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SURGICAL TREATMENT OF LOCAL RENAL CELL CARCINOMA RECURRENCE. SURGICAL ASPECTS AND ONCOLOGICAL RESULTS

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Abstract

Introduction. Treatment of local RCC recurrence is a serious surgical and therapeutic problem. There is no single standard strategy for the treatment of locally recurrent RCC. **Objective:** to evaluate the short- and long-term results of surgical treatment of patients with local RCC recurrence. **Material and Methods.** Among all participants (n=53), 48 patients had isolated local RCC recurrence (group 1), and 5 had synchronous metastases (group 2). All patients had one or more local foci of RCC and underwent radical removal of all foci from May 2007 to January 2024. In distant metastases, metastasectomy was performed. **Results.** Laparotomy was the preferred access (75.4 %). The average duration of surgery was 167.5 minutes in group 1 and 300 minutes in group 2 (p=0.008). In the early postoperative period, 10 people had postoperative complications. The median follow-up period was 68.17 ± 9.17 (95 % CI 17.00; 112.50) months in group 1 and 79.60 ± 12.17 (95 % CI 47.50; 123.50) in group 2 (p=0.493). The median RFS in group 1 was 139.86 ± 11.02 (95 % CI 119.00; 154.50) months and 100.67 ± 10.22 (95 % CI 91.00; 121.00) months in group 2 (p=0.375), while the local RFS was 174.80 ± 12.22 (95 % CI 139.00; 194.50) and 126.00 ± 11.40 (95 % CI 109.20; 142.40) months in groups 1 and 2, respectively (p=0.352). The median PFS was 193.00 ± 11.22 (95 % CI 172.02; 209.50) months in group 1 and 121.13 ± 11.14 (95 % CI 111.00; 146.43) months in group 2 (p=0.266). The median OS was 149.70 ± 11.20 (95 % CI 123.12; 161.43) months in the group 1 and 56.50 ± 11.20 (95 % CI 33.20; 78.42) months in the group 2 (p=0.169). The 5-year CSS was 85.7 % in group 1 and 40 % in group 2 (p=0.096). The 10-year CSS rate was 81 % and 4 % in groups 1 and 2, respectively (p=0.109). **Conclusion.** Surgical intervention is effective treatment for local recurrence, providing good oncological outcomes; however, size and proximity to neighboring organs can significantly impact the risk of perioperative complications.

Key words: local renal cell carcinoma recurrence, surgical treatment, short- and long-term results.

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ОПЕРАТИВНОЕ ЛЕЧЕНИЕ ПАЦИЕНТОВ С МЕСТНЫМ РЕЦИДИВОМ РАКА ПОЧКИ. ХИРУРГИЧЕСКИЕ АСПЕКТЫ И ОНКОЛОГИЧЕСКИЕ РЕЗУЛЬТАТЫ

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Аннотация

Введение. Лечение местного рецидива почечно-клеточного рака (ПКР) представляет серьезную хирургическую и терапевтическую проблему. В настоящее время отсутствует единая стандартная стратегия лечения местно-рецидивирующего ПКР. **Цель исследования –** оценка краткосрочных и долгосрочных результатов хирургического лечения пациентов по поводу локального рецидива ПКР в МНИОИ им. П.А. Герцена. **Материал и методы.** Среди 53 пациентов у 48 (90,6 %) был выявлен изолированный местный рецидив ПКР (1-я группа), кроме того, у 5 (9,4 %) обнаружены еще и отдаленные синхронные метастазы (2-я группа). У всех пациентов выявлен один или несколько локальных очагов ПКР в зоне предшествующего лечения, по поводу чего было проведено хирургическое лечение в период с мая 2007 г. по январь 2024 г. При наличии отдаленных метастазов (n=5) выполнена метастазэктомия. **Результаты.** Лапаротомия была предпочтительным доступом (75,4 %). Средняя продолжительность операции в 1-й группе составила 167,5 мин, во 2-й – 300 мин (p=0,008). В раннем послеоперационном периоде у 10 человек были послеоперационные осложнения. Медиана наблюдения в 1-й группе составила 68,17 ± 9,17 (95 % CI 17,00; 112,50) мес, во 2-й – 79,60 ± 12,17 (95 % CI 47,50; 123,50) мес (p=0,493). Медиана ВБР в 1-й группе составила 139,86 ± 11,02 (95 % CI 119,00; 154,50) мес, во 2-й – 100,67 ± 10,22 (95 % CI 91,00; 121,00) мес (p=0,375), в то время как медиана лВБР составила 174,80 ± 12,22 (95 % CI 139,00; 194,50) и 126,00 ± 11,40 (95 % CI 109,20; 142,40) мес соответственно (p=0,352). Медиана ВБП в 1-й группе – 193,00 ± 11,22 (95 % CI 172,02; 209,50) мес, во 2-й группе – 121,13 ± 11,14 (95 % CI 111,00; 146,43) мес (p=0,266). Медиана ОВ в 1-й группе – 149,70 ± 11,20 (95 % CI 123,12; 161,43) мес, во 2-й группе – 56,50 ± 11,20 (95 % CI 33,20; 78,42) мес (p=0,169). Пятилетняя ОСВ в 1-й группе составила 85,7 %, во 2-й – 40 % (p=0,096), 10-летняя – 81 % и 4 % соответственно (p=0,109). **Заключение.** Хирургическое вмешательство является эффективным методом лечения местного рецидива ПКР, обеспечивая хорошие онкологические результаты, однако размер рецидивного очага и его близкий контакт с соседними органами могут оказывать значительное влияние на риск периоперационных осложнений.

Ключевые слова: местный рецидив почечно-клеточного рака, хирургическое лечение, непосредственные и отдаленные результаты.

