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Surgical treatment of locally advanced kidney cancer in the T3a–c stage

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ABSTRACT

BACKGROUND: Kidney cancer is a common pathologic condition, which ranks the 3rd place among urologic cancers. In 4–10% of patients, while growing it metastasizes upward the venous vessels up to the thoracic vena cava and right atrium. Selection of the optimal tactics for surgical treatment of such patients still remains a complex and unsolved task.

AIM: To assess the surgical treatment findings for the patients suffered from kidney cancer with tumor invasion in the renal and inferior vena cava.

MATERIALS AND METHODS: 115 patients with renal cell carcinoma complicated by tumor invasion into renal and inferior vena cava have been operated in North-Western State Medical University named after I.I. Mechnikov from 2003 to 2023. They were 76 (66.1%) men and 39 (33.9%) women, their mean age was 67.0 ± 4.1 . Stage T3a covered 53 (46.1%), T3b — 33 (28.7%) and T3c 29 (25.2%) patients. Metastatic lesion of one lymph node was observed in 21 (18.3%) and of multiple nodes in 6 (5.2%) patients. Distant metastases were found in 26 (22.6%) patients: in the lungs in 9.6% and in the adrenal glands in 5.2%. All patients were treated with radical nephrectomy, removing blood trombi from the inferior vena cava system. Eight (7.0%) of them, received the treatment by the method developed in the clinic, which consists in preliminary endovascular extraction of the cranial trombus part. Another 3 (2.6%) patients were treated using cardiopulmonary bypass machine.

RESULTS: Early postoperative complications developed in 36 (31.4%) patients. The most common and severe of them were pulmonary embolism (4.4%) and acute cardiovascular insufficiency (10.4%). These complications appeared the causes of death of 4 patients. The mortality rate was 3.5%. The three year survival rate in the T3a group was 70.6%, T3b group — 66.0% and T3c group — 50.6% ($p < 0.05$).

CONCLUSIONS: Nephrectomy with vena cava thrombectomy is a radical surgical treatment. Its complexity increases as the tumor thrombus spreads further through the venous system and in some cases requires an interdisciplinary approach.

Keywords: kidney cancer; inferior vena cava; tumor venous thrombosis.

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Оперативное лечение местно-распространенного рака почки в стадии Т3а–с

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АННОТАЦИЯ

Актуальность. Рак почки является частым патологическим состоянием и занимает 3-е место в структуре онкоурологических заболеваний. У 4–10 % больных по мере своего роста он распространяется вверх по венозным сосудам вплоть до грудного отдела полой вены и правого предсердия. Выбор оптимальной тактики хирургического лечения таких пациентов до сих пор остается сложной и до конца нерешенной задачей.

Цель — оценить результаты хирургического лечения больных раком почки с опухолевой инвазией в почечную и нижнюю полую вену.

Материалы и методы. С 2004 по 2023 г. в клиниках урологии СЗГМУ им. И.И. Мечникова были оперированы 115 больных почечноклеточным раком, осложненным опухолевой инвазией в почечную и нижнюю полую вену. Мужчин было 76 (66,1 %), женщин 39 (33,9 %), средний возраст составил $67,0 \pm 4,1$ года. Стадия Т3а имела место у 53 (46,1 %), Т3б — у 33 (28,7 %) и Т3с — у 29 (25,2 %) пациентов. Метастатическое поражение одного лимфоузла наблюдалось у 21 (18,3 %) больного, множественное — у 6 (5,2 %). У 26 (22,6 %) больных выявлены отдаленные метастазы: в легких у 9,6 % и в надпочечниках у 5,2 %. Всем пациентам выполнена радикальная нефрэктомия с удалением тромбов из системы нижней полой вены, у 8 (7,0 %) из них по разработанному в клинике методу, заключающемуся в предварительной эндоваскулярной экстракции краниальной части тромба. Еще у 3 (2,6 %) пациентов был использован аппарат искусственного кровообращения.

Результаты. Ранние послеоперационные осложнения развились у 36 (31,4 %) больных. Наиболее частыми и тяжелыми из них стали тромбоэмболия легочной артерии (4,4 %) и острая сердечно-сосудистая недостаточность (10,4 %). Они и оказались причинами смерти 4 пациентов. Летальность составила 3,5 %. Трехлетняя выживаемость в группе Т3а составила 70,6 %, Т3б — 66,0 %, Т3с — 50,6 % ($p < 0,05$).

Выводы. Нефрэктомия с тромбэктомией из полой вены является радикальным хирургическим лечением. Сложность его возрастает по мере распространения опухолевого тромба по венозной системе и в ряде случаев требует междисциплинарного подхода.

