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Research Article



Local recurrences after radical cystectomy in bladder cancer patients

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BACKGROUND: Radical cystectomy is the standard treatment for patients with muscle-invasive bladder cancer and superficial neoplasms in cases of resistance to intravesical immunochemotherapy.

AIM: To establish the frequency of local pelvic recurrence in patients with bladder cancer after radical cystectomy.

MATERIALS AND METHODS: From 1997 to 2022 radical cystectomy was performed in 407 patients with bladder cancer: 344 (84.5%) men and 63 (15.5%) women. Orthotopic urinary diversion methods were performed in 302 (74.2%) patients, including gastrocystoplasty — 24 (5.9%), ileocystoplasty — 253 (63.8%) and sigmocystoplasty — 25 (6.1%) patients. Continent skin diversion of urine was performed in 13 (3.2%) patients, ureter transplantation into the sigmoid colon — in 42 (10.3%) patients, and ureterocutaneostomy — in 50 (12.3%) patients.

RESULTS: Local recurrence in the pelvis after radical cystectomy was observed in 33 (8.1%) patients: 27 (81.8%) men and 6 (18.2%) women. The average age of men with relapses was 58.7 ± 11.7 years (from 43 to 73 years), women — 50.0 ± 7.8 years (from 24 to 65 years). Simultaneous metastatic lesions of internal organs were detected in 6 (18.2%) patients. Local pelvic recurrence after radical cystectomy occurred more often in lymphopositive patients with extravesical spread of the primary low-grade tumor. The median time from radical cystectomy to detection of pelvic recurrence was 7.0 months, from the moment of detection of pelvic recurrence to the death of the patient — 4.5 months.

CONCLUSIONS: The frequency of local pelvic recurrence of bladder cancer after radical cystectomy is 8.1%. The survival rate of patients with local pelvic recurrence is extremely low.

Keywords: bladder cancer; radical cystectomy; local pelvic recurrence.

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Научная статья

Местные рецидивы после радикальной цистэктомии у больных раком мочевого пузыря

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Актуальность. Радикальная цистэктомия — стандартный метод лечения больных мышечно-инвазивным раком мочевого пузыря и поверхностной формой новообразования в случаях резистентности к внутрипузырной иммунохимиотерапии.

Цель — установить частоту локального тазового рецидивирования у больных раком мочевого пузыря после радикальной цистэктомии.

Материалы и методы. С 1997 по 2022 г. радикальная цистэктомия выполнена 407 больным раком мочевого пузыря: 344 (84,5 %) мужчинам и 63 (15,5 %) женщинам. Ортотопические методы отведения мочи были применены 302 (74,2 %) пациентам, в том числе гастроцистопластика — 24 (5,9 %), илеоцистопластика — 253 (63,8 %) и сигмоцистопластика — 25 (6,1 %). Накожная континентная деривация мочи была выполнена 13 (3,2 %) пациентам, пересадка мочеточников в сигмовидную кишку — 42 (10,3 %), уретерокутанеостомия — 50 (12,3 %).

Результаты. Локальный рецидив в малом тазу после радикальной цистэктомии наблюдали у 33 (8,1 %) пациентов: 27 (81,8 %) мужчин и 6 (18,2 %) женщин. Средний возраст мужчин с рецидивами составил $58,7 \pm 11,7$ года (от 43 до 73 лет), женщин — $50,0 \pm 7,8$ года (от 24 до 65 лет). Одновременное метастатическое поражение внутренних органов выявлено у 6 (18,2 %) больных. Локальный тазовый рецидив после радикальной цистэктомии чаще возникал у лимфоположительных пациентов с экстравезикальным распространением первичной опухоли низкой степени дифференцировки. Медиана времени от радикальной цистэктомии до выявления тазового рецидива составила 7,0 мес., с момента выявления тазового рецидива до смерти пациента — 4,5 мес.

Выводы. Частота локального тазового рецидива рака мочевого пузыря после радикальной цистэктомии составляет 8,1 %. Выживаемость больных с наличием местного тазового рецидива исключительно низкая.

Ключевые слова: рак мочевого пузыря; радикальная цистэктомия; локальный тазовый рецидив.

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BACKGROUND

Bladder cancer (BC) is the second most common neoplasm of the genitourinary system [1, 2]. In the majority of patients with BC, a superficial neoplasm is verified at the time of diagnosis, and in 20%–40% of cases, a muscle-invasive or extravesical form of the neoplasm is detected. Metastases are detected in approximately half of the patients with invasive BC during diagnosis [3–5]. Radical cystectomy (RC) with pelvic lymphadenectomy with/without adjuvant polychemotherapy is considered a standard treatment for patients with muscle-invasive BC and superficial neoplasm in cases of resistance to intravesical immunotherapy [6–8]. Although RC is the gold standard for the surgical treatment of BC, at least a third of the patients have relapses, and they die from disease progression [9–11]. The main cause of BC-related mortality in patients who underwent RC is distant metastases. Moreover, long-term survival after local pelvic recurrence is extremely rare [12–14]. Thus, the incidence of local recurrences, along with distant metastasis, must be investigated when assessing the BC-related mortality of patients who underwent RC. After RC, pelvic recurrences of urothelial cancer occur relatively rarely, with their incidence ranging from 4% to 34%, depending on the primary tumor stage [1, 2, 4, 5, 10, 15–26].

