cell carcinoma with keratinization with invasion of the entire thickness of the biopsy was detected. The patient was admitted for further examination and treatment at the Federal State Budgetary Institution Ak. E. N. Meshalkin's with a diagnosis of stage III cervical cancer (T1bN1M0). In August 2012 a course of combined radiation therapy was carried out a remote stage in combination with radiomodification, then a course of intracavitary gamma therapy using the Multisource, the Fletcher system: ROD - 5 Gy, 2 fractions per week, 6 fractions. Thus, SOD was 30 Gy, EQD2 per t.V. = 70 Gr. EQD2 per T.A. = 80-90 Gr. In May 2014, progression was recorded, metastases were detected in the para-aortic lymph nodes. According to MSCT dated May 13, 2014. Conglomerates of retroperitoneal lymph nodes up to 4 cm. Then, at the Federal State Budgetary Institution Ak. E. N. Meshalkin's a course of conformal stereotaxic remote beam therapy was carried out using the "VMAT" method (rotation with modeling according to the intensity of irradiation), E=10 MeV, in the 5p/week mode with irradiation of the conglomerate of retroperitoneal lymph nodes in

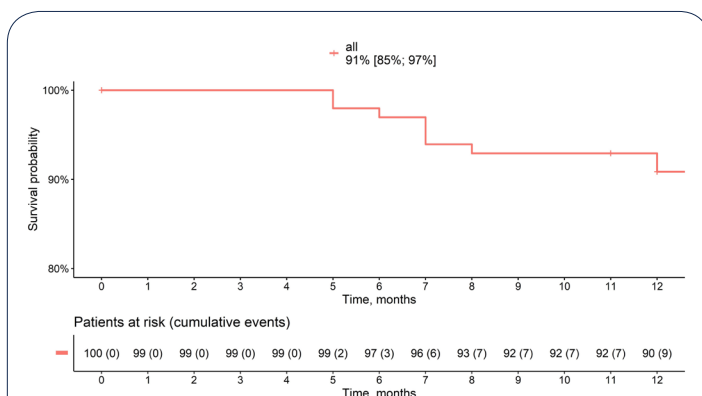


Figure 1: Survival of patients with recurrent cervical cancer for 12 months from the end of primary treatment.

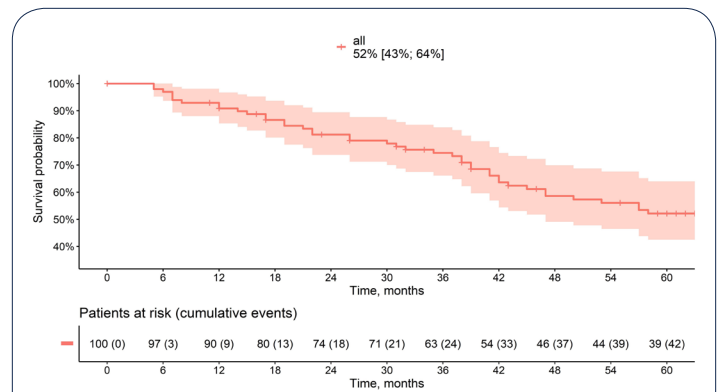


Figure 2: Survival of patients with recurrent cervical cancer for 60 months (5 years) from the end of primary treatment.

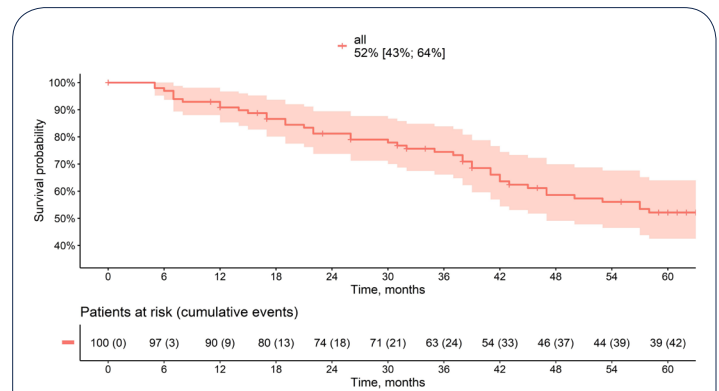


Figure 3: Five-year survival depending on the location of recurrence.