Introduction

Renal cell carcinoma (RCC) accounts for approximately 3 % of all cancers and ranks 14th among the most common cancers [1, 2]. In 2020, over 400,000 new cases of kidney cancer were detected worldwide [3]. The incidence is highest in Western countries, with an approximately 2 % annual increase over the past 2 decades.

Surgery is the main treatment of the renal cancer. The stage of the disease, including the size and prevalence of the tumor, determines the operation [4]. Kidney resection is preferable at stage T1a, providing excellent oncological control with optimal preservation of the kidney functional state and with the technical possibility of surgery at later stages. Nephrectomy (NE) is recommended to treat patients with T1b-T4 stages and in cases where resection is not technically possible because of individual factors [5].

The literature shows the 1.8 % to 40 % local recurrence rate after primary treatment of kidney cancer [6–8]. Isolated local kidney cancer recurrence is quite low, and several studies showed its prevalence ranging from 1 to 2 % [9–11]. In most cases, the disease relapses within the first 5 years after surgery, [12] while in 6–10 % of the cases it develops later (up to 45 years) [13, 14].

Treatment of local RCC recurrence is a serious surgical and therapeutic problem, since almost half of patients with local recurrence may experience synchronous metastases significantly worsening the overall prognosis of the disease [5, 11]. There is no single standard strategy for the treatment of locally recurrent RCC, and several approaches are suggested as surgical treatment, thermal ablation, radiation therapy, systemic drug therapy, and follow-up with no treatment. The optimal sequence of treatment for patients with local RCC recurrence is still under discussion [11]. The literature shows no alternative treatment for local kidney cancer recurrence surpassing R0 resection in the oncological results [5].

Objective

Our study is aimed at evaluating the short- and long-term results of surgical treatment of patients with local RCC recurrence in the Moscow Scientific Research Oncological Institute named after P.A. Herzen to determine the role of surgical intervention in the treatment of this group of patients.

Material and Methods

For this study, 53 patients of all sexes with local RCC recurrence were selected, of whom 5 had distant metastases. All patients underwent surgical treatment from May 2007 to January 2024 at the Moscow Scientific Research Oncological Institute named after P.A. Herzen. The local recurrence was a tumor node detected after radical removal of the primary kidney tumor of the same histological type in its bed or a tumor developing in the kidney bed, regional lymph nodes, and ipsilateral adrenal gland after nephrectomy. In primary thermal ablation, the local recurrence was represented by a tumor node previously exposed to ablation [15, 16].

The preoperative parameters of patients, intraoperative data, and the features of the postoperative period and subsequent follow-up were analyzed retrospectively based on the prospectively collected database of the Institute. All patients had one or more local foci of RCC in previous treatment (thermal ablation, kidney resection, or nephrectomy). The essence of the operation was the radical removal of all foci, followed by a morphological examination of the surgical material. In distant metastases (n=5), metastasectomy was performed. The preoperative examination included the medical history, primary treatment, clinical, laboratory, and instrumental examination data (mainly abdominal and retroperitoneal space MSCT with intravenous contrast). In cases when MSCT with intravenous contrast was not possible, the abdominal and retroperitoneal space ultrasound or MRI was performed.

Preoperative data of the patients included gender, age, body mass index (BMI), primary treatment (kidney resection, nephrectomy, ablation), access in case of primary surgery (laparotomy, laparoscopy), pathomorphological characteristics of primary RCC (pT stage, Fuhrman malignancy score, histological subtype, tumor size, synchronous metastases), characteristics of local RCC recurrence (location, number, and size), and time of the recurrence diagnosis.

The study evaluated the following intraoperative parameters: nature of access, type of surgery, time of surgery, intraoperative complications, intraoperative blood loss, transfused blood, and technical features of the surgical aid. We evaluated the following postoperative criteria: postoperative complications (according to the Clavien–Dindo classification), intensive care unit stay, hospital stay, and mortality. In pancreatic resection, we evaluated specific complications of pancreatic surgery: biliary congestion, stagnation of gastric contents, and postoperative pancreatic fistula (POPF).

Further monitoring of patients was carried out on the basis of physical examination, blood chemistry tests (assessment of the kidney function) and instrumental examination data: chest, abdominal and retroperitoneal space MSCT with intravenous contrast every six months for the first 2 years, and then annually. We evaluated the following long-term results: recurrence rate, its location, and 5 main oncological indices: relapse-free survival (RFS), local relapse-free survival (LRFS), overall survival (OS), cancer-specific survival (CSS), progression-free survival (PFS). We defined RFS as the time from the surgical treatment of a local RCC recurrence to the detection of a new recurrence, including a long-term one. We defined LRFS as the time from the surgical treatment of a local RCC recurrence to the detection of a new local recurrence. OS was defined as the period from surgical treatment of a local RCC recurrence to the death of a patient from any cause or to the last observation. CSS is the period from surgical treatment of a local RCC recurrence to the patient's death from RCC, provided that other causes of death are excluded. We defined PFS as the time from the surgical treatment of a local RCC recurrence to the detection of metastases.

Statistical analysis was performed using the IBM SPSS v.26.0 program, survival rates were estimated using the Kaplan-Meyer method. Quantitative parameters were compared using the Mann-Whitney test, qualitative parameters were compared using the x^2-test and Fisher's exact test. The $p<0.05$ was significant.

Results

Among all participants (53 people), 48 (90.6 %) patients had isolated local RCC recurrence (group 1), and 5 (9.4 %) had remote synchronous metastases besides the local process (group 2). The local recurrence was detected in 37.7 % after kidney resection, in 52.9 % after nephrectomy, and in 9.4 % after primary radiofrequency thermoablation (p=0.093). In group 2, all patients with a primary tumor were treated with nephrectomy. In group 1, the average time to relapse was 23.50 months (7.50; 59.50), in group 2, 13.8 months (p=0.068). In 77.1 % patients from group 1 and in 20 % from group 2, local recurrence was true, occurring 12 months or more after primary treatment, and contin-

ued tumor growth was noted in 22.9 % and 80 % in groups 1 and 2, respectively (p=0.007). Table No. 1 presents the main preoperative indices for both groups.