Ключевые слова: рак почки; нижняя полая вена; опухолевый венозный тромбоз.

Как цитировать

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BACKGROUND

Surgical approach to patients with locally advanced renal cancer (RC) and invasion into the renal vein and inferior vena cava remains a pressing issue in modern urologic oncology [1–4]. RC is the 3rd most common urologic cancer after prostate cancer and bladder cancer [5, 6]. Global epidemiological evidence shows that over 400,000 new RC cases have been recorded annually over the past decade, i. e. about 2.0% of all newly diagnosed malignant neoplasms.

The distinctive feature of RC is its ability to extend to the vein lumen [6, 7] by gradually invading the intraorganic network with subsequent growth through the renal vein into the lumen of the inferior vena cava (IVC). In some cases, the neoplasm may reach the right atrium cavity and prolapse into it. According to various authors, venous invasion occurs in 4–10% of patients [4, 8]. Until recently, most of them were considered incurable [7]. Today, cancer-specific survival of patients with renal cell carcinoma (RCC) complicated by tumor invasion into the vein lumen is comparable to that of patients with locally advanced cancer without vascular invasion. Despite the positive outcomes, the choice of the best surgical approach to patients with invasion is still challenging and, if necessary, requires an interdisciplinary approach [2, 3, 9, 10].

This study *aims* to evaluate the outcomes of surgical approaches to patients with renal cancer and invasion into the renal vein and inferior vena cava.

MATERIALS AND METHODS

From 2004 to 2023, 115 patients with renal cell carcinoma complicated by invasion into the renal vein and inferior vena cava were operated and observed in

the urology clinics of I.I. Mechnikov North-Western State Medical University, including 76 men (66.1%) and 39 women (33.9%). The average age of the patients was 67.0 ± 4.1 . The patients included 53 (46.1%) patients with stage T3a disease, 33 (28.7%) patients with stage T3b disease, and 29 (25.2%) patients with stage T3c disease. Clear cell renal cell carcinoma was diagnosed in 88 (76.5%) patients, 19 (16.5%) patients had papillary renal cell carcinoma, and 8 (6.7%) patients had chromophobe renal cell carcinoma. Twenty-one (18.3%) patients had metastasis in one lymph node, and 6 (5.2%) patients had multiple metastases. Distant metastases were detected in 26 (22.6%) patients, including lungs (9.6%) and the adrenal glands (5.2%). Forty-nine (42.6%) patients had creeping tumor thrombi, 21 (18.2%) patients had occlusive tumor thrombi, and 45 (39.1%) patients had free-floating tumor thrombi. All patients underwent surgery. Surgery types are shown in Table 1.

Table 1 shows that laparoscopy was used in 12 (22.6%) of 53 patients with stage T3a tumors. The surgery time in such patients was 92 ± 8.3 min, and 97 ± 10.2 min for open nephrectomy in the remaining patients. The average blood loss during laparoscopic nephrectomy with thrombectomy was 239 ± 7.3 mL versus 435 ± 9.1 mL in open surgery cases ($p < 0.05$). The average hospital stay after laparoscopic radical nephrectomy with thrombectomy was 9.3 days versus 16.1 days in open surgery cases ($p < 0.05$).

The operated patients with RCC included 33 (28.7%) patients with invasion into the subhepatic IVC (T3b), including 17 (51.5%) cases, when the tumor thrombus extended from the renal vein by no more than 2 cm. Such patients had nephrectomy, and marginal IVC clipping with renal vein removal. In 16 cases (48.5%), thrombosis extended higher, but did not advance beyond the diaphragm.

Table 1. Types of surgeries for patients suffered from kidney cancer with tumor invasion into the renal and inferior vena cava

Таблица 1. Виды хирургических вмешательств, выполненных больным раком почки с опухолевой инвазией в почечную и нижнюю полую вену

Surgery type	Number of surgeries	
	abs.	%
Open nephrectomy, marginal inferior vena cava clipping and removal of the renal vein	58	50.4
Laparoscopic nephrectomy, marginal inferior vena cava clipping and removal of the renal vein	12	10.4
Transverse clipping of the inferior vena cava, hepatic veins and iliac veins, vena cava thrombectomy, marginal resection of the vein and thrombectomy	16	13.9
Nephrectomy, thrombectomy, inferior vena cava clipping above the diaphragm	18	15.7
X-ray endovascular thrombectomy followed by open nephrectomy and the remaining tumor thrombectomy	8	7.0
Nephrectomy with thrombectomy and cardiopulmonary bypass	3	2.6
Total	115	100.0

