

A.V. Tobohov, R.R. Vinokurov, A.V. Maksimov, V.N. Nikolaev

## CURRENT STATUS OF DIAGNOSIS AND SURGICAL TREATMENT OF RENAL CELL CARCINOMA

### ABSTRACT

The article presents a review of the prevalence of renal cell carcinoma, used at the moment of classification of the disease. The instrumental methods of diagnosis of renal cell carcinoma and surgical treatment at the present stage of development of medicine are shown. Various methods of surgical interventions and approaches to the choice of a method of surgical treatment of the disease and therefore different results are described. The authors gave the analysis of results of surgical treatment of renal cell carcinoma based on data published in the current medical literature, including the use of laparoscopic techniques.

**Keywords:** renal cell carcinoma, diagnosis of kidney tumors, laparoscopic partial nephrectomy, open partial nephrectomy.

### INTRODUCTION

Renal cell carcinoma (RCC), it is one of the especially significant in urology oncological diseases due to the high frequency of morbidity and mortality. In the world of renal malignancies are gaining growth rate. So in Russia according to the monograph V.I. Chissova et al. provided Statistics 2010, which revealed 516.874 new cases of malignant kidney education, women 54.0%, and men 46.0%. The absolute number of men newly diagnosed with RCC diagnosed 2000-2010 was increased from 7646 to 10286 people, women from 5959 to 8437. The average age of patients was 61.7 years (60.4 for men, 63.1 for women) [6]. In men, kidney cancer occurs in 2 times more often than women. [7] The structure of mortality from cancers to share RCC worldwide accounts for 2.7% of men and 2.1% for women [56]. In Russia, the number of deaths from 2000-2010, the RCC with men from 4450 to 5223, women from 2822 to 3030. In other words the death rate from kidney cancer rose from 5.01 to 6.01 per 100 thousand. Population, the percentage of growth in 17, 38% [52]. According to Siegel R.L. over the past five years (2007-2011 y.), the overall death rate from cancer has decreased from 215.1 in 1991 to 168.7 per 100 thousand. population decreased by 22% in 2011. The subsequent reduction in mortality from RCC can be accelerated by the widespread use of new knowledge in the field of cancer control in all strata of the population [45]. Siegel R., et al write identification 58240 new cases of kidney cancer and 13,040 deaths from RCC recorded in the US in

2010 [45].

**Classification.** To date, the practice of using multiple types of classifications of kidney cancer. Historically, Russia is widely used classification of renal tumors, the proposed NA Krajewski et al. (1981) [24]. In this classification, the following types of RCC on the histological structure: clear cell RCC - 73.7%, granular cell (dark cell) SIC - 17.5%, Spindle (sarcomatoid) RCC - 3.7%, ferrous RCC - 5.1%. However, in 1996 the idea of the morphological structure of kidney tumors has been revised (Heidelberg) and adopted by the working classification, called "Heidelberg" or "Maynts". It is based on cytogenetics and kidney tumors at early classification W. Thoenes (1986) [13]. 1. The clear cell RCC, RCC chromophilic 2. 3. papillary RCC, chromophobe RCC 4., 5. oncocytomas 6. cancer of the ducts of Bellini, 7. neuroendocrine cancer.

Known as the TNM system (2009), describes the anatomy of the spread of destruction and consists of three parts (TNM).

The classification of malignant tumors in the so-called "stage" of the process is based on the postulate that high survival for localized tumors than than the common beyond the organ lesions [9].

In 1981, S.A. Fuhrman et al. proposed a classification system tumors, which take into account the index of the cell nucleus, the degree of differentiation of tumor cells Fuhrman system [1].

- Grade 1 (G1) - high-grade tumors;
- Grade 2 (G2) - moderately differentiated tumor;
- Grade 3-4 (G 3-4) - low-grade tumor.