The average number of tumor nodes in group 1 was 1.77, in group 2, 3.40 (p=0.004). The local recurrence was diagnosed at the place of residence mainly by multispiral computed tomography (83 %), and more rarely by magnetic resonance imaging (3.8 %) and ultrasound examination of the kidneys (13.2 %). In group 2, distant foci were found in the liver in 2 (40 %) cases and in the lungs in 3 (60 %) cases.

Laparotomy was the preferred access (75.4 %), especially in cases with a large mass and when laparotomy was performed for the primary tumor. Laparoscopic access was used in 13 cases (all from the group of isolated local recurrence), of which 23.1 % after primary laparotomy, 61.5 % after primary laparoscopic surgery, and in no one case conversion was required. Laparotomy was surgery of choice for local recurrence after radiofrequency thermoablation in 60 % of cases and laparoscopy in 40 % of the cases. The high percentage of laparotomy in this group is explained by the severity of postoperative adhesions in these cases after primary RFA and the high risk of intestinal damage during potential laparoscopic access. Table No. 2 summarizes the access options.

In the group of isolated local recurrence, in 13 (27.1 %) cases after previous kidney resection, the size, location, and postoperative changes in the surrounding tissues allowed a repeated kidney resection, including 3 cases with a single functioning kidney as an absolute indication for organ resection. In one case, a kidney resection was attempted but subtotal tumor invasion into the pelvicalyceal system prompted nephrectomy. In one case from group 2, the site of previous liver resection because of the tumor invasion into the organ formed a bed for local kidney cancer recurrence. This patient underwent repeated liver resection using intraoperative ultrasound of the organ because of local recurrence. Only one patient from group 1 underwent intraoperative radiation therapy (IORT) due to the massive lesion with multiple (4) tumor nodes in the fiber of the bed of the removed kidney with spread to the neighboring organs and tissues (small intestine, colon, and their mesentery).

In group 1, the removal of local recurrence after nephrectomy required resection of neighboring organs because of local tumor invasion involving the surrounding tissue and a pronounced scarring in the previous operation: spleen in 14.6 %, small intestine in 4.2 %, mesentery of the small or large intestine in 4.2 %, inferior vena cava in 14.6 %, pancreas in 6.3 %, adrenal gland in 31.3 %, anterior abdominal wall in 2.1 %, renal pedicle in 16.7 %, rib in 2.1 %, peritoneum in 4.2 %, omentum in 4.2 %, diaphragm in 8.3 %, psoas major muscle in 12.5 %, and gallbladder in 2.1 %. In 2 cases, blunt isolation and intimal application of the tumor node with electrocoagulation of the liver defect allowed us to avoid liver resection.

In group 2, some cases required also the removal or resection of adjacent organs and tissues: spleen in 20 %, adrenal gland in 60 %, renal pedicle in 40 %, inferior vena cava in 40 %, liver in 20 %, mesentery of the small or large intestine in 20 %, and diaphragm in 60 %. Also in this group, 3 patients underwent simultaneous metastasectomy of foci in the lungs, among whom, one patient additionally underwent removal of intrathoracic lymph nodes and sub-segmental bronchus. Table 3 presents summary of the extent of surgery in both groups.

Marginal resection of the inferior vena cava was performed in 9 cases, with one case from the distant metastasis group: when a tumor thrombus was removed from the renal vein (4) and when the tumor node was intimately adjacent to the vessel (5, of which 1 was in the group of distant metastasis). In 6 cases (5 in group 1, one in group 2), the inferior vena cava resected with compression, with the vessel clamping with a Satinsky clamp for 20 minutes (17.5; 80) and 5 minutes on average in groups 1 and 2, respectively. The average size of the IVC defect was 24.78 and 11.5 mm in groups 1 and 2, respectively. Prolene-5.0 thread was used for suturing the defect of the IVC with a continuous suture. In one case from group 1, to prevent narrowing of the lumen of the vein in the resection area, the large IVC defect (40 mm) was covered by a fragment of the pericardium using a Prolene-5.0 atraumatic thread. After that, an anastomosis was additionally formed using a reinforced graft with an atraumatic Prolene-5.0 suture.

Table 4 presents intraoperative parameters and perioperative complications associated with surgical treatment for local RCC recurrence. The average duration of surgery was 167.5 minutes (121.25; 213.75) in group 1 and 300 minutes (222.50; 402.5) in group 2 (p=0.008); the average blood loss was 300 ml (100; 700) in group 1 and 700 ml (350; 2000) in group 2 (p=0.098). In 15 cases, intraoperative transfusion of blood components was required (13 of them in group 1, 2 in group 2). No one case required the autohemotransfusion Sell-saver system or additional transfusion of blood components in the early postoperative period because of blood loss. In group 1, kidney resection (in 12 patients) was performed with the renal artery compression in 66.7 % (8 patients) with 20 minutes of ischemia on average; in other cases (33.3 %) resection was performed under zero ischemia. In one case, surgery on a single kidney was accompanied with temporary local finger clamping of the parenchyma to prevent the acute renal failure in the early postoperative period. The initial hemoglobin level after surgery decreased by 17.40 g/l on average in group 1 and by 18.8 g/l in group 2 (p=0.926), and creatinine levels increased by 7.65 mmol/l (0.68; 26.8) in group 1 and by 2.48 mmol/l in group 2 (p=0.386).

