

RESULTS OF TRIMODAL THERAPY FOR INVASIVE BLADDER CANCER

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Abstract:

Bladder cancer most of these tumors are represented by urothelial cancer and can be characterized by varying degrees of differentiation and invasiveness. In many cases, Bladder cancer develops against the background of generalized metaplasia of the entire urothelium from the renal pelvis to the urethra. This explains the tendency for multiple tumors to appear and Bladder cancer to recur after resection. Urothelial cancer cells can also migrate and implant into other areas of the urothelium, which makes it difficult to determine the causes of a re-detected tumor: incomplete removal of the primary, migration and implantation of cancer cells, multiple tumors or a different combination of them.

Keywords: bladder cancer, relapse, trimodal therapy.

Introduction

Relevance of the study: The incidence of RMP worldwide and in Uzbekistan tends to increase steadily. In Uzbekistan, the incidence was 3.1 per 100,000 population in 2021, in 2015 this figure was 3.2. The proportion of patients actively identified from the number of patients with newly diagnosed RMP in Uzbekistan in 2015 and 2021 was 14.2% and 16.5%, respectively. The proportion of patients with a morphologically confirmed diagnosis from the number of patients with newly diagnosed RMP in Uzbekistan in 2015 and 2021 was 89.8% versus 94.8%. The proportion of patients registered in oncological institutions in Uzbekistan for 5 years or more since the diagnosis of RMP in 2015-2021 was 36.3% and 37.3%, respectively. The proportion of patients with stage I–II tumor process from the number of patients with newly diagnosed RMP in Uzbekistan in 2015-2021 amounted to 50.0% and 55.4%. Mortality of patients from RMP in the Republic of Uzbekistan for 2015 and 2021. (abs. number and per 100,000 population) varied between 1.0 and 0.8, respectively. (Tillyashaykhov M.N., Sh.N.Ibragimov, Dzhanlich S.M., 2022)

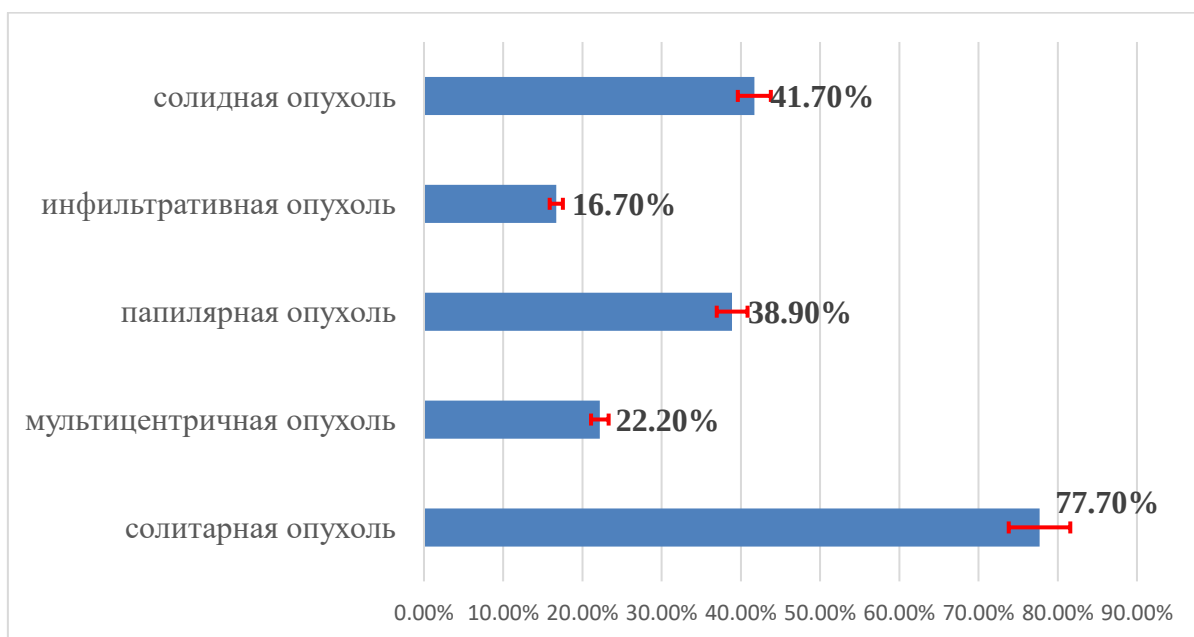
Local or disseminated metastases develop in at least 5% of patients with highly and moderately differentiated superficial papillary carcinoma and in 20% of patients with low-differentiated superficial RMP (including in situ carcinoma) (Trapeznikov N.N., Axel E.M., 2003).