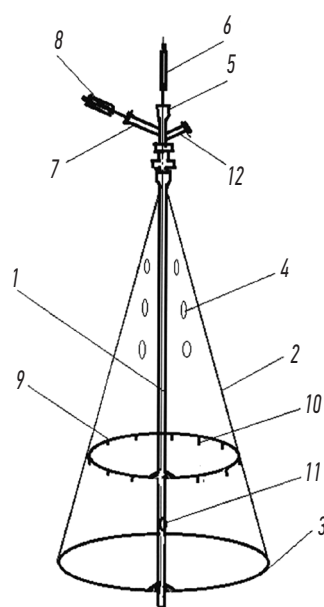


Fig. 1. Thrombectomy device. 1 — polyurethane catheter; 2 — conical synthetic catch-bag; 3 — external nitinol loop; 4 — holes for maintaining blood flow during retrieval; 5 — input nozzle; 6 — control handle; 7 — port; 8 — control grip; 9 — additional internal nitinol loop; 10 — hooks for securing the tumor thrombus; 11 — additional opening for contrast agent inflow; 12 — port for administering the contrast agent

Рис. 1. Тромбозэкстрактор. 1 — полиуретановый катетер; 2 — конусообразная синтетическая ловушка-мешок; 3 — наружная режущая нитиноловая петля; 4 — отверстия для сохранения кровотока в процессе захвата; 5 — патрубок для ввода; 6 — рукоятка управления; 7 — порт; 8 — рукоятка управления дополнительной внутренней петлей; 9 — дополнительная внутренняя нитиноловая петля; 10 — крючки для фиксации опухолевого тромба; 11 — дополнительное отверстие для поступления контрастного вещества; 12 — порт для введения контрастного вещества

Such patients had open nephrectomy with transverse clipping of the IVC, hepatic veins and iliac veins, vena caval thrombectomy with marginal resection of the vein and tumor thrombectomy. Thoracolumbotomy was used in all 33 cases. This method is beneficial as it allows avoiding entry into the abdominal cavity and the additional risk of tumor cell dissemination. It always provides a convenient approach to the abdominal IVC, regardless of the patient's body type.

Twenty-nine of the most complex patients with RC and tumor thrombus extension into the thoracic IVC and the right atrium were operated using different techniques. In 5 (17.2%) patients with left kidney cancer, we used the surgical approach proposed by Davydov. However, as it has a disadvantage of limited approach to heart cavities and the thoracic IVC, we use a method that involves thoracophrenolumbolaparotomy in the VII or VIII intercostal space from the mid-subclavian line to the umbilicus. Thirteen (44.8%) patients were operated using this technique. Its advantages include the ability to provide wide approach to the thoracic IVC and the right atrium by minimizing the risks of fragmentation and detachment of the tumor thrombus. Nephrectomy with thrombectomy in the right atrium using a cardiopulmonary bypass was performed in 3 (10.3%) patients. Another 8 (27.6%) patients had open nephrectomy in combination with preliminary X-ray endovascular thrombectomy in the lumen

of the thoracic IVC (invention patent No. 2798727 dated 06/23/2023). Endovascular thrombectomy was performed through the internal jugular vein using a thrombectomy device developed by us (utility patent No. 210500 dated 04/18/2022). It ensures high reliability of capturing, holding, and removing tumor thrombi from the vein lumen and reduces the surgery time (Figure 1).

RESULTS AND DISCUSSION

Early postoperative complications in patients undergoing surgery for RC with T3a–c venous invasion are shown in Table 2.

Table 2 shows that early postoperative complications occurred in 36 (31.4%) patients with RCC and venous invasion, including the most frequent and severe, such as pulmonary embolism (4.4%) and acute heart failure (10.4%), causing the death of 4 patients. The mortality rate was 3.5%.

Depending on the degree of occlusion of the renal vein by tumor, patients with stage T3a tumors were divided into two groups. The first group included 23 (43.4%) patients with partial occlusion of the renal vein lumen by tumor, and the second group included 30 (56.6%) patients with complete occlusion of the renal vein by the tumor. The study groups were not homogeneous by gender, and each group included 2/3 of men and 1/3 of women.