In 10 cases, intraoperative ultrasound examination was performed (2 of them in group 2) to determine the margins of resection to increase the radicality of

Table 1/Таблица 1

Main preoperative indices of patients

Основные предоперационные показатели пациентов

Preoperative indices/ Предоперационные показатели		Patients with isolated local recurrence (n=48)/ Больные с местным рецидивом (n=48)	Patients with local recurrence and distant metastases (n=5)/ Больные с местным рецидивом и отдаленными метастазами (n=5)	p-value
Gender/Пол	Male/Муж	29 (60.4 %)	4 (80 %)	0.390
	Female/Жен	19 (39.6 %)	1 (20 %)	
Age/Возраст		59.38	57.80	0.964
BMI/ИМТ		29.12	26.95	0.386
The primary treatment/ Первичное лечение	Kidney resection/Резекция почки	20 (41.7 %)	0	0.093
	Nephrectomy/Нефрэктомия	23 (47.9 %)	5 (100 %)	
	RFAs/РЧА	5 (10.4 %)	0	
The access in the primary operation/ Доступ при первичной операции	Laparoscopy/Лапароскопия	17 (35.4 %)	0	0.141
	Laparotomy/Лапаротомия	26 (54.2 %)	5 (100 %)	
T-stage of the primary tumor/ Т-стадия первичной опухоли	rT1a/1b	14/17	0/0	0.159/0.106
	rT2a/2b	7/0	1/1	0.747/0.002
	pT3a/3b	9/1	0/1	0.288/0.045
	pT4	0	2	<0.001
The grade of malignancy of the primary tumor/ Степень злокачественности первичной опухоли	1–2	27 (56.3 %)	1 (20 %)	0.099
	3–4	21 (43.7 %)	4 (80 %)	
The size of the primary tumor (mm)/ Размер первичной опухоли (мм)	Less than 40 mm/Менее 40 мм	17 (35.4 %)	0	0.106
	Over 40 mm/Более 40 мм	31 (64.6 %)	5 (100 %)	
Histotype of the primary tumor/ Гистотип первичной опухоли	Light cell/Светлоклеточный	44 (91.7 %)	5 (100 %)	0.115
	Papillary/Папиллярный	1 (2.1 %)	0	
	Other/Другое	3 (6.2 %)	0	
The time before the local relapse/ Время до появления рецидива	Continued growth (up to 12 months)/ Продолженный рост (до 12 мес)	11 (22.9 %)	4 (80 %)	0.007
	True local relapse (over 12 months)/ Истинный рецидив (более 12 мес)	37 (77.1 %)	1 (20 %)	
Average time to local recurrence (months)/ Среднее время до появления рецидива (мес)		23.50 (7.50; 59.50)	13.8	0.068
The number of recurrent nodes/ Количество рецидивных очагов	1	30 (62.5 %)	0	0.007
	Over 1/Более 1	18 (37.5 %)	5 (100 %)	
The size of the recurrent tumor node/ Размер рецидивного очага	Less than 40 mm/Менее 40 мм	29 (60.4 %)	3 (60 %)	0.986
	Over 40 mm/Более 40 мм	19 (39.6 %)	2 (40 %)	

Notes: BMI – body mass index; RFA – radiofrequency thermoablation; created by the authors.

Примечания: ИМТ – индекс массы тела; РЧА – радиочастотная абляция; таблица составлена авторами.

Table 2/Таблица 2

Access options in primary and repeated operations

Соотношение доступов первичной и повторной операций

The primary treatment (access)/ Доступ при первичной операции	Laparotomy access of repeated surgery/ Лапаротомный доступ при повторной операции (n=40)	Laparoscopic access of repeated surgery/ Лапароскопический доступ при повторной операции (n=13)	p-value
Laparotomy/Лапаротомия (n=31)	28 (52.8 %)	3 (5.7 %)	0.011
Laparoscopic/Лапароскопический (n=17)	9 (16.9 %)	8 (15.1 %)	
Thermal ablation/Термоабляция (n=5)	3 (5.7 %)	2 (3.8 %)	

Note: created by the authors.

Примечание: таблица составлена авторами.

Table 3/Таблица 3

Extent of surgery

Объем хирургического вмешательства

Extent of surgery/Объем хирургического вмешательства	Number of cases/ Число случаев
Patients with isolated local recurrence/Пациенты с изолированным местным рецидивом (n=48)	
Kidney resection/Резекция почки	13
Removal of a local recurrence from the kidney bed with resection/removal of ≤3 adjacent organs/tissues/ Удаление местного рецидива из ложа почки с резекцией/удалением ≤3 соседних органов/тканей	18
Removal of local recurrence from the kidney bed with IORT, retroperitoneal lymphadenectomy, resection of the mesentery of the colon/ Удаление местного рецидива из ложа почки с ИОЛТ, забрюшинной лимфаденэктомией, резекцией участка брыжейки толстой кишки	1
Removal of a local recurrence from the kidney bed with resection/removal of >3 adjacent organs/tissues/ Удаление местного рецидива из ложа почки с резекцией/удалением >3 соседних органов/тканей	4
Nephrectomy/Нефрэктомия	1
Nephrectomy with resection/removal of adjacent organs/tissues/ Нефрэктомия с адреналэктомией, удалением почечной ножки	8
Retroperitoneal lymphadenectomy/Забрюшинная лимфаденэктомия	3
Patients with isolated local recurrence with underlying distant solitary foci/ Пациенты с изолированным местным рецидивом на фоне отдаленных солитарных очагов (n=5)	
Removal of local recurrence from the kidney bed, with resection/removal of adjacent organs/tissues + + removal of the lung metastasis, sub-segmental bronchus, and removal of intrathoracic lymph nodes/ Удаление местного рецидива из ложа почки с резекцией/удалением соседних органов/тканей + + резекция легкого	2
Removal of local recurrence from the kidney bed with with resection/removal of adjacent organs/tissues + liver resection/ Удаление местного рецидива из ложа почки с резекцией/удалением соседних органов/тканей + резекция печени	3

Notes: IORT – intraoperative radiation therapy; created by the authors.

