

MONITORING THE RESULTS OF CERVICAL CANCER TREATMENT BASED ON DATA FROM THE SAMARKAND REGIONAL BRANCH OF THE REPUBLICAN SPECIALIZED SCIENTIFIC AND PRACTICAL MEDICAL CENTER OF ONCOLOGY AND RADIOLOGY.

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Abstract. Cervical cancer is one of the most common malignancies among women. It is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women. This pathology remains a global public health problem, particularly in developing countries. According to GLOBOCAN 2022, 604,000 new cases and 342,000 deaths from cervical cancer were registered worldwide in 2020.

Study Objective: To investigate the factors leading to unsatisfactory outcomes (early recurrence, prolonged growth, one-year mortality and survival) after combined and comprehensive treatment of patients with cervical cancer.

Study Materials and Methods: A retrospective analysis of outpatient records and medical histories of 1,221 patients with cervical cancer treated between 2014 and 2023 was conducted, based on data from the Samarkand Regional Branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology.

Data from anamnesis, clinical, laboratory, morphological, and instrumental examinations obtained from patients with cervical cancer, outpatient records, medical histories, and cancer registry records.

Keywords: cervical cancer, recurrence, prolonged growth, chemotherapy, external beam irradiation.

Introduction. Cervical cancer (CC) is one of the most common malignant tumors among women. It is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women. According to GLOBOCAN 2022, in 2020, 604,000 new cases and 342,000 deaths from CC were registered worldwide.

Currently, the standard treatment for cervical cancer, consisting of a combination of surgery, radiation therapy, and chemotherapy, has been developed for early-stage and locally advanced cervical cancer [2].

Even though traditional radical treatment methods, including surgery, chemotherapy, and radiation therapy (RT), are available for early-stage and locally advanced cervical cancer, recurrence and metastasis of this pathology are still observed due to its heterogeneous manifestations.

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Data from anamnesis, clinical and laboratory data, morphological, and instrumental examination data were obtained from patients with cervical cancer, as well as outpatient records, medical histories, and cancer registry records. The following examinations were performed: gynecological examination, colposcopy, cervical tumor biopsy, chest X-ray, abdominal and pelvic ultrasound, pelvic and abdominal MRI before and after treatment, and PET-CT as indicated.

General clinical overview of the study. Despite screening measures, the study data show that the incidence of cervical cancer increases year after year among women of childbearing age. This means that by age group, the average incidence among women aged 18-25 is 10.25% ($\pm 3\%$), among women aged 26-35 it is 27.5% ($\pm 3\%$), and among women aged 36-45 it is 38.5% ($\pm 2\%$) (Table 1).

Table 1.

Distribution of patients by age group according to FIGO.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total quantity	n=89	n=92	n=127	n=141	n=108	n=141	n=134	n=138	n=134	n=117
18-25	12 13,5	0	2 1,6	8 5,7	4 3,7	6 4,3	9 6,7	9 6,5	12 9,0	12 10,2
26-35	16 18,0	14 15,2	24 18,9	32 22,7	36 33,8	48 34,0	34 25,4	38 27,5	24 18,0	29 24,8
36-45	30 33,7	45 49,0	42 33,0	56 40,0	42 38,9	52 36,8	45 33,6	51 37,0	42 31,3	45 38,5
46-55	29 32,6	23- 25,0	29 22,8	37 26,2	17 15,7	26 18,4	28 20,9	24 17,0	32 28,3	23 19,6
56 and older	2 2,3	10 10,8	16 12,6	8 5,7	9 8,3	9 6,4	18 13,4	16 11,6	18 13,4	8 6,8

A study of disease stage among newly diagnosed cervical cancer patients from 2014 to 2023 revealed the following: stage II diagnosis was approximately 53%, and stage III diagnosis was up to 26.5%. This suggests that screening and early diagnosis of cervical cancer over the past 10 years have not reduced the rate of locally advanced cervical cancer diagnoses (Table 2).

Table 2.