Materials and methods of research: As part of a prospective study, the effectiveness of trimodal therapy was analyzed in 36 patients with invasive bladder cancer. The evaluation of treatment results was carried out on the basis of medical documentation, including medical histories, outpatient records and dispensary observation data. The catamnesis was traced back to December 31, 2023.

Demographic characteristics of the cohort: men made up 83.3% (n=30), women – 16.7% (n=6). The age range ranged from 43 to 82 years, with an average value of 62.7 ± 0.7 years. The largest proportion of patients, 15 (41.6%), belonged to the age group of 61-70 years.

The diagnostic algorithm included a comprehensive examination. Distribution by stages: T2a – $44.4 \pm 5.76\%$ (n=16), T2b – $55.6 \pm 6.93\%$ (n=20). The absence of regional and distant metastases was verified in all patients. Histological examination of biopsies in all cases revealed urothelial cancer.

Solitary tumors were diagnosed in $77.7 \pm 6.9\%$ (n=28) of patients, multifocal tumors in $22.2 \pm 6.93\%$ (n=8). By the nature of growth: papillary neoplasms were detected in 38.9% (n=14) of cases, solid - in 41.7% (n=15), infiltrative - in 16.7% (n=6).



At the initial stage of therapy, all patients underwent transurethral resection (TUR) and repeated TUR (RETOUR) of the bladder. Subsequent remote radiation therapy was performed on the device _ in static mode using four input fields of 8 x 10 cm each. The fields were arranged in the form of two front and two rear, with an angle of inclination of their central axes of radiation to the horizontal plane of 40 °. This configuration provided coverage of the primary tumor and regional lymph nodes.

The results of the study:

When determining the therapeutic target, the following criteria were used: 1) the upper border is between the articulation of the L5 and S1 vertebrae; 2) the lower border is the lower edge of the occlusion opening or the lower sections of the sciatic tubercles (when the tumor spreads to the urethra); 3) the lateral borders are along the edges of the walls of the bone pelvis with an indentation of 1-1.5 cm inside. When planning, they tried to exclude the posterior wall of the rectum from the irradiation zone.

Indications for radical radiation therapy were: 1) single or multiple tumors more than 3 cm in diameter; 2) subtotal or total damage to the bladder; 3) localization of the neoplasm in the neck or Lieto triangle.

Radiation therapy was performed in the hypofractionation mode of the dose. The single focal dose was 2 Gy, the total focal dose was 55 Gy. Treatment was carried out in a split course with an interval of 2-3 weeks between stages after reaching a dose of 30-40 Gy. Cisplatin was used as a radiosensitizing agent at a dose of 100 mg/m² every 3 weeks.

During trimodal therapy, 13 (36.1%) patients had reactions in the form of cystitis. The treatment was carried out without interruption of radiation or in between courses. Further follow-up revealed complications in the form of radiation cystitis in 7 (19.4%) patients: mild in 2 (5.6%), moderate in 4 (11.1%), severe in 1 (2.8%) patients. All patients with complications underwent conservative therapy with a positive effect.

The subsequent treatment tactics were determined depending on the results of radical radiotherapy. The clinical effect, including cases of complete and partial tumor regression, was evaluated 1-2 months after completion of irradiation using clinical, endoscopic, ultrasound and X-ray examination methods according to WHO recommendations. The assessment was carried out in 29 (80.6%) patients; 7 (19.4%) patients did not show up for a follow-up examination after radiotherapy and refused further treatment.