Примечания: ИОЛТ – интраоперационная лучевая терапия; таблица составлена авторами.

surgical intervention: in 5 cases, endophytic growth of the tumor node or its small size prompted the kidney ultrasound during organ resection, of which 3 during surgery on a single kidney. In 1 case, intraoperative ultrasound was required to determine the margins of psoas muscle resection, in 1 case because of the detection of a fixed tumor thrombus in the segmental renal vein and in 1 case because of intraoperative detection of suspicious nodes in the omentum tissue. In 2 cases, intraoperative liver ultrasound was performed, one combined with a cito cytological examination of a solitary suspicious liver lesion confirming metastatic damage, requiring organ resection to maximize cytoreduction.

In all cases, in both groups of isolated local recurrence and of distant metastasis, a pronounced adhesion in the previous operation was the main technical problem, causing intraoperative complications in most cases, which increased the operation time. The operations complicated by: opening of the pleural cavity during excision of a tumor node or mobilization of the kidney in 9 cases (7 in the group of isolated local recurrence, 2 in the group of distant metastasis), of which 7 cases required resection of the diaphragm (4 in group 1 and 3 in group 2). The minimum size of the diaphragm defect was 1 cm, the maximum one was 5.5 cm. In all cases, the defect was sutured with a continuous atraumatic Vicryl-1.0 thread suture with the installation of an insurance drainage into the pleural cavity. In 4 patients out of 8 (50 %), splenectomy was performed because of serous membrane removal for 1.5–2.2 cm during the mobilization of the splenic angle of the colon showing the spleen involvement (3 patients in the group of isolated local recurrence and 1 patient in the group of distant metastasis). In 3 cases, the intimate attachment of the tumor node to the intestinal wall (2 of small intestine and 1 of colon), serous membrane removal occurred, requiring suturing of the defect with a continuous suture with Vicryl-4.0 thread (2 cases in the group of isolated local recurrence and 1 case in the group of distant metastasis). In group 1, an aortic defect of no over 1 mm was found during mobilization of the single left kidney and was sutured with an atraumatic Z-shaped Prolene-5.0 suture. In group 1, excision of the deeply invaded tumor node resulted in opening of the pelvicalyceal system in two patients, which in one case required the installation of an ureteral stent into the upper urinary tract followed by suturing of the defect with a continuous Vicryl-4.0 suture, and nephrectomy in the other case.

In the early postoperative period, 10 people had postoperative complications, of which 7 cases developed in the group of isolated local recurrence (14.6 %) and 3 cases in the group of distant metastasis (Table

Table 4/Таблица 4

Intraoperative parameters and perioperative complications

Интраоперационные параметры и периоперационные осложнения

Parameters/Параметры		Patients with isolated local recurrence (n=48)/ Больные с местным рецидивом (n=48)	Patients with local recurrence and distant metastases (n=5)/ Больные с местным рецидивом и отдаленными метастазами (n=5)	p-value
Duration of the operation (min)/Длительность операции (мин)		167.5 (121.25; 213.75)	300 (222.50; 402;5)	0.008
Blood loss (ml)/Кровопотеря		300 (100; 700)	700 (350; 2000)	0.098
Duration of ischemia in case of kidney resection (min)/ Продолжительность ишемии в случае резекции почки (мин)		20	-	
Transfusion of blood components/Переливание компонентов крови		13 (27.1 %)	2 (40.0 %)	0.034
Average transfusion volume (ml)/ Средний объем трансфузии (мл)	Freshly frozen plasma/ Свежезамороженная плазма	600 (320;930)	1020.00 (652.50; 1052.50)	0.178
	Packed red blood cells/ Эритроцитарная масса	331.50 (75; 652)	240	0.437
Duration of IVC clamping (min)/ Продолжительность пережатия НПВ (мин)		20 (17.5; 80)	5	0.137
Performing intraoperative ultrasound/ Проведение интраоперационного УЗИ		8 (16.7 %)	2 (40.0 %)	0.004 0.021
Opening of the pleural cavity/Вскрытие плевральной полости		7 (14.6 %)	2 (40.0 %)	0.020
Deserization of the spleen/Десерозация селезенки		3 (6.25 %)	1 (20.0 %)	0.032
Colon deserization/Десерозация кишки		2 (4.2 %)	1 (20 %)	0.032
Aortic defect/Дефект аорты		1 (2.1 %)	–	
Opening of the pelvicalyceal system components/ Вскрытие компонентов ЧЛС		2 (4.2 %)	–	
Average preoperative hemoglobin level (g/l)/ Средний предоперационный уровень гемоглобина (г/л)		139.39	131.80	0.140
Average postoperative hemoglobin level (at discharge) (g/l)/ Средний послеоперационный уровень гемоглобина (на момент выписки) (г/л)		122.03	113.00	0.187
Average preoperative creatinine level (mmol/l)/ Средний предоперационный уровень креатинина (мкмоль/л)		103.70	101.00	1.000
Average postoperative creatinine level (at discharge) (mmol/l)/ Средний послеоперационный уровень креатинина (на момент выписки) (мкмоль/л)		118.750 (98.80; 131.68)	103.48	0.148
Average intensive care unit stay (h)/ Средняя продолжительность нахождения в реанимации (ч)		11.25	24.00 (18.50; 79.50)	0.010
Average length of stay in hospital (days)/ Средняя продолжительность нахождения в стационаре (дни)		8.92	15.20	0.014

Notes: IVC – inferior vena cava, PCS – pelvicalyceal system; created by the authors.

Примечания: НПВ – нижняя полая вена, ЧЛС – чашечно-лоханочная система; таблица составлена авторами.

Table 5/Таблица 5

Postoperative complications according to Clavien-Dindo classification

Послеоперационные осложнения по Clavien–Dindo

The stage of postoperative complications according to classification/ Степень послеоперационных осложнений по Clavien–Dindo	Patients with isolated local recurrence (n=48)/ Больные с местным рецидивом (n=48)	Patients with local recurrence and distant metastases (n=5)/ Больные с местным рецидивом и отдаленными метастазами (n=5)
Stage 1/1 степень	–	1
Stage 2/2 степень	1	2
Stage 3a/3a степень	3	–
Stage 4a/4a степень	2	–
Stage 5/5 степень	1	–

Note: created by the authors.