Patient stage distribution.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total number	n=89	n=92	n=127	n=141	n=108	n=141	n=134	n=138	n=134	n=117
Stage I	21 23,6	14 15,2	10 7,87	8 5,67	17 15,74	19 13,5	18 13,43	25 18,1	19 14,2	16 13,67
Stage II	38 42,7	46 50	55 43,3	58 41,1	53 49	66 46,8	68 50,74	65 47	68 50,7	62 53
Stage III	23 25,8	25 27,2	54 42,5	61 43,3	30 27,78	52 36,8	40 29,85	42 30,4	41 30,6	31 26,5
Stage IV	7 7,9	7 7,6	8 6,3	14 9,9	8 7,4	4 2,8	8 5,97	6 4,35	6 4,5	8 6,84

The table data show that the prevalence of the disease among women of childbearing age (18-45 years) is higher, with an average prevalence of $67 \pm 3\%$. Among women of socially active, working age (26-55 years), the average prevalence was $82.6 \pm 3\%$. Currently, the risk group for cervical cancer includes women of reproductive age (36-45 years). This suggests that, to effectively detect cervical cancer early, careful consideration must be given to the age group of women selected for screening.

A 10-year study revealed that exophytic tumor growth averaged $48.4\% + 3\%$, endophytic growth was detected in up to 35%, and mixed tumor growth was observed in up to 19% of cervical cancer patients (Table 3).

Table 3.

Distribution of cervical cancer patients by tumor growth pattern

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total number	89	92	127	141	108	141	134	138	134	117
Exophytic growth	49- 55,0	46- 50,0	67- 53,0	69- 49,0	46- 42,6	78- 55,3	56- 41,8	66- 47,8	58- 43,3	54- 46,1
Endophytic growth	29- 32,6	38- 41,3	48- 37,8	54- 38,3	33- 30,5	46- 32,6	52- 38,8	58- 42,0	44- 32,8	41- 35,0
Mixed tumor growth	11- 12,3	8- 8,7	12- 9,4	18- 12,76	29- 26,8	17- 12,0	28- 20,9	14- 10,4	32- 23,8	22- 18,8

The tumor's morphological type is important for determining treatment strategy and prognosis. A histological analysis of primary biopsy and postoperative specimens from 1,221 patients

revealed squamous cell cervical cancer (SCC) in 672 cases, representing an average of 55.2% ($\pm 4.8\%$) (Table 4).

Table 4.

Distribution of Cervical Cancer Patients by Histological Type.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total number	89	92	127	141	108	141	134	138	134	117
Squamous cell carcinoma	46-51,7	55-59,8	82-64,5	75-53,2	62-57,4	72-51,0	74-55,2	70-50,7	72-53,7	64-54,7
Nonkeratinizing squamous cell carcinoma	34-38,2	33-35,8	29-22,3	58-41,1	38-35,18	55-39,0	54-40,3	53-38,4	51-33,8	38-32,5
Adenocarcinoma	8-9,0	3-3,2	6-4,7	6-4,2	7-6,5	12-8,5	4-3,0	12-8,7	8-5,9	12-10,2
Clear cell carcinoma	1-1,1	1-1,1	1-0,8	2-1,4	2-1,8	2-1,4	2-1,5	3-2,2	3-2,2	3-2,5

The tumor's morphological type is of primary importance in treatment planning and prognosis in cervical cancer.

The majority of cervical cancers are squamous cell nonkeratinizing cancers, which are easily treated with specific treatment methods. However, the majority (56%) of patients presented with regional metastasis. Despite population-based screening, treatment outcomes remained largely unchanged over the past 7 years (2014-2020).

Table 5.

Distribution of patients by tumor grade G for squamous cell nonkeratinizing cervical cancer.

Squamous cell nonkeratinizing		2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
		n=33	n=33	n=29	n=58	n=38	n=55	n=54	n=53	n=51	n=38
G1	6-18,0	11-33,3	14-48,3	20-34,5	12-31,6	15-27,3	12-22,2	11-20,7	16-31,3	6-15,8	
G2	15-44,0	18-34,5	9-31,0	22-38,0	20-52,6	24-43,6	37-68,5	36-68,0	24-47,0	22-58,0	
G3	10-29,4	3-9,0	5-17,2	14-24,1	5-13,2	14-25,4	4-7,4	4-7,5	8-	8-21,1	

										15,7	
	G4	3-8,8	1-3	1-3,4	2-3,4	1-2,6	2-3,6	1-1,8	2-3,8	3-6,0	2-5,3

According to the G gradation of the tumor of squamous cell keratinizing cervical cancer, the following data were obtained from the initially diagnosed patients (668 patients): G1 squamous cell cervical cancer - 198 (29.64%) patients, G2 squamous cell cervical cancer - 347 (52%) cases, G3 squamous cell cervical cancer - 100 (15%), squamous cell cervical cancer G4 - 23 (3.4%) (Table No. 1).