Table 2. Early complications in operated patients with kidney cancer and tumor invasion in stages T3a–c

Таблица 2. Ранние послеоперационные осложнения у оперированных пациентов с раком почки и опухолевой инвазией в стадиях Т3а–с

Early postoperative complications	Number of patients		Outcome	
	abs.	%	Recovery	Death
Postoperative bleeding	8	7.0	8	–
Narrowing of the vena cava	2	1.7	2	–
Pulmonary embolism	5	4.4	2	3
Surgical wound infection	1	0.9	1	–
Gastrointestinal bleeding	6	5.2	6	–
Liver and kidney failure	1	0.9	1	–
Acute heart failure	12	10.4	12	1
Infective endocarditis	1	0.9	1	–
Total	36	31.4	33	4

In both groups, the majority of patients had clear cell renal cell carcinoma (82.6, 66.7%, respectively); the papillary renal cell carcinoma was detected 3 and 4 times less frequently in each group (13.0, 23.3%, respectively), and chromophobe renal cell carcinoma was the least detected tumor: 1 (4.3%) and 3 (10.0%) patients in the groups. The analysis showed that the distribution by tumor thrombus type did not have significant differences ($\chi^2 = 0.007$; $p = 0.997$).

Three-year relapse-free survival of patients with stage T3a disease in the groups of partial and complete renal vein occlusion by tumor masses differed significantly (86.6 and 79.6%, respectively; log-rank test: $\chi^2 = 0.43$; $p = 0.57$). In the partial renal vein occlusion group, the average time to relapse was 52.4 ± 3.2 months versus 50.8 ± 3.0 months in patients with complete renal vein occlusion. These data are shown in Figure 2.

We studied the surgical treatment outcomes of 26 patients with RC and invasion into the thoracic IVC and right atrium (T3c). They were divided into three groups by the surgery type. The first group included 5 patients operated using a transdiaphragmatic approach to the intrapericardial IVC proposed by Davydov. The second group included 13 patients who underwent thoracophrenolombolaparotomy in the VII or VIII intercostal space from the mid-subclavian line to the umbilicus. The third group included 8 patients who underwent the minimally invasive surgery, an X-ray endovascular thrombectomy followed by nephrectomy, proposed by us. Surgical approaches were compared by the surgery time, blood loss, length of hospital stay, postoperative complications, and three-year survival after surgery (Table 3). The surgery time and blood loss were significantly lower with X-ray endovascular thrombectomy in combination with open nephrectomy.

In the midline laparotomy group, 1 (20.0%) patient had postoperative bleeding and required another surgery.

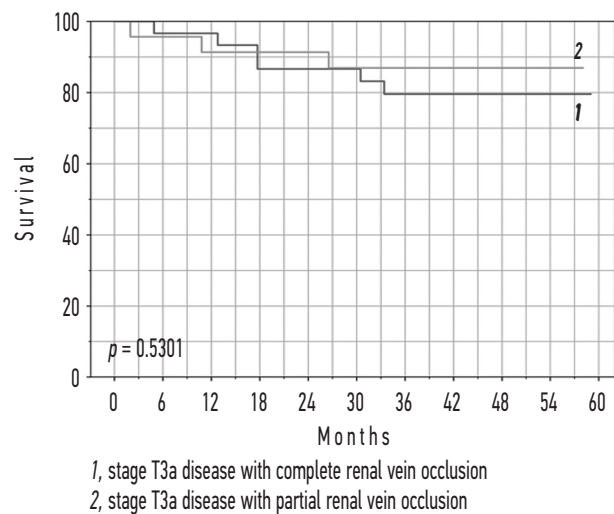


Fig. 2. Three-year recurrence-free survival in patient groups with various degrees of renal vein obstruction in pT3a stage

Рис. 2. Трехлетняя безрецидивная выживаемость в группах пациентов с разной степенью обтурации почечной вены в стадии pT3a

Another 1 patient (20.0%) had fatal pulmonary embolism. After thoracophrenolombolaparotomy, 3 (23.1%) patients had gastrointestinal bleeding, 4 (30.7%) patients had acute heart failure, and 2 (15.4%) had postoperative bleeding. Another 1 patient (7.7%) also had fatal pulmonary embolism. In the group of X-ray endovascular thrombectomy and nephrectomy, gastrointestinal bleeding occurred in 1 (12.5%) patient, and 2 (25.0%) patients had acute heart failure. The highest number of postoperative complications was recorded in the thoracophrenolombolaparotomy group (76.9%).

Lymph node involvement affected long-term survival of patients. Three-year survival at stage N0 (76.4%) was significantly higher versus patients with N1 stage disease ($p = 0.0003$). The data are shown in Figure 3.