Примечание: таблица составлена авторами.

Table 6/Таблица 6

Long-term oncological results

Отдаленные онкологические результаты

Parameter/Показатель	Patients with isolated local recurrence (n=48)/ Больные с местным рецидивом (n=48)	Patients with local recurrence and distant metastases (n=5)/ Больные с местным рецидивом и отдаленными метастазами (n=5)	p-value
Median follow-up (months)/Медиана наблюдения (мес)	68.17 ± 9.17 (95 % CI 17.00; 112.50)	79.60 ± 12.17 (95 % CI 47.50;123.50)	0.493
Repeated local recurrence/Повторный местный рецидив	7 (14.6 %)	0	0.359
Disease progression/Прогрессирование процесса	9 (18.8 %)	3 (60 %)	0.036
Death of patients/because of the underlying disease/ Смерть пациентов/из них по причине основного заболевания	15 (31.3 %)/9 (18.8 %)	4 (80 %)/4 (80 %)	0.031
Local treatment of local recurrence, surgery/ Локальное лечение местного рецидива, хирургия	2 (4.2 %)	0	0.754
Local treatment of local recurrence, RFA/ Локальное лечение местного рецидива, РЧТА	1 (2.1 %)	0	0.754
Local treatment of local recurrence, radiation therapy/ Локальное лечение местного рецидива, лучевая терапия	1 (2.1 %)	0	0.754
Local treatment of tumor metastasis, embolization of vessel feeding the node/Локальное лечение опухолевого метастаза, эмболизация сосуда, питающего узел	1 (2.1 %)	0	0.754
Systemic therapy/Системная терапия	5 (10.4 %)	3 (60 %)	0.003
Median recurrence-free survival (months)/ Безрецидивная выживаемость (мес)	139.86 ± 11.02 (95 % CI 119.00; 154.50)	100.67 ± 10.22 (95 % CI 91.00; 121.00)	0.375
Median local recurrence-free survival (months)/ Локальная безрецидивная выживаемость (мес)	174.80±12.22 (95 % CI 139.00; 194.50)	126.00 ± 11.40 (95 % CI 109.20; 142.40)	0.352
5-year local recurrence-free survival/ 5-летняя локальная безрецидивная выживаемость	90.5 %	100 %	0.422
10-year local recurrence-free survival/ 10-летняя локальная безрецидивная выживаемость	90.5 %	100 %	0.422
Median progression-free survival (months)/ Выживаемость без прогрессирования (мес)	193.00±11.22 (95 % CI 172.02; 209.50)	121.13 ± 11.14 (95 % CI 111.00; 146.43)	0.266
5-year progression-free survival/ 5-летняя выживаемость без прогрессирования	83.3 %	60 %	0.370
10-year progression-free survival/ 10-летняя выживаемость без прогрессирования	81 %	60 %	0.460
Cancer-specific survival rate (months)/ Канцер-специфическая выживаемость	151.66 ± 10.39 (95 % CI 132.20; 173.42)	55.00 ± 11.28 (95 % CI 38.24; 79.40)	0.052
5-year cancer-specific survival/ 5-летняя канцер-специфическая выживаемость	85.7 %	40 %	0.096
10-year cancer-specific survival/ 10-летняя канцер-специфическая выживаемость	81 %	40 %	0.109
Median overall survival rate (months)/ Общая выживаемость (мес)	149.70 ± 11.20 (95 % CI 123.12; 161.43)	56.50 ± 11.20 (95 % CI 33.20; 78.42)	0.169
5-year overall survival/5-летняя общая выживаемость	87.5 %	40 %	0.042
10-year overall survival/10-летняя общая выживаемость	75 %	40 %	0.252

Note: created by the authors.

Примечание: таблица составлена авторами.

No. 5). We found the following Clavien Dindo complications: grade 1 in one patient (marked suppuration of the postoperative wound on the 4th day after the operation; treated with local antibacterial and anti-inflammatory therapy), grade 2 in 3 patients (one patient developed occlusive thrombosis of muscular veins of the middle and upper third of the left tibia not expanding to the tibial vein on day 6 after surgery, diagnosed by ultrasound and effectively treated with anticoagulants; one patient developed occlusive thrombosis in both legs, diagnosed by ultrasound on day 4 and effectively treated with anticoagulants; one patient developed necrosis of the tail of the pancreas on day 3, requiring lavage of the abdominal cavity through a safety drain with dioxidine solution and change of antibiotic therapy), grade 3A in 3 patients (one patient developed reactive pleurisy from the side of rib 12 resection two days after surgery, the curative pleural puncture was performed with evacuation of 500 ml of serous-hemorrhagic discharge; two patients developed floating thrombi in the common femoral vein on day 12, treated with implantation of OPTEASE (Cordis) vena cava filter through the jugular access); grade 4A in 2 patients (one patient developed acute respiratory failure on day 2, the severe physical status prompted transferring to ICU for conservative treatment and observation; one patient developed acute renal failure requiring hemodialysis on day 3 after the resection of a solitary kidney), and grade 5 in one patient (resulting in the progressing of cardiovascular failure and death in the first day after surgery). None of the patients who underwent pancreatic resection had complications associated with organ resection in the postoperative period. The average intensive care unit stay in the early postoperative period was 11.25 hours in group 1, 24.00 (18.50; 79.50) hours in group 2 (p=0.010), the average hospital stay after surgery was 8.92 days in group 1 and 15.20 days in group 2 (p=0.014).