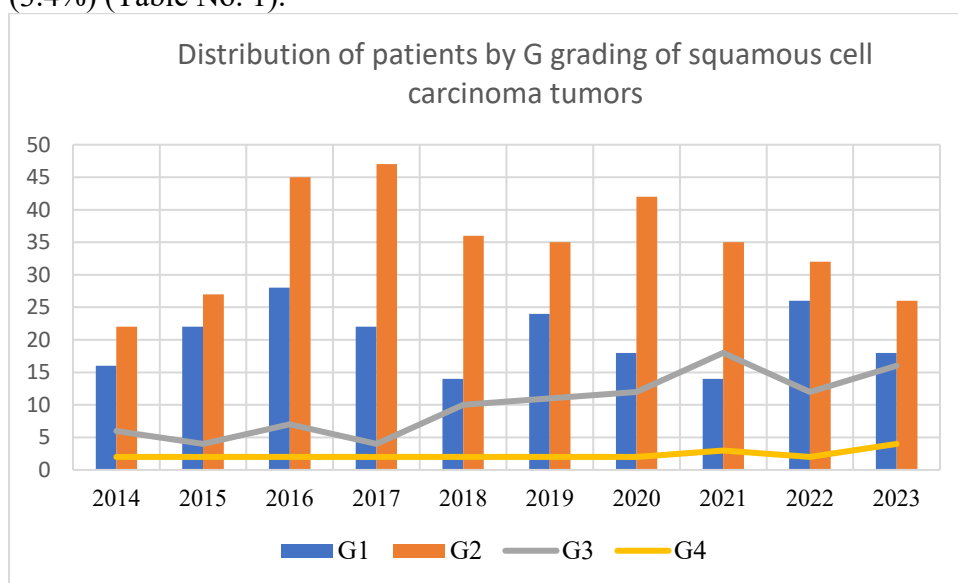


Fig. 1. Distribution of patients by G grading of squamous cell cervical cancer tumor (n=668). For stage IIb cervical cancer, 166 (88.3%) of 188 patients underwent polychemotherapy. Twenty-two patients (11.7%) received concomitant radiation therapy abroad. For stage IIIa cervical cancer, 44 of 112 patients underwent surgery. Forty-two patients received polychemotherapy. Of these, 22 received concomitant radiation therapy abroad. Of the 173/125 patients with stage IIIb cervical cancer, 6-8 courses of polychemotherapy were administered. 22 (19.7%) patients received combined radiation therapy abroad. Treatment outcomes were nearly identical, with a mean recurrence period of 12+4 months. Stage IV patients received palliative chemotherapy and symptomatic treatment. Since 2020, with the introduction of radiotherapy devices, radiation therapy has been included in the treatment of cervical cancer. According to the table, 60 of the 389 patients diagnosed with early cervical cancer underwent surgical treatment only.

Table 12.

Treatment methods for patients with cervical cancer from 2020 to 2023.

By stage	Surgical treatment only	Surgical Treatment +	Combine d	Combin ed radiatio	chemoth erapy only	Symptomati c treatment

		combined radiation therapy	radiation therapy	n therapy + chemotherapy		
I st (n=60)	60-100					
IIa st (n=106)	4-3,8	94-88,7		8-7,5		
IIb st (n=89)	-	-	37-41,6	28-31,5	24-26,9	
IIIa st (n=36)		18-50,0	6-16,7	12-33,3		
IIIb st (n=78)			22=28,2	44-56,4	12-15,4	
IV st(n= 20)			2-10,0	4-20,0	9-45,0	5-25,0
Total number of patients n= 389	64	120	65	82	53	5

Stage IIa was detected in 106 patients, of whom 4 patients underwent surgery alone, and 94 patients received surgery followed by combined radiation therapy. Eight patients received chemotherapy alone due to extragenital pathology. Stage IIb was detected in 89 cases, of which 37 patients received combined radiation therapy alone, and 28 patients received combined radiation and polychemotherapy.

Twenty-four patients received only courses of polychemotherapy due to contraindications to radiation therapy.