**Diagnosis.** Currently, there are various methods of diagnosis of RCC. Non-invasive diagnostic methods of our time as ultrasound and CT, MRI led to a change in the method of examination of patients with RCC, in addition, to increase the detection rate of the earlier stages of the disease [32,27]. Ultrasound is a common screening methods of radiation diagnosis of renal neoplasms [47]. CT is the most valuable diagnostic value, which is the main and the main method of diagnosis of kidney structures. The most common solid and solid-cystic tumor types that occur regardless of the lower or upper pole. The existence of a cystic component, due to the presence of hemorrhage and necrosis areas that clearly differentiated with the help of CT. Typical fibrous renal capsule as hyperechogenic rim at the periphery of the tumor, clearly delineating the tumor and normal kidney tissue. However, at low tumor cell differentiations kidney fibrous capsule can be infiltrated and inflamed. During the CT scan with contrast may diagnose a tumor the size of 0.5 mm. determine the location in relation to the segments, boundaries and goal kidney [16]. Practice shows that CT also allows you to see an increase in regional lymph nodes along the aorta and inferior vena cava, blood clots in the hollow and renal veins, and distant metastases. How to write Zagoria R.J. and Wolfman N.T. doubts about the results of CT scans occur only when non-directional search for renal tumors [56]. Implementation of multiplanar and three-dimensional reconstructions allows the doctor to evaluate complex vascular architecture

of the kidneys and urinary tract. ICB renal cancer patients compared to standard CT can more accurately determine the stage of the disease and metastasis, provides information for determining the amount and the method of surgical treatment [23]. Patients suffering from intolerance to iodinated contrast agents, MRI is an excellent alternative. [26] Take into account that an MRI scan about 24% of kidney tumors reserves without differentiation [56]. Unlike CT MRI worse displaying tumor calcification, which can lead to diagnostic errors. However, MP angiography is considered to be an accurate method for the detection of venous tumor invasion [33]. As the data of other studies of MRI in the detection sensitivity of the inferior vena cava thrombosis reaches 80-100%, which corresponds angiography with selective catheterization of the inferior vena cava [53]. Taking into account the peculiarities of metastasis, a set of mandatory surveys for staging contains X-ray light, and with a reasonable suspicion of metastases in the lungs to do CT chest. Radioisotope scan skeleton renografiya radionuclide that can play a major role in addressing the many issues in the further treatment.

**Treatment.** Surgery is the only effective treatment for kidney cancer. To date, use these types of surgery: combined, by extension, radical nephrectomy and simple. When choosing a need to take into account the fact that access must be less traumatic, and more, provide access to the object operation [1]. As is known, the standard treatment for localized renal cell carcinoma is radical removal of kidneys from the time of its introduction (S.J. Robson et al., 1963). In domestic medicine nephrectomy for renal tumor performed the first SP Fedorov in 1923. The principles of the operation have not changed since the days of C.S. Robson and typically include early bandaging a. renalis, subsequent ligation v. renalis and their intersection, kidney removal is Gerota fascia, along with the surrounding perirenal fiber, removing the ipsilateral adrenal gland. However, the choice of access execution lymphadenectomy currently remain controversial [55]. Advanced kidney removal involves almost the same amount of transactions that radical removal. However, it a regional lymphadenectomy is performed

after diagnosis of metastatic lymph node.