The surgical material was examined morphologically and compared with the pathomorphological conclusion from the material after the initial operation, based on which the following results were obtained. In most cases, the recurrent tumor had a structure similar to the primary one. Only in 9 (18.75 %) cases in group 1, the tumor structure changed with the development of: granular cell component (n=1), papillary component (n=2), eosinophilic cell component (n=2), tumor histotype change from light cell RCC to renal cell papillary cancer with focal light cell changes (n=1), indicating the independent growth of a "new" tumor in place of the previous one but not a true relapse. In 3 cases in group 1, recurrence was represented by a benign tumor (xanthogranuloma, tubulo-interstitial nephritis with "thyroidization" of the kidney, and epithelioid cell angiomyolipoma, one case each). Tumor progression was assessed for primary and recurrent tumors by comparing the Furman grade. The analysis showed no significant change in this index in the groups. In total, 14 people (13 in group 1, one in group 2) showed a change in the malignancy grade without a clear trend, with a decrease in 15.1 % and an increase in 11.3 % (p=0.047) of the cases. In the group of isolated local recurrence, one case had a multifocal tumor growth and was represented by 3 nodes, 2 of which originated in the bed of previously removed nodes, while all tumors were of the same histological structure.

In the long-term postoperative period, patients were offered follow-up, the results of which were provided to the attending physician in person or by telephone contact. The median follow-up was 68.17 ± 9.17 (95 % CI 17.00; 112.50) months in group 1 and 79.60 ± 12.17 (95 % CI 47.50; 123.50) months in group 2 (p=0.493). The following results were obtained. The median recurrence-free survival in group 1 was 139.86 ± 11.02 (95 % CI 119.00; 154.50) months and 100.67 ± 10.22 (95 % CI 91.00; 121.00) months in group 2 (p=0.375), while the local recurrence-free survival was 174.80 ± 12.22 (95 % CI 139.00; 194.50) and 126.00 ± 11.40 (95 % CI 109.20; 142.40) months in groups 1 and 2, respectively (p=0.352). Patients with a registered repeated local recurrence (n=7) in the group of isolated local recurrence underwent repeated surgical excision in 2 cases, stereotactic radiation therapy in 1 case, RFTA of the tumor node in 1 case, and monitoring recommended because of the benign character of the previously removed tumor and its insignificant size (up to 2cm) in 1 case. The remaining patients (n=2) underwent systemic therapy because of distant metastases with underlying local focus. The effect of repeated treatment was achieved in all patients. The median progression-free survival of the oncological process was 193.00 ± 11.22 (95 % CI 172.02; 209.50) months in group 1 and 121.13 ± 11.14 (95 % CI 111.00; 146.43) months in group 2 (p=0.266). Among patients with established progression of the tumor (n=12: 9 in the group of isolated local recurrence, 3 in the group of distant metastasis), 8 patients (66.7 %) received systemic therapy with an effect and one patient (8.3 %) underwent embolization of the left and right intercostal afferent arteries in the lumbar vertebra L2, feeding the tumor conglomerate. The remaining patients (n=3) died before the start of systemic therapy. The median overall survival was 149.70 ± 11.20 (95 % CI 123.12; 161.43) months in the group of isolated local recurrence and 56.50 ± 11.20 (95 % CI 33.20; 78.42) months in the group of distant metastasis (p=0.169). The 5-year cancer-specific survival was 85.7 % in the group of isolated local recurrence and 40 % in the group of distant metastasis (p=0.096). The 10-year cancer-specific survival rate was 81 % and 4 % in groups 1 and 2, respectively (p=0.109) (Table No. 6)

Discussion

The literature describes various local treatments for local RCC recurrence, and the choice depends on the previous treatment, the size and location of the recur-

rent lesion, the physical status of the patient, and the technical capabilities and experience of the operating surgeon. There is no single standardized algorithm for treating patients with local RCC recurrence, and surgical excision of the latter is a very difficult technical task. The authors also emphasize that such an operation often requires resection of neighboring organs (spleen, colon or pancreas), which further complicates surgical intervention [17–19].

Some authors consider surgical intervention the most effective to treat local recurrence; however, size and proximity to neighboring organs can impact significantly the risk of perioperative complications [16]. Salvage surgery is an effective treatment option for local RCC recurrence after nephron-sparing surgery (NSS), especially when the size or location of the tumor does not allow thermal ablation. Repeated surgery is associated with more serious perioperative complications (from 17 to 58 %), in part because of severe postoperative fibrosis [16]. Unfortunately, currently only a few studies explore this topic, which makes it difficult to assess the effectiveness of the surgical method of treating local RCC recurrence after NSS. Despite the high risks, repeated NSS can provide good functional results and control the cancer. Johnson et al. examined 46 patients after repeated kidney resection, all survived with an average follow-up period of 56 months. In 19.6 % of cases, repeated surgery was required for additional local relapses or de novo tumors with an average follow-up period of 50 months [20]. In our series of cases, repeated relapse with an average follow-up of 68.17 months occurred in 7 (14.6 %) patients in the isolated local relapse group, while two of them had synchronous distant metastases at diagnosis of local relapse. After kidney resection, only one patient with a single kidney in the early postoperative period required hemodialysis because of acute renal failure.

In most studies, open access was preferred, but both laparoscopic [20] and robotic access options are described in the literature [21]. Scientists concluded that laparoscopic access may be applicable in some cases with a small recurrent lesion that does not affect neighboring organs. Our results confirm the possibility of repeated laparoscopic surgery after previous treatment, urging a conversion in no one case. Despite the higher risk of perioperative complications up to organ removal in kidney resection with local intrarenal recurrence, it is the only treatment for patients with a single kidney, since nephrectomy can lead to terminal renal failure.

