ACADEMICIA
An International Multidisciplinary Research Journal
(Double Blind Refereed & Peer Reviewed Journal)

DOI: 10.5958/2249-7137.2021.00966.6

MODERN TECHNOLOGIES IN THE DIAGNOSIS AND TREATMENT OF KIDNEY CANCER

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ABSTRACT

Renal cell carcinoma (RCC) diagnosis and management have undergone significant shifts in the recent past. MSCT makes it possible to assess not only the prevalence of the tumor process, but also the calyx-pelvic system and vessels; In the past 10 years, due to the technological advancements, laparoscopic nephrectomy has become the popular and effective method of the treatment and a less traumatic alternative to open radical nephrectomy. Laparoscopy may not be used only for removal of the neoplasm, but also for biopsy of the tumor. Over the past years, cryodestruction of neoplasms has become widespread since it is possible to carry out the procedure in real time under the control of ultrasound, CT or MRI. This review aims to highlight recent evidence that has emerged in the diagnosis and management of this complicated oncologic issue.

KEYWORDS: *Renal cell carcinoma, Multispiral computed tomography, Telomeres, laparoscopic approach, Microwave therapy, Chemo ablation.*

INTRODUCTION

Modern technology has greatly improved the diagnosis and treatment of kidney cancer. The algorithm for examining patients has changed: after detecting a neoplasm during ultrasound,

multispiral computed tomography (MSCT) is performed, which allows us to abandon excretory urographyand complex vascular research. MSCT makes it possible to assess not only the prevalence of the tumor process, but also the calyx-pelvic system and vessels [1]. In planning an organ preserving surgery obtaining spatial three-dimensional position of the neoplasm, renal vessels and the calyx-pelvic system with modeling the of possible anatomical changes after removal of part of the organ might be significantly informative. Both MSCT and magnetic resonance imaging (MRI) allow us to consider the presence and extent of a tumor venous thrombus, and MRI with suppression of the signal from paranephrium- about invasion into the kidney fibrous capsule, which facilitates the differential diagnosis of the pT1a, b and pT3a stages of the disease.

Despite the enormous possibilities of tomography, in some cases (suspicion of a benign tumor, severe intercurrent condition, etc.) it is necessary to establish the morphological structure of the neoplasm before the operation. This allows perform only a biopsy, the informative value of which reaches 90%. In order to increase informativeness of a biopsy it is used the determination of telomerase activity [2]. The enzyme telomerase is a ribonucleoprotein complex that synthesizes the terminal DNA sequences - telomeres. Telomeres protect the ends of chromosomes from enzymatic destruction, prevent fusion of chromosomes with each other and are necessary fordoubling of genetic material during division of cells. High activity of this enzymeis observedin embryonic, stem, germ cells of a person, as well as in macrophages and leukocytes; Although information about this enzyme is encoded in the DNA of all cells there is no telomerase activity in most somatic cells. In the process of malignant transformation of the cell, telomerase is activated, which provides the malignant cells to divide unlimitedly.Most malignant tumors are characterized by high telomerase activity. A kidney tumor is no exception.

In the past 10 years, due to the advancements in technology laparoscopicnephrectomy has become popular effective method of the treatment and a less traumatic alternative to open radical nephrectomy in a certain population of patients [3]. The first laparoscopic nephrectomy due to kidney cancer was performed in 1990 by Clayman R.V. [4]. Today, laparoscopic nephrectomy is widely used. Compared to open surgery, it reduces postoperative pain as well as the patient's stay in the hospital and the period his recovery after surgery [5].

Most authors perform laparoscopic radical nephrectomy in cases of small (<8 cm) local renal cell carcinomas without local invasion, renal vein thrombosis or lymphadenopathy. For laparoscopic kidney cancer surgery there are three approaches are used: transperitoneal, retroperitoneal and assisted.

Clay man R.V. was the first to use the transperitoneal laparoscopic approach [6]. Retroperitoneal access is an analogue of open lumbotomy nephrectomy, it makes possible to reach the renal vessels without opening the abdominal cavity. Assisted laparoscopic nephrectomy facilitates the training of surgeons in open surgery and serves as an alternative to the conversion of laparoscopic surgery to open surgery, and is also used for large tumors. It has been described [7] a modified assisted laparoscopic surgery with an additional gel port in the groin or on the border of the epi- and mesogastric region for manual manipulations in the wound. There are [8] the advantages of this technique: the use of the alternating manual and instrumental tissue dissection with laparoscopic assisted nephrectomy combines the possibilities of endosurgical and traditional approaches. Every of three access options for laparoscopic nephrectomy has its advantages and

disadvantages and can be chosen by the surgeon depending on his/her preferences, but it is necessary to ensure compliance with oncological requirements. The results of 5-year survival of patients' with kidney cancer that underwent laparoscopic surgery are comparable to those with open surgery (Table 1) [5, 9 - 15].