#### **Laparoscopic radical nephrectomy (LRN).**

Laparoscopy remained exclusively a diagnostic method for a long time, until in 1983, Z. Kurt et al. I not made a laparoscopic appendectomy, since laparoscopic surgery has been gaining a place in the different surgical specialties. In 1990, Clayman first realized laparoscopic nephrectomy at oncocytomas [56]. The terms of use of laparoscopic surgery in the treatment of urological diseases each year continues to grow [48]. Sor1soa1 et al. (1991) published the results of the first radical laparoscopic nephrectomy in RCC [14]. Over the past decade known urologists around the world have repeatedly demonstrated that laparoscopic nephrectomy in RCC is feasible and most preferable than open surgery. Today more and more evidence that the T1 and T2 laparoscopic nephrectomy is becoming a serious alternative to open surgery [56]. In 1999 Cervais et al. raised the bar even higher with laparoscopic nephrectomy in patients with T3a and T3b tumors even as cytoreductive surgical intervention prior to immunotherapy. It was found that these patients recovered significantly better than similar patients who underwent open surgery, as they were able to start a course of immunotherapy for 1 month before [50]. The results of 64 patients after laparoscopic radical nephrectomy and 69 - after open radical nephrectomy. In this retrospective multicenter survey shows that the 5-year survival rate after LRN is the same after the traditional open surgery [35]. According to the same Permpongkosol S et al. (2005), a ten-year survival rate after laparoscopic radical nephrectomy was significantly higher than with conventional surgical approach. [36] At this time, the treatment of RCC by means of open and laparoscopic techniques. The greatest number of successful operations obtained by laparoscopic surgery, but they have drawbacks such as the need for pneumoperitoneum.

#### **Laparoscopic assisted radical nephrectomy (LARN) - a version of the standard laparoscopic surgery.**

With this operation, it uses standard laparoscopic instruments, first create a pneumoperitoneum and a laparoscope is inserted. After an additional incision

in the abdominal cavity is entered free hand surgeon, thereby reducing the risk of iatrogenic damage of tissue dissection and retracts bodies [41]. In 1996, Dr. Nacada performed the first laparoscopic-assisted nephrectomy. In the same year in the United States approved the use of the first hand-held laparoscopic port, which later became the most popular. [33]

Laparoscopic assisted radical nephrectomy for renal cell carcinoma T2N0M0 in our country for the first time performed a professor OV Teodorovich in 2002 at the Department of endoscopic urology RMAPO [17]. Methods of assisted laparoscopy (AL) suited to laparoscopic surgery, which require an intact removal of a relatively large volume of tissue, which in the case of the classical method would entail an extension of the operational section of the trocar [44]. Positive moment assisted surgery is that the surgeon's hand helps in localization of structures and instruments of governance in the three-dimensional space, whereas in conventional laparoscopic surgery is often lost focus. Moreover, at the surgeon can control AL situations that may require open conversion, for example, massive bleeding. AL may also be used as an alternative, which is preferred transition from open to laparoscopic surgery [38]. AL surgery usually requires less trocars and working tools than traditional laparoscopy. A number of other advantages, the introduction of the hand into the abdominal cavity, which enables the operator to the tactile sense of the ability to carry out palpation of the kidneys and other tissues, excretion blunt manner, control bleeding, and so on. According Nakada et al. (2001), the average time assisted laparoscopic nephrectomy in 18 patients was 220.5 minutes, while traditional open radical nephrectomy - 117.8 min [34]. However, the average stay (3.9 days after laparoscopy assisted nephrectomy versus 5.1 days after open radical nephrectomy), stay on a piece of disability (26.8 days after nephrectomy laparoscopically assisted versus 52.2 days after traditional open nephrectomy), the average duration of return to normal working life (28 days after nephrectomy laparoscopically assisted versus 150 days after open radical nephrectomy) speak in favor of laparoscopically

assisted radical nephrectomy. Lee SE et al. (2003) compares the results of the open nephrectomy and laparoscopic nephrectomy assisted 104 patients. According to him the length of laparoscopically assisted surgery was 194.9 minutes. against 180.7 minutes. with traditional open nephrectomy. The volume of blood loss higher in open surgery (262.8 ml versus 182.8 mL), were also observed significantly good performance early postoperative period: the start of feeding (2.6 vs. 3.2 days), the duration of an insurance drainage (2.6 day compared to 3.2) and the average length of hospital days (6.8 days vs. 8.9 at LARN after open surgery) [20]. As a result, the use of fewer ports and cleavage with cut muscles may reduce unwanted surgical complications.