Thirty-six cases were identified with stage IIIa, of which 18 patients received surgery and combined radiation therapy, six patients received combined radiation therapy, and 12 patients received combined radiation therapy and polychemotherapy.

Seventy-eight patients were identified with stage IIIb, of which 22 patients received combined radiation therapy, 44 patients received combined radiation therapy followed by chemotherapy. Twelve patients received chemotherapy alone.

Twenty patients with stage IV disease were diagnosed: two patients received combined radiation therapy, four patients received combined radiation therapy and polychemotherapy, nine patients received polychemotherapy, and five patients received symptomatic treatment.

Radiotherapy: Combined radiation therapy is considered a standard treatment for squamous cell cervical cancer. However, the effectiveness of radiotherapy does not always produce the expected favorable results. In recent years, complications such as local carcinomatosis and pelvic ascites have been observed after combined radiation therapy for 9+3 months.

The following complications, which are rarely observed during treatment or after radiotherapy, were identified (post-radiation erosive cystitis, proctitis, rectal tumor, pelvic carcinomatosis, and ascites) during chemotherapy (Table 9).

Table 8.

Post-radiation complications of cervical cancer (n= 267).

Complications	Кол-во	В процентах
Post-radiation erosive cystitis	12	4,5%
Post-radiation proctitis	14	5,24%
Post-radiation rectal tumor	5	2%
Post-radiation skin burn	14	5,2%
Urinary tract stricture	6	2,24%
Thrombophlebitis of the lower extremities	8	3%
Leukopenia	26	9,7%
Post-radiation hemorrhoidal bleeding	5	2%
Progression of distant lymph node metastasis (subclavian lymph nodes, mesenteric lymph nodes with ascites)	6	2,5%

Treatment results for patients with stage Ib-IIa cervical cancer after traditional extended hysterectomy with adnexa and lymphadenectomy followed by combined radiation therapy and chemotherapy yielded expected results when using a second chemotherapy regimen.

Furthermore, patients who underwent laparoscopic extended hysterectomy with adnexa and lymphadenectomy also had favorable results. This surgical option helps reduce the risk of postoperative complications, including adhesions, chronic abdominal pain, urinary and defecation difficulties, intestinal obstruction, postoperative cysts, and prolapse of internal organs.

When comparing traditional extended hysterectomy with appendages with a minimally invasive surgical treatment method—laparoscopic extended hysterectomy with lymphadenectomy—the following data were revealed (Table 9).

Table 9.

Characteristics of the surgical treatment method for cervical cancer.

Indicators	Traditional laparotomy; Extended hysterectomy with lymphadenectomy	Laparoscopic; Extended hysterectomy with lymphadenectomy
Surgery duration	150-180	90-110min
Duration of anesthesia	160-200min	100-130 min
Blood loss during surgery	240-280ml	160-180 ml



Volume of lymph nodes removed	Removal of 11 groups of lymph nodes	Removal of only the affected lymph nodes
Injury to adjacent pelvic organs	Up to 20%	10%
Postoperative rehabilitation period	24-36 days	20 days
Wound healing time	15-28 days	14-18 days
Postoperative complications		
Early adhesive disease	12%	4%
Lymphorrhea	23%	-
Lymphcysts	3-5%	-
Secondary wound healing	5%	-
Postoperative hernia below the scar	12%	-
Ureteral stricture due to adhesions	7%	2%
Cystovaginal/rectovaginal fistula	4%	1%

With traditional laparotomy, extended hysterectomy with appendages and lymph node dissection, postoperative complications are 16-20%, including injury to adjacent pelvic organs, lymphorrhea, lymphadenopathy, postoperative adhesions of the abdominal and pelvic organs, ureteral stricture due to adhesions, and cysto-/rectovaginal fistulas, which can prevent the initiation of adjuvant chemotherapy and radiotherapy. Furthermore, postoperative recovery is extended to 40 days. The use of minimally invasive surgery in gynecologic oncology not only increases survival rates but also reduces socioeconomic costs.

The advantages of traditional laparotomy include: minimal trauma, shorter hospital stays, a shorter recovery period, and earlier initiation of subsequent treatment (combined radiation therapy or chemotherapy). Furthermore, minimally invasive procedures such as laparoscopic extended hysterectomy have the following favorable results: damage to adjacent pelvic organs is less than 10%, compared to 20% with traditional surgical treatment.