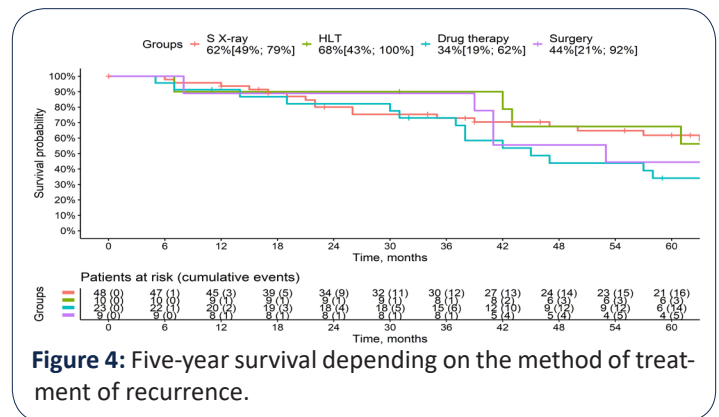


Figure 4: Five-year survival depending on the method of treatment of recurrence.

the ROD 3 Gy to SOD 48 Gy (equivalent to SOD 60 Gy) (Figure. 5). The treatment was carried out using IGRT image control technology. Currently, the patient has been under observation for more than 10 years, there are no signs of recurrence of the disease, the patient is under dispensary observation (Figure 6,7).

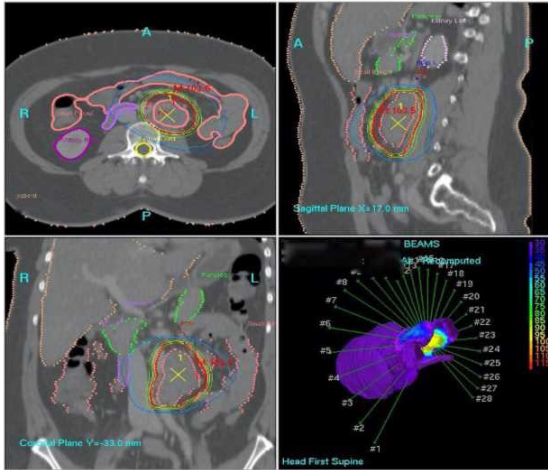


Figure 5: CT-topometric planning of stereotaxic irradiation of para-aortic lymph Nodes.

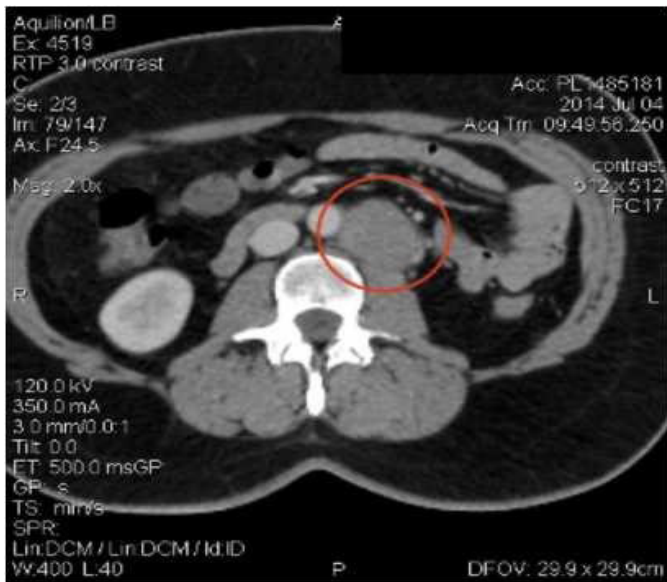


Figure 6: Before para-aortic lymph node irradiation.