#### **Open partial nephrectomy.**

The world's first operation of partial nephrectomy (PN) is fixed and performed by Dr. Simon in 1870, a patient with hydronephrosis, and later Dr. Vizen Czerny first performed RP over the tumor [18]. PN was originally proposed as an alternative method of choice of surgical treatment of patients with a single kidney tumors, congenital anomalies, systemic disease, with a reduction in filtration and excretory functions, as well as with bilateral kidney damage. The analysis of clinical and diagnostic information 14647 patients, which for the period from 1988 to 2001. performed surgical treatment due to the size of RCC with less than 7 cm Education found that conserving surgery was performed only in 1401 (9.6%) patients. Worth to note that the number of execution times in the ER increased from 1988 to 2001 (4.6% and 17.6%, respectively,  $p < 0.001$ ). In the period 1988-1999 gg. tumor having a size of 2 cm. RP was performed in 14% of cases, and from 2000-2001. in 42% of cases. When tumor size of 2 to 4 cm. The performance of nephron-sparing surgery has increased from 5% to 20%, respectively, analogical period [31]. After the data is carried out retrospective studies, as well as their frequency of decreased PN, organ surgery for localized forms of cancer has become the standard of care [37,10] have shown. The highlight of partial nephrectomy is the clamping of the renal artery, which time has a major role in the future of kidney

function. In assessing the complexity of the surgical technique of resection depend on the location of the tumor, the presence of tumor in the middle segment or have kidney gate increases during ischemia (55 min. To 34 min. In patients with the presence of tumor in the upper and lower segments ( $p < 0.05$ ). Fergany according to data in 2000 on the basis of the research results of a 10-year follow-up of patients with PN was performed. of the 107 patients, 96 (90%) surgery was performed on absolute grounds, in 42 (39%) preoperative period revealed a decrease in kidney function. 5 and 10 year survival rates were 88.2% and 73%, respectively. In 52 patients (49%) had stable renal function for the weight of the observation period [17]. According to the data analysis in 1454 patients in which the PN produced or PAD, no reliable differences recurrent survival was not found in the group of patients with a tumor size of up to 4.0 cm., and in patients with tumor sizes ranging from 4.0 to 7.0 cm. Mortality at step T1a turned 2.2% and 2.6% in the PPR and PH ( $p = 0.8$ ), respectively, at step T1b - 6.2% and 9%, respectively ( $p = 0.6$ ). During the RRP for a long time was considered the standard in the art partial nephrectomy, it is indented 1 cm. From the edge of the tumor, to achieve intaknogo surgical margins [11].

Currently, the question of the distance from the tumor to the resection margin still remains debated. In retrospective studies conducted in 69 patients who underwent RRP was performed, Castilla et al. an 8-year period of observation it was found out that the creation of a negative surgical margin is sufficient to achieve the appearance of recurrence, regardless of its width [15]. Piper et al. write that the observed 67 patients for 60 months, which proves to achieve absence of local recurrence of the tumor enough to indent the edge of 1 mm. [38]. At present, the existing clinical guidelines of the European Association of Urology partial nephrectomy in RCC indicated for all patients with clinical stage T1, with minimal surgical indented [28].

#### **Laparoscopic partial nephrectomy.**

The first partial nephrectomy using endovideosurgical technology (LPN) was performed Winfield et al. In 1992, a patient with a kidney stone. While argon