A key component of assessing cervical cancer treatment outcomes is determining one-year mortality among patients newly diagnosed and receiving specialized treatment. Furthermore, the ratio of one-year mortality to the incidence of advanced cases (stages III–IV) plays a significant role in assessing treatment outcomes. According to statistics from the Republic of Uzbekistan, one-year mortality among cervical cancer patients has tended to decrease in recent years due to the use of new-generation chemotherapy agents and targeted therapy (Table 10).

Table 10.
One-year mortality.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Republic of Uzbekistan	146	139	171	190	195	178	194	168	144	148
	11.1	10,1	11,4	13	12,6	9,6	11,8	9,2	7,8	7,9

Samarkand Region	7 7,8	16 17,4	15 11,8	13 9,2	10 9,2	7 5	12 9	9 6,5	6 4,5	6 5,1
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According to the table, the percentage of cases in the Samarkand region is lower than in the Republic, ranging from 2.1-3.4%.

Furthermore, a retrospective analysis revealed that 63.2% of women with cervical cancer complete the 5-year follow-up duration.

An analysis of mortality rates up to the first year of follow-up and 5-year survival rates for the period 2014–2023 revealed that one in five patients (19.2%) dies within the first year after cervical cancer verification.

Table 11.

5-Year Survival Rate in the Samarkand Region.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total number of patients	746	719	736	770	765	779	828	808	828	816
Of which, alive for 5 years	371	381	341	282	267	257	267	279	269	300
Of which, newly diagnosed	56	62	47	59	36	48	56	54	52	48

Discussion

The results of this study confirm the importance of a comprehensive approach to cervical cancer (CC) treatment and highlight the need to consider the individual characteristics of each case. An analysis of data from 1,221 patients revealed that, despite the implementation of screening programs, the problem of diagnosing and treating advanced CC remains a pressing issue. This underscores the importance of finding ways to improve early diagnosis and optimize treatment strategies.

An important aspect is the choice of treatment modalities, particularly the inclusion of radiation therapy. Results have shown that combined radiation therapy is not always sufficiently effective as adjuvant therapy, which may be due to various factors, including tumor genetic characteristics and individual sensitivity to radiation therapy. Therefore, studying prognostic factors and developing more individualized treatment approaches is relevant. The study highlights the importance of tumor morphological type and differentiation for treatment planning and prognosis in cervical cancer. An analysis of treatment outcomes for various histological tumor types revealed that nonkeratinizing squamous cell carcinoma responds best to specific treatment. However, it should be noted that a significant proportion of patients present at late stages, which complicates treatment and worsens the prognosis.

Thus, the conducted study allows us to identify the main directions for improving the results of cervical cancer treatment: improvement of screening programs for early detection of the disease, development of individualized approaches to the choice of treatment tactics taking into account the morphological characteristics of the tumor and development of new treatment methods, including targeted drugs and immunotherapy.



When studying treatment outcomes, the percentage of disease recurrence after combined treatment (surgery + chemotherapy, APC) without radiation therapy and with traditional treatment methods (i.e., combination treatment with radiation therapy) was almost identical. When using second-line chemotherapy (paclitaxel or gemcitabine), the effectiveness of radiation therapy increased by 70%, and complications associated with radiation therapy were reduced. Three-year survival increased by 16-18%, while one-year mortality remained virtually unchanged.

With second-line chemotherapy, the recurrence rate was reduced by 20%. Since 2023, targeted therapies have been widely used in cervical cancer treatment, with favorable results extending the recurrence-free period of combined treatment for cervical cancer.

Follow-up of patients receiving combined treatment (surgery + chemotherapy) with second-line chemotherapy also showed significantly improved results. Survival and recurrence-free periods for combined treatment (surgery + chemotherapy with second-line agents + targeted therapy) average 19+5 months.

Conclusions.

Modern gynecologic oncology advocates a personalized, comprehensive approach to cervical cancer treatment. While each newly diagnosed case represents one cancer, and although it may be of the same type, the immune response, resistance, and body composition are unique.

The reasons for unsatisfactory results depend on each patient's response to combined and comprehensive treatment.

The body's response is a genetically encoded protective complex that must be implemented during treatment of every case of cervical cancer.

Genetics research—identifying molecular markers for cervical cancer in each patient—means a personalized approach to diagnosis and treatment expands the possibilities for improving the expected treatment outcomes for this pathology.