Table 3. Comparative assessment of surgical treatment methods for patients with kidney cancer at stage T3c, *n* = 26
Таблица 3. Сравнительная оценка методов хирургического лечения больных раком почки в стадии Т3с, *n* = 26

Parameter	Surgical technique			
	Midline transdiaphragmatic approach to the thoracic inferior vena cava (<i>n</i> = 5)	Thoracophrenolumbo-laparotomy in the VII or VIII intercostal space (<i>n</i> = 13)	X-ray endovascular thrombectomy with open nephrectomy (<i>n</i> = 8)	<i>p</i>
Average surgery time, min	326 ± 23	256 ± 19	214 ± 12	<0.05
Average blood loss, mL	2580 ± 50	2377 ± 43	1425 ± 27	<0.05
Length of hospital stay, patient day	22.0	20.1	19.0	≥0.05
Early postoperative complications, %	40.0	76.9	37.5	<0.05
Mortality rate, %	20.0	7.7	–	<0.05

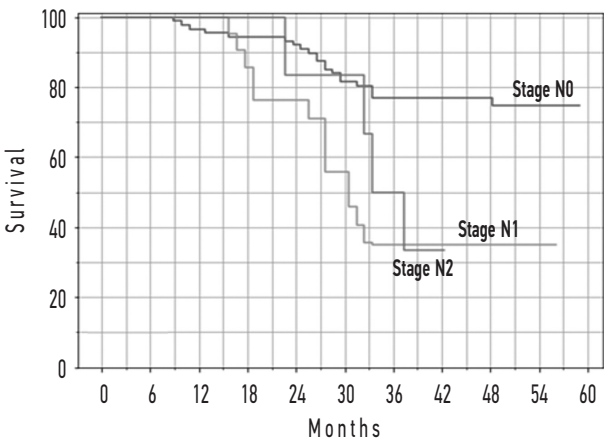


Fig. 3. Three-year overall survival of operated patients depending on the extent of lymph node involvement according to Kaplan–Meier, *p* = 0,0000
Рис. 3. Трехлетняя общая выживаемость оперированных пациентов в зависимости от степени поражения лимфоузлов по Каплану–Мейеру, *p* = 0,0000

When analyzing overall three-year survival depending on T stage, we expectedly had worse outcomes in the T3c group. The proportion of survivors in the T3a group was 70.6%, 66.0% in the T3b group, 50.6% in the T3c group (*p* < 0.05).

The first paper on a successful nephrectomy with thrombectomy above the diaphragm was published in 1970 [1, 3, 9]. Significant prognostic factors of survival include the amount of thrombus removal, invasion into the paranephric body, regional lymph node involvement, and distant metastasis [2, 7, 8]. According to our data, the main predictor of survival in this group of patients is the degree of invasion into the inferior vena cava and the regional lymph node involvement. The main difference between nephrectomy with thrombectomy and a mere radical nephrectomy is the need for surgical release and resection of the inferior vena cava, which turns a conventional abdominal surgery into a vascular one and

may have certain technical difficulties [3, 4, 8]. The development of surgical techniques, modern capabilities of cardiopulmonary bypass, hypothermia, adoption of liver transplantation techniques, and improvement of anesthetic management have allowed to change the surgical strategy by minimizing the risk of intra- and postoperative complications. The extent of surgery for an intraluminal tumor depends on the extent of thrombus spread in the venous network. The higher the tumor thrombus, the more appropriate is the use of an interdisciplinary surgical approach, including in cases of cardiopulmonary bypass surgery [1, 3].

CONCLUSION

Nephrectomy with thrombectomy is the only radical modality of tumor thrombus treatment in renal cancer cases. The surgical approach to such patients is complex and primarily depends on the degree of thrombus spread up the vena cava. X-ray endovascular thrombectomy followed by nephrectomy is a promising and minimally invasive technique for removing tumor thrombi from the thoracic IVC. The use of a cardiopulmonary bypass in cases of intra-atrial tumor invasion allows to significantly reduce the possibility of fatal intraoperative thromboembolism by tumor during open-heart surgery and ensures the radical surgical treatment.

ADDITIONAL INFO

Author’s contribution. 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. Personal contributions of each author: B.K. Komyakov — analysis of the obtained data, manuscript editing; A.T. Salsanov — collection of clinical material, work with medical records, article writing; V.B. Matveev — analysis of the

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Consent for publication. The authors obtained written consent from patients for the publication of medical data.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед

публикацией. Личный вклад каждого автора: Б.К. Комяков — анализ полученных данных, редактирование рукописи; А.Т. Салсанов — сбор клинического материала, работа с историями болезни, написание статьи; В.Б. Матвеев — анализ полученных данных, редактирование рукописи; В.А. Зубарев — подготовка рукописи к печати, оформление и перевод статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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