TABLE 1: RESULTS OF LAPAROSCOPIC RADICAL NEPHRECTOMY

Author	Number	Stage	*renal-bed or fossa recurrence*	5-year specific survival rate,%	average observation period,mon
Cadeddu J.A. et al.[9]	157	T1—2N0M0	0	91	19,2
Walther M.Met al. [22]	11	≥T2NxM1	0	—	—
Ono Y. et al [10]	147	T1—2N0M0	0	96	30
Gill I.S. et al. [12]	53	T1—2N0M0	0	—	13
Dunn M.D. et al. [5]	61	T1—2N0M0	0	—	25
Chan D.Y. et al. [13]	67	T1—2N0M0	0	95	35,6
Portis A.J. et al. [14]	64	T1—2N0M0	1	98	54
Stifelman M.D. et al. [15]	108	T1—3N0M0	0	93	14

Tumors to be removed with laparoscopic radical nephrectomy (stage pT1), can be removed with open resection of the kidney [3, 16]. Modern technologies make it possible to carry out laparoscopic organ-preserving surgeries for kidney cancer [17].

Laparoscopic surgery for cancer is associated with the risk of dissemination of the neoplasm and the development of metastases. There are reports of cutaneous metastases and metastases at the sites of laparoscopic port placement after laparoscopic lymp hadenectomy for prostate cancer [18] and bladder cancer [19]. The work [20] provides data on 1098 urological laparoscopic operations for malignant neoplasms, while there were 8 local recurrences and 2 cases of metastases in the ports. In kidney cancer, according to the authors, the frequency of local recurrence amounted to 2.2%; metastases in the places of installation of laparoscopic ports were not registered. Currently, only 3 cases of metastases in ports after laparoscopic radical nephrectomy have been described [21].

Traditionally, laparoscopic radical nephrectomyis performed for kidney cancer at T1-2N0M0. The maximum sizes of the neoplasm, subject to laparoscopic removal, are discussed, and the

limitations are to a greater extentassociated with the "comfort" of the surgeon, rather than with technical difficulties [3]. If initially laparoscopic surgery was carried out at clinical stage T1-2, then in the subsequent described [9, 15] successful laparoscopic removal of many neoplasms that according to the data of morphological studies, they belonged to the pT3a stage. Moreover, laparoscopic the operation can be performed for advanced (pT3b) and metastatic (M1) kidney cancer.

So, Walther M.M. et al. [22] showed that patients with metastatic kidney cancer who performed laparoscopic cytoreductivenephrectomy, recovered faster after surgery, had less pronounced postoperative pain and shorter time to treatment with interleukin 2 compared to patients undergoing open nephrectomy. However, the author reports that in 5 out of 11 cases, laparoscopic the operation was transformed into an open one.

Performing laparoscopic nephrectomy with venous tumor invasion of renal cancer into the renal and inferior vena cava is limited due to the technical difficulties of laparoscopic thrombectomy. Nevertheless, here, too, there are technical innovations. Allowed to perform laparoscopic radical nephrectomy for renal cancer pT3b with renal thrombus level I [23], and during operations on animals - and with renal thrombus level II – IV [24]

Recently, there have been reports of authors [25, 26] about the use of a laparoscopic access for kidney tumors. There was used a laparoscopic approach, and not laparoscopic surgery, since the technique itself does not differ from the standard one when using the transperitoneal operative approach [3]. With laparoscopic surgery, as with open surgery, it is necessary to observe oncological requirements, such as lymphadenectomy [27].

Laparoscopy may not be usedonly for removal of the neoplasm, but also for biopsy of the tumor. There is a large number of works confirming the great diagnostic value of a kidney biopsy [28, 29]. Visualization of the organ is possible not only through ultrasound scanning, but also with laparoscopic and retroperitoneoscopic access. Limb J. et al. [30] used a laparoscopic approach to elucidation of the nature of 57 cystic neoplasms kidneys (28 patients had Bosniak II category and in 29 - III). In all observations, transperitoneal laparoscopic imaging of the neoplasm and aspiration of the contents cysts for cytological analysis followed by biopsy of the cyst wall. 11 (19%) patients were diagnosed with cystic kidney cancer. In nonethere was no recurrence of cancer or dissemination of cancer cells in the port or peritoneum.

If removal of the neoplasm of the kidney is impossible (severe intercurrent background, senile age, small size of the neoplasm or reluctance of the patient), then one of the options for minimally invasive surgery for kidney cancer can be chosen - cryodestruction, radiofrequency ablation, laser ablation, focused high-power ultrasound exposure, microwave thermal ablation, chemoablation with the introduction of ethanol and others into the tumor substances. The role of these methods is being studied; it is possible that that some of them will be at the forefront of the treatment of localized small kidney tumors.