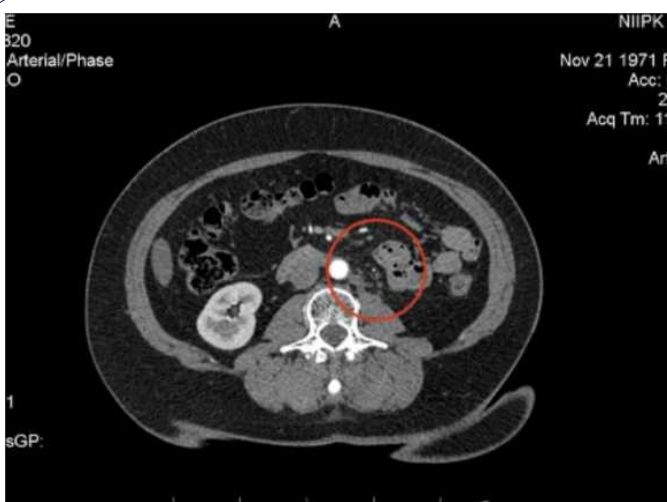


Figure 7: After irradiation of paraaortic lymph nodes.

Discussion

The data obtained by us were analyzed in comparison with the data of similar studies presented in the modern literature. Thus, according to the results of the study by Perez CA et al. most often, recurrences were detected in the vaginal stump, in the small pelvis, as well as in the form of distant metastases [8]. The most common distant sites were para-aortic lymph nodes (81%), lungs (21%) and supraclavicular lymph nodes (7%), the frequency of which was associated with the stage of the disease: at stage IA it was 0-3%, 13-16% at stage IB, 22-31% at stage IIA, 22-26% at stage IIB, 32-39% at stage III, and 75% at stage IVA, which is absolutely comparable with our results [9,10]. It should be noted that our study did not calculate the number of patients with CC relapses in relation to the total number of treated CC patients, which makes it difficult to interpret the data [11,12]. According to M. Peiretti et al. the frequency of pelvic recurrences after radical hysterectomy and pelvic lymphadenectomy varies depending on the specific risk factors for each patient [13]. Patients with such relapses after surgical treatment had a more favorable prognosis compared with patients with relapses after the use of primary radiation therapy alone, which also coincides with our results [14]. It should be noted that our study is not without limitations due to its retrospective nature, small sample size, and the lack of long-term results in the treatment of recurrent cervical cancer, which indicates the need and prospects for continuing the current study [15].

Conclusions

- Despite the early stages of the disease and the effectiveness of treatment methods, relapses were recorded in 54% of cases in patients with stages I (18%) and II (36%) of the disease, which confirms the need for more frequent and long-term monitoring of a group of patients with early stages of cervical cancer. .
- Local recurrences most often occurred in patients with stage I disease (55% of cases), while locoregional recurrences were more often detected in patients with stage III disease (62.5%). Given this nature of recurrence, during the observation period, an examination by an oncogynecologist, colposcopy, pathomorphological examination, ultrasound of the pelvic organs and abdominal cavity, and CT is necessary.
- The most common localizations of distant cervical cancer metastases are bones and lungs (35.8% each), brain and liver (14.2% each). Among distant lymphogenous metastases are inguinal and supraclavicular lymph nodes (50% each).
- Late relapses (more than 12 months) occurred in 65% of cases, regardless of the stage of the disease, which dictates the need for a longer follow-up of patients after treatment with cervical cancer.
- One of the most effective methods for treating recurrent cervical cancer is stereotaxic conformal radiation therapy; in this sample, it was used regardless of age, stage of the process, type of primary treatment, and results of pathomorphological examination.

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Conflict of interest: The authors declare no conflict of interest.

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