coagulator was used, the operation was carried out for 6 hours. In the course of LPN noted easier postoperative period, in comparison with standard access [54]. A year later, a group of authors led by McDougall described with the first laparoscopic partial nephrectomy performed for RCC [30]. Janetschek G et al. in 2000 we conducted the OSR analysis, namely comparison of OSR ( $n = 73$ ) and wedge laparoscopic partial nephrectomy ( $n = 25$ ) performed 98 patients diagnosed with RCC. The average age of patients 62.3 years, median tumor - 3.8 cm in the group OSR and 1.9 cm in the group of laparoscopic partial nephrectomy wedge... According to the data presented in the group OSR average time duration of surgery was 142 minutes (86 minutes - 230 min), the average amount of blood loss - 170 ml. (0 ml - 1500 ml.), Postoperative complications - 8.0%. In the group of laparoscopic wedge resection average time duration of the operation was 163.5 minutes. (90 minutes - 300 min), the average amount of blood loss - 287 ml. (20 ml - 800 ml), postoperative complications were observed in 8% of patients. According to the histopathological study of RCC was diagnosed in 87 patients, 2 patients - oncocytomas, from 1 - kidney adenoma, and 1 unknown-metastaz other malignant tumors, in 4 - multylokulare cyst, and 1 - kidney abscess. For up to 22 months. OSR observation group and laparoscopic wedge resection not been a local recurrence without distant metastases [21]. Stifelman et al. We proposed a method for the LRS using "hands" assisted operations, based on the experience of this procedure in 11 patients. The average operation time 273 min., The average amount of blood loss 319 ml. All operations were carried out without warm ischemia, harmonic scalpel was used in conjunction with argon coagulation. The average volume of the tumor was 1.9 cm. According to the Pathology Report angiomyolipoma in 7 patients, and 4 RCC [51]. In 2003, the published data of the comparative analysis of early postoperative complications following LPN ( $n = 100$ ) and RN ( $n = 100$ ), 200 patients completed RCC tumor is not more than 7 cm. At the Cleveland Clinic. Mean tumor size was 2.8 cm. In the group of LRP and 3.3 cm.



In the LPN group and in the latter group was significantly greater in patients with tumors greater than 4 cm ( $p < 0.001$ ), with the defeat of the only kidney ( $p = 0.002$ ), more malignancies were detected ( $p = 0.002$ ). Mean operative time was 3 hours and 3.9 hours in the LPN group and PN, respectively ( $p < 0.001$ ), blood loss - 125 ml. and 250 ml. ( $p < 0.001$ ), and during ischemia renal parenchyma - 27.8 minutes. and 17.5 min. ( $p < 0.001$ ), respectively. Functional results in both groups were comparable, the mean preoperative serum creatinine level was 1.0 mg / dL (88.4 mmol / L) and 1.0 mg / dl (88.4 mmol / L) ( $p = 0.52$ ) and the average serum creatinine levels after the operation - 1.1 mg / dl (97.24 mmol / l) and 1.2 mg / dL (106.08 mmol / l) ( $p = 0.65$ ) and Group PFU LPN respectively. LPN was associated with a higher frequency of intraoperative complications (5% vs. 0%,  $p = 0.1$ ). According to the frequency of postoperative complications did not differ between groups (11% in the LPN group versus 2% in the PN group,  $p = 0.01$ ), however, urological complications (urinary drip, kidney hematoma, haematuria) were more frequent in the LPN group [20]. In addition a group of authors led by Simmons shows that carefully selected patients with clinical stage T1b-T3a and tumors greater than 4 cm., LRS allows to achieve oncologic outcomes comparable with those after the PN. In the period from April 2001 to December 2005, 75 patients performed LPN, PN - 35 patients. Mean tumor size was larger in the group of PN (5.3 cm. Against 4.9 cm.,  $P = 0.03$ ), this group often detected tumor spread beyond the kidney capsule (33% vs. 9%,  $p = 0.006$ ). Median follow-up was 57 months (27 months - 79 months) in the PN and 44 months (27 months - 85 months) in the group of LPN ( $P = 0.1$ ). General and tumor - specific survival in both groups were the same and amounted to 89% and 97%. Relapse-free survival was 97% in the LA group and 94% in the group of LRP ( $p = 0.43$ ). Functional results were better after LPN and the average decline in glomerular filtration rate was 13 ml / min to 24 ml / min PN group ( $p = 0.03$ ) [46].