Over the past years, cryodestruction of neoplasms has become wide spread since it is possible to carry out the procedure in real time under the control of ultrasound, CT or MRI. The use of this method is devoted to a large number of works, first used it Barone G.W. in 1988 [31]. In a recent publication, Cestari A. et al. [32] reported about cryodestruction of a kidney tumor in 37 patients. Depending on from the location of the neoplasm, the procedure was performed trans- or

retroperitoneally. In averagethe operation took 194 minutes, and the blood loss was 165 ml. After the operation, the patients were under MRI control for 24 months or more, in addition, a biopsy was performed from the area of the tumor, which was subjected to cryodestruction, 6 months later. In none of observations did not detect cancer cells. Complications were registered in 14.6% of cases [33]. The principle of radiofrequency ablation (RFA) is that a needle inserted percutaneously or openly into the tumor creates local hyperthermia. Modern RFA can destroy a tumor 2–5 cm in size [34]. Some publications [35, 36] have demonstrated good results.RFA for kidney tumors. Multicenter studies of RFA complications showed their low frequency (7.4%). Complications were associated mainly with pain or paresthesia at the site of introduction of probes [33].

As an ablative technique, microwave thermotherapy was first used by Kigure T. [37] on VX-2 tumor models in rabbits. Recently Iinuma M. et al. [38] published their own data on the use of microwave ablation in the treatment of kidney tumors in 13 patients. Preliminary results show that all patientsdestruction of the tumor was noted after the procedure. Moreover, when compared with the control group, which performed an open nephrectomy, it turned out that after microwave ablation, significantly fewer complications were recorded. Terai A. et al. [39] performed laparoscopic resection of the kidney using microwave ablation in 19 patients. Postoperative complications include the formation of a urinary fistula, arteriovenous fistula, and wrinkling of the operated organ. 19 months after surgery CT scan showed no relapse or distant metastases. Similar data were presented by other researchers [40, 41]. Microwave thermotherapy has many advantages. Many clinics are equipped with microwave thermotherapy devices used for liver surgery, but they can be adapted for ablation of tumors of other organs, including kidney. Chemoablationis achieved by injecting chemicals into the tumor tissue. For this, various substances can be used. Percutaneous administration of ethanol into a tumor is more often used to destroy liver neoplasms [42]. In urologythis method has been applied in prostate cancer [43]. Its use in kidney tumors is being studied. Naitoh Y. et al. [44] injected ethanol into a neoplasm of the kidney in white rats and showed that none the tumor that underwent this procedure did not enlarge. After the 3rd injection, tumor growth was significantly suppressed, and after the 5th tumor, almostcompletely destroyed. Histologically detecteddegenerative necrosis,Rehman J. et al. [45] for the purpose of ablation injected into the kidneys of pigsacetoaceticacid. At the sites of acid injection, tissue necrosis was noted. The authors propose in the future to use this method in combination with other minimally invasive kidney tumor treatment options, for example cryodestruction or radiofrequency ablation.

Kohrmann K.U. et al. [46] report the possibility of using high-intensity focused ultrasound (High Intensity Focused Ultrasound - HIFU). Wu F. et al. [47] used HIFU for late-stage kidney tumors in 13 patients and noted that the blood supply of all neoplasms either decreased or was absent and the tumors themselves were significantly reduced.

Other methods of minimally invasive surgery of kidney tumors have also appeared. Prapavat V. et al. [48] suggested using laser-induced thermotherapy (LITT). Dick E.A. et al. [49] used it in 9 patients with an inoperable tumor kidney and have shown that the method is safe and reduces tumor volume by an average of 45%.

Solomon S.B. et al. [50] on the kidneys of dogs showed the possibility of using ablation by γ-radiation (Interstitial Photon Radiation Ablation) on a par with other minimally invasive

techniques. David Y. et al. [51] note that this method is effective with ablation of hyper vascularized tissues of interest is the Hydro-Jet technique, the principle of which is to use a directed jet water that acts like a sharp knife. Generator Hydro-Jet is mainly used for resection of highly vascularized liver tissue. ShekarrizH Et al. [52] first used this method with laparoscopic resection of the kidney in animals. It has been noted that the Hydro-Jet preferentially cuts off the renal parenchyma, leaving the intrarenal vessels and the renal pelvis system intact. Large vessels were then clipped and dissected. Minimal bleeding was easily stopped by coagulation.

The introduction of new technologies made it possible to revise the algorithm for examining patients with kidney tumors, as well as expand the possibilities of their treatment. In the future, an even earlier than when using ultrasound, tumor diagnosis kidneys; the existing screening method will be replaced by research for a tumor marker of kidney cancer. Of course, there are observations when the identity of the neoplasm remains unclear (parenchyma or pyelocaliceal system, tumor of the upper segment of the kidney with invasion of the adrenal gland or primary neoplasm of the adrenal gland with invasion into kidney, etc.). In these cases, the definition of a tumor marker would be extremely useful.

When planning the volume of lymp hadenectomy and to substantiate the feasibility of removing the adrenal gland, an isotope diagnostic method is required, when the radiopharmaceutical is associated with a monoclonal antibody to kidney cancer antigens (according to analogies with prostatsinth). Such a "renascent" will make it possible to visualize not only the tumor in the kidney, but also metastases in lymph nodes, adrenal gland, distant micro metastases. In order to improve the results of treatment, to suppress micro metastases, new "tools" of immunotherapy are needed. Thus, modern technologies open up new perspectives bothin the diagnosis and treatment of kidney cancer.

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