The clinical effect was achieved in 31 patients, which is 86.1% of the estimated cases. Complete tumor regression was recorded in 13 (36.1%) patients. These patients were strictly monitored at the dispensary with regular checkups every 3 months, including mandatory cystoscopy and ultrasound monitoring. When detecting a relapse, the issue of surgical treatment, mainly organ-preserving, was considered. The volume of surgery was determined by the size and location of the tumor and did not depend on the time elapsed after the end of radiation therapy.

Stabilization and progression of the tumor process after trimodal therapy were found in almost equal numbers of cases, amounting to 11.1% (4 patients) and 8.33% (3 patients), respectively. During stabilization, two patients underwent cystectomy, and the rest had contraindications to it. These patients, as well as patients who had a progression of the oncological process, were treated symptomatically.

The results of radical radiation therapy for invasive bladder cancer are clearly presented in Table 20.

Table 1 The effectiveness of trimodal therapy in patients with invasive bladder cancer.

	The absolute number	%
Full regression	13	36,1±3,2
Partial regression	16	44,4±2,9
Stabilization	4	11,1±2,3
Progression	3	8,33±3,1

As a result of the trimodal therapy of invasive bladder cancer, partial regression of the neoplasm was most often observed in 16 (44%) patients.

The study analyzed the effectiveness of trimodal therapy depending on the stage of the tumor process and the total focal radiation dose. At stage T2, the clinical effect was observed in 87.4% of patients, with complete tumor regression recorded in 43.7% of patients. In patients with stage T2b, the clinical effect was noted in 85.5% of cases, which is slightly lower than in T2a. It is noteworthy that the frequency of stabilization of the process was comparable in all stages. Disease progression was not observed at T2a, but reached a maximum (5%) at stage 2b, which is statistically significant ($p<0.001$).

Table 2 The effectiveness of radiation therapy depends on the stage of the tumor process.

	T2a n=16		T2b n=20	
	abs	%	abs	%
Full regression	7	43.7±4.4%	7	35.5±3,4%
Partial regression	7	43.7±4,4%	10	50±0.1
Stabilization	2	12.5±2.2%	2	10±0.3
Progression	0	0	1	5±0.1

During long-term follow-up of 36 patients with invasive bladder cancer, relapses were detected in 7 (19.5%) patients. The time interval before recurrence varied from 6 to 48 months, with an average of 18.9 months after completion of treatment. Morphologically, recurrent tumors predominantly had a urothelial growth pattern of 28 (77.7%), adenocarcinoma 3 (8.3%) and squamous cell forms 4 (11.2%) were less common.

After histological confirmation of recurrence, patients underwent surgical interventions in different volumes. Cystectomy was required in only one case. Chemotherapy was prescribed to 2 patients with inoperable relapses. No effect was obtained. In one case, a contraindication to special types of treatment was revealed.

Repeated recurrence was observed in 6 (16.7%) patients. At the same time, relapses were detected twice in 4 (11.1%), three times and four times equally often in 2 (5.5%) patients, respectively. In case of repeated relapses, 5 (13.9%) patients underwent a

bladder tour, and 14 (1.8%) underwent symptomatic treatment. The timing of subsequent relapses varied. The minimum period after the first and second relapse was 3.3 months, and the maximum was 12.7 months, respectively.

Distant metastases were detected in 3 (8.3%) patients who were under medical supervision after treatment. There were single cases in 2 (5.6%) patients, and multiple cases in 1 (2.8%) patients. On average, long-term metastasis was observed 24.3 months after the end of special treatment, and the minimum period was 7 months, and the maximum was 37 months.

The quality of life in 36 patients with invasive bladder cancer in the long-term period after radical radiation therapy was monitored. Frequent exacerbation of complications of special treatment requiring intensive conservative therapy was observed in 6 (16.7%) patients. The remaining 30 (83.3%) have a completely satisfactory quality of life, moreover, patients live with their bladder.

Conclusion:

An analysis of the literature data and the results of our own research, conducted using evidence-based medicine methods, allows us to conclude that trimodal is highly effective as one of the leading methods of treating invasive bladder cancer. It should be noted that trimodal is contraindicated in patients with severe concomitant pathology, cancer intoxication, severe anemia and chronic renal failure.

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