Further studies confirmed the results on the technical feasibility and preserved effect of laparoscopic access in surgery for local RCC recurrence [22]. Scientists agree that the access option depends not only on the technical capabilities but also on the experience of the surgeon [22–25]. The literature reported several cases of using robotic technology for these [26]. In 2015, a group of scientists reported the treatment of 3 patients with isolated retroperitoneal RCC recurrence. In all cases, robotic transperitoneal access was used in combination with intraoperative laparoscopic ultrasonography to locate the tumor. In this series of cases, no conversions were performed on any patient, while all tumor foci were successfully removed within healthy tissues (R0). The successful postoperative period allowed the discharge on the first day. During 2 years of follow-up, none of them had repeated relapses [26]. The authors emphasize the great advantages of this access: reducing the time of ischemia and surgery, reducing blood loss, improving visualization, facilitating access to the tumor node, greater comfort for the surgeon, safety because of greater mobility of working tools, and shortening hospitalization. We agree that minimizing access may be justified for a group of patients, while ensuring less morbidity from the treatment and early rehabilitation of patients.

The treatment of local recurrence after nephrectomy is the most difficult task because of the high risk of metastasizing [27]. The literature describes quite different oncological results of such treatment. Boorjian et al. [28] reported a 2-year progression-free survival of 29.3 %, whereas Russell et al. [29] found 3-year progression-free survival of 40.5 %, while some patients underwent adjuvant or neo-adjuvant systemic drug therapy. Of note, Boorjian et al. [28] showed the similar results of treatment after surgical removal of recurrence in retroperitoneal lymph nodes to those of lymphadenectomy in view of metastases during primary NE.

The 2019 pathomorphological study showed a negative surgical margin (R0) after surgery in 5 (41.6 %) out of 12 patients. Progression of the disease after surgery was observed in 7 patients (58.3 %) with metastatic lesions in lungs, bones, and liver. All of them were treated with life-saving targeted therapy [28]. Our study included multiple patients with an average follow-up of over 5.6 years but only 22.6 % had progression (9 people in group 1, 3 people in group 2). Thomas et al. [30] reported the following results of surgical treatment of patients for local RCC recurrence after NE: 42 (41.2 %) patients showed no signs of the disease after surgery, which eliminated the need for further therapy. The 5-year cancer-specific survival rate in the subgroup of isolated local RCC recurrence was 52 %, comparable to the 51 % from the Itano et al. study [9] and the 69.2 % 4-year cancer-specific survival rate of patients after surgery for RCC recurrence after nephrectomy in an Argentine study [27]. The fairly convincing data were also provided in 2020, with the 60 % 5-year OS in the group of isolated local recurrence and the 80 % in the group of local recurrence with underlying distant metastases. The mean OS showed no critical difference between the groups: 98.4 months in the isolated local recurrence and 116.0 months in the local recurrence with underlying distant metastases (p=0.881). The groups did not differ in cancer-specific survival: 98.4 months in the group of isolated local recurrence and

116.0 months in the group of local recurrence with underlying distant metastases (p=0.265) [31]. Our series of patients showed quite impressive results, adjusted for a significant numerical advantage in the group of isolated local relapse. The 5-year cancer-specific survival reached 85.7 % in isolated local recurrence and 40.0 % in that with underlying distant metastases (p=0.072), while the 10-year CSS was 81.0 % and 40.0 % in these groups (p=0.086).

One study evaluated the surgical removal of a recurrent venous tumor thrombus after nephrectomy. Parker et al. [32]. found complete removal of a venous tumor thrombus in primary NE in 9 out of 13 patients. Surgical excision of a recurrent venous tumor thrombus was successful in 11 cases. After 12 months of follow-up, all patients died from relapse and/or metastatic disease.

The literature also evaluated the effect of IORT in major relapses, when a complete surgical excision of the tumor is technically impossible or may be unsafe. The advantages of such a combination still need to be confirmed. One study in only 14 patients found no significant difference in survival rates between the groups of patients with and without IORT, despite the larger average recurrent node in the IOLT group (7.5 cm vs. 4.5 cm). We performed IORT because of the large tumor lesion (4 nodes) in the mesentery of the small and large intestine only in one case [33].

Systemic therapy seems to be relatively effective in locally relapsing RCC, [34] and the relative radioresistance of RCC has limited the possibilities of radiation therapy in the treatment of these patients. In the metastatic process, even in the era of combination therapy, metastasectomy can significantly increase chances of recovery and survival rates, especially in the oligometastatic process, providing longer recurrence-free intervals and a good physical status of the patients [35]. Complete metastasectomy is associated with better survival and symptom control compared with no or incomplete metastasectomy [36]. Our study did not evaluate and compare oncological results in performing and not performing metastasectomy in patients with metastatic RCC with underlying local recurrence. However, there were no significant differences in survival rates when compared with the isolated local recurrence, which shows the effect of metastasectomy, especially in the oligometastatic process. There is no standard management strategy for patients with metastatic RCC with underlying local recurrence, even in potentially resectable metastases.

Limitations

This study has several limitations. It was based on a retrospective analysis of a selected group of patients who were treated in one specialized institution. The cohort we selected was heterogeneous and included patients with recurrent lymph nodes, soft tissues, and psoas muscles.

Conclusion

The treatment for local RCC recurrence is selected considering a wide range of factors: the primary RCC treatment, the clinical and pathomorphological characteristics of the tumor, the nature and size of local recurrence, and the physical status of the patient. Surgical intervention is the most effective treatment for local recurrence, providing good oncological outcomes; however, size and proximity to neighboring organs can significantly impact the risk of perioperative complications.

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Compliance with Ethical Standards

The study was conducted in accordance with ethical principles outlined in the Declaration of Helsinki approved by Ethics Committee of P.A. Hertsen Moscow Oncology Research Institute (3, 2nd Botkinsky Drive, Moscow, 125284, Russia), protocol No. 1390 dated October 12, 2020.

Voluntary informed consent

Written informed voluntaries consents were obtained from the patients for the publication of data in medical journal.

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Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью и добросовестностью любой части работы.

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