MATERIALS AND METHODS

From 1997 to 2022, RC was performed in 407 patients with BC, including 344 (84.5%) men and 63 (15.5%) women. Orthotopic urinary diversion methods were used in 302 (74.2%) patients, including gastrocystoplasty in 24 (5.9%) cases, ileocystoplasty in 253 (62.2%), and

sigmocystoplasty in 25 (6.1%). Continent cutaneous diversion of urine was performed in 13 (3.2%) patients, transplantation of the ureters into the sigmoid colon in 42 (10.3%), and ureterocutaneostomy in 50 (12.3%).

In the follow-up period, patients underwent a follow-up examination every 6 months during the first 2 years and then annually, which included laboratory tests, including a blood test for prostate-specific antigen, ultrasonography, spiral computed tomography (CT) or magnetic resonance imaging (MRI) of the abdominal cavity and small pelvis, excretory urography, dynamic renal scintigraphy, and osteoscintigraphy. Moreover, the functional state of the upper urinary tract and urinary reservoir, degree of metabolic disorders, and oncological status of the patients were evaluated. Local pelvic recurrence was defined by CT or MRI as a tissue density mass of ≥ 2 cm below the aortic bifurcation.

RESULTS

Local recurrence in the pelvis after RC was detected in 33 (8.1%) patients, including 27 (81.8%) male and 6 (18.2%) female patients. The mean age of the male patients with relapses was 58.7 ± 11.7 (43–73) years and that of women was 50.0 ± 7.8 (24–65) years. Simultaneous metastatic liver damage was diagnosed in six (18.2%) patients, and in three (9.1%) of them, simultaneous damage to the skin, lungs, or bones was also detected. No distant metastases were detected in 27 (81.8%) patients. The pathomorphological stages of BC in patients who underwent RC and had local recurrence in the small pelvis are presented in Table 1.

The surgical margin of the urethra was positive in a patient with stage pT1N0M0G2 and a patient with lymphopositive disease. The percentage of patients with

Table 1. Distribution according to the pTNM system of patients with bladder cancer with local recurrence in the small pelvis after radical cystectomy, $n = 33$

Таблица 1. Распределение по системе pTNM больных раком мочевого пузыря с местным рецидивом в малом тазу после радикальной цистэктомии (РЦ), $n = 33$

Stage according to the pTNM system	Number of patients with local recurrence after RC				
	Women		Men		
	<i>n</i>	%	<i>n</i>	%	
pT0N0	–	–	–	–	
pT1N0	–	–	1	3.0	
pT2N0	pT2aN0	1	3.0	4	12.1
	pT2bN0	1	3.0	7	21.2
pT3N0	pT3aN0	–	–	–	–
	pT3bN0	–	–	3	9.1
pT4N0	pT4aN0	2	6.1	3	9.1
	pT4bN0	–	–	–	–
N+	2	6.1	9	27.3	
Total	6	18.2	27	81.8	

recurrence depending on the primary tumor stage and the stage-wise median time from the moment of surgery to the local recurrence diagnosis are presented in Table 2.

The median time from surgery to pelvic recurrence was 7.0 (1.5–45.7) months. Extravesical tumor expansion or metastatic lesion of the lymph nodes was detected in 19 (57.6%) patients. In 14 (42.4%) patients, BC was organ-limited and lymphonegative. In addition, the median time from RC to pelvic recurrence correlated significantly with the pathologic stage. It was 14.9 months at stage \leq pT2, pN0 and 5.3 months at stage $>$ pT2, N+. In 20 (60.6%) of 33 patients, pelvic recurrence was suspected based on clinical symptoms, and in 13 (39.5%) cases, it was suspected based on CT or MRI findings. Clinical symptoms manifested as pain (in the perineum, lower abdomen or back, and side, with irradiation to the lower

limb) in 7 (21.2%) patients, swelling of the lower limb in 5 (15.2%), intestinal paresis in 3 (9.1%), and constipation in 1 (3.0%). Relaparotomy for small bowel obstruction was performed in 4 (12.1%) patients, and pelvic recurrence was diagnosed intraoperatively.

Regarding the incidence of pelvic recurrence in patients in whom different methods of urinary diversion were used, the probability of local recurrence was not dependent on the method of urinary diversion. The distribution of patients with pelvic recurrence depending on the method of urine diversion is presented in Table 3.

Tumor recurrence was localized on the lateral wall of the pelvis in 14 (42.4%) patients, presacral region in 4 (12.1%), pararectally in 5 (15.2%), and iliac fossa in 2 (6.1%), and several localizations as a single conglomerate were detected in 8 (24.2%) patients.