## CONCLUSION

Thus, the analysis of the literature shows that laparoscopic surgery

technique in RCC is effective and minimally invasive techniques compared to traditional surgery. Also, the advantages of laparoscopic nephrectomy methods compared with traditional methods are a minimal incision of the anterior abdominal wall, shorter hospital stay, faster recovery and all this significantly expands the indications for treatment of volumetric endosurgical kidney structures. RP provides the best long-term results in patients with local renal cell carcinoma. Compared with radical nephrectomy preservation of renal parenchyma eliminates the inconveniences associated with the duration of survival. The most important arguments for conserving surgery for kidney cancer are clearly increasing number of small renal tumors diagnosed sizes, operative technique conserving surgery is well designed, which allows to minimize the number of complications or avoid them completely. But despite the success of surgical treatment, kidney cancer is still quite a complex disease, in diagnostic and in therapeutic terms.

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#### The authors:

Tobohov Alexander Vasilevich - Professor, MD, Head of the Department of Hospital Surgery and radiation diagnosis, M.K. Ammosov North-Eastern Federal University.

Address: 677019, Yakutsk, Sergelyakh Highway 4

Phone number 8 (4112) 395644

E-mail: [avtobohov@mail.ru](mailto:avtobohov@mail.ru)

Nikolaev Vladimir Nikolaevich - PhD, associate professor of hospital surgery and radiation diagnosis, M.K. Ammosov North-Eastern Federal University.

Address: 677019, Yakutsk, Sergelyakh Highway 4

Phone number 8 (4112) 395644

E-mail: [w.nik@mail.ru](mailto:w.nik@mail.ru)

Vinokurov Ruslan Ruslanovich - graduate student, doctor RBN#1-NCM, [vinocurovrr@mail.ru](mailto:vinocurovrr@mail.ru);

Maximov Alexander Vasilevich - Head. Dep. Urology RBN#1-NCM.

V. G. Ignatiev, V. M. Mikhailova, T. S. Dyagileva, I. A. Holto-sunov, L. A. Krivoschapkina

## THE APPLICATION EXPERIENCE OF SIMPONI (GOLIMUMAB) IN THE SECOND LINE OF BIOLOGICAL THERAPY (AFTER INFLIXIMAB) IN THE PATIENT WITH ULCERATIVE COLITIS

### ABSTRACT

The article presents the clinical case analysis of the patient with diagnosis: ulcerative colitis of overall affection with clinical-laboratory results. The effect of baseline therapy with transition to genetically engineered biological therapy with the medicine "infiximab". The development of secondary resistance to the medicine "infiximab" and prescription of "golimumab" in the second line of biological therapy.

**Keywords:** ulcerative colitis, infiximab, golimumab.

### INTRODUCTION

The relevance of inflammatory bowel disease (further IBD) in different regions of the world considerably varies. So, the frequency of ulcerative colitis (further UC) according to different researchers makes from 21 to 268 cases, and the Crown disease (further CD) from 9 to 199 cases per 100 thousand population, reaching the maximal indicators in the countries of Scandinavia, North America, Canada, Israel. The incidence increase of UC is 5-20 cases a year, CD - 5-15 cases a year per 100 thousand population.

According to epidemiological researches abundance of IBD in the European part of Russia makes 20,4 per 100 thousand population for UC and 3,7 per 100 thousand population for CD.

It is important to note that IBD develop mainly at the young age (mean age of the patients - 20-40 years).

The peculiarity of disease incidence in our country is a triple dominance of the severe complicated IBD forms with a high lethality due to late diagnostics. IBD within the first year of the disease is diagnosed only in 25% of cases,

in other cases the diagnosis was made 3-12 years since the beginning of clinical symptoms. The frequency of complications makes 55% for CD diagnosis during the period up to three years, for later diagnostics — in 100% of cases. Heavy complications develop in 29% of cases at late diagnostics of UC.

IBD is diagnosed on the basis of assessment of complaints, anamnesis, clinical picture of disease, data of a complex of endoscopic, radiological, histologic and laboratory tests.

For many years the treatment of IBD