Table 2. Time of occurrence of pelvic recurrence after radical cystectomy depending on the stage of the primary tumor in patients with bladder cancer, $n = 33$

Таблица 2. Время возникновения тазового рецидива после радикальной цистэктомии (РЦ) в зависимости от стадии первичной опухоли у больных раком мочевого пузыря, $n = 33$

Stages according to the pTNM system	Total number of patients, n	Number of patients with local recurrence after RC, n	Percentage of patients with local recurrence of the total number	Median time to pelvic recurrence, months
pT0N0	21	–	–	–
pT1N0	22	1	4.5	8.5
pT2N0	pT2aN0	5	6.1	19.5
	pT2bN0	97	8	10.3
pT3N0	pT3aN0	16	–	–
	pT3bN0	38	3	7.9
pT4N0	pT4aN0	49	5	10.2
	pT4bN0	8	–	–
N+	74	11	14.9	5.5
Total	407	33	8.1	7.0

Table 3. Distribution of patients with bladder cancer with local recurrence in the small pelvis after radical cystectomy depending on the method of urine diversion, $n = 33$

Таблица 3. Распределение больных раком мочевого пузыря с местным рецидивом в малом тазу после радикальной цистэктомии в зависимости от метода деривации мочи, $n = 33$

Derivation method	Number of patients, n	Number of patients with pelvic recurrence (n)	Percentage of patients with pelvic recurrence, depending on the method of urine diversion
Gastrocystoplasty	24	2	8.3
Ileocystoplasty	253	21	8.3
Sigmocystoplasty	25	2	8.0
Continent cutaneous diversion	13	2	15.4
Ureterosigmoanastomosis	42	2	4.8
Ureterocutaneostomy	50	4	8.0
Total	407	33	8.1

Table 4. Distribution of patients with bladder cancer with local recurrence in the small pelvis after radical cystectomy depending on the histopathological gradation of the primary tumor, $n = 33$

Таблица 4. Распределение больных раком мочевого пузыря с локальным рецидивом в малом тазу после радикальной цистэктомии в зависимости от гистопатологической градации первичной опухоли, $n = 33$

Histopathological grade	Number of patients			
	Women		Men	
	<i>n</i>	%	<i>n</i>	%
G1	1	3.0	2	6.1
G2	4	12.1	21	63.6
G3–4	1	3.0	4	12.1
Total	6	18.2	27	81.8

The distribution of patients with local recurrence in the pelvis, depending on the histological grading of the primary tumor, is provided in Table 4. In patients with local recurrence, G2 and G3–4 primary tumors were detected in 30 (90.9%) of 33 patients.

DISCUSSION

The incidence of pelvic recurrences of BC after RC is estimated in a rather wide range and depends on various factors, primarily on the disease stage. Thus, in the study by Ozbir et al. [27], 49 (14.1%) of 347 patients who underwent surgery had a local recurrence. Local recurrence developed in 8.2% of cases with an organ-limited disease, 17.6% with an extravesical disease, and 23.2% with a lymphopositive form. Kim et al. [10] conducted a retrospective study of 160 patients with stage \geq pT3 BC and a history of RC. In these patients, local recurrence developed in 55 (34.3%) patients. The local recurrence rate was significantly higher in patients with a positive surgical margin than in those without this sign (28% and 10%, respectively, $p = 0.004$). In a study by V. Murthy et al. [28], local recurrence developed in 31 (16%) of 188 patients with BC after RC, and the average period from the surgery to local recurrence was 8.2 months. Depending on the prevalence of the tumor process (category T), lymph node involvement (N), and lymphovascular invasion, the authors identified groups with low, medium, and high risks of local BC recurrence, with their cumulative potential for recurrence of 7.1%, 21.6%, and 35%, respectively. In the present study, the rate of local pelvic recurrence was 8.1%, which was comparable to the results of the above studies. The probability of local recurrence in patients with BC who underwent RC was higher with a greater prevalence of primary tumor (category T), lymph node lesions, and lymphovascular invasion. Our study also demonstrated that the degree of tumor differentiation is significant in the development of local recurrence. The low degree of BC differentiation causes a high probability of local recurrence. In the

present study, 90.9% of patients with a local recurrence had G2 and G3–4 primary tumors. Obviously, moderate and low differentiation indicates the aggressive nature of the primary tumor. In addition, the number of patients with local recurrence depends on the disease stage, where the higher the stage, the greater the percentage of patients with pelvic recurrence (6.9% with pT2aNO, 12.8% with pT4aNO, and 14.8% with N+). The median time from RC to the diagnosis of pelvic recurrence was 7.0 months, and the median time from recurrence detection to patient death was 4.5 months. The frequency of local recurrence was not dependent on the method of urine diversion.

CONCLUSIONS

The results of this study indicate that local pelvic recurrence after RC occurs more often in lymphopositive patients with extravesical expansion of G2–G3 primary tumors. With a local pelvic recurrence of BC, the survival rate of patients is extremely low.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. The contributions of each author: B.K. Komyakov — research concept and design, surgical treatment; A.E. Saad — collection and processing of material, diagnostic studies, literature review; V.A. Fadeev, T.H. Al-Attar — collection and processing of material, surgical treatment, literature review; A.V. Sergeev — analysis of the data obtained, literature review, surgical treatment, writing the text.

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