



LAPAROSCOPIC CRYOABLATION OF RENAL TUMORS: INITIAL EXPERIENCE

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ABSTRACT

With the widespread use of x-ray imaging, echography, computerized tomography, magnetic resonance imaging, diagnosis of small kidney malignancies as well as renal cell carcinoma have increased. Surgical treatment of renal tumors with clinical cT1b stage is the radical nephrectomy. Partial nephrectomy is considered to be a gold standard in the surgical treatment of small kidney masses in stage 1 cT1b. However, treatment guidelines have recently changed in patients with renal tumors with cT1b. When establishing a patient with renal tumor in the cT1b stage the first treatment line should be partial nephrectomy. Partial nephrectomy is associated with perioperative complications in about 20% of cases, which causes significant comorbidity. Following the introduction of renal cryoablation at the end of the 1990s, urologists broadened the role of cryoablation to treat cT1b stage tumors in selected patients. Renal cryoablation is a recommended therapeutic alternative in a specific patient population, namely elderly patients, patients with multiple concomitant diseases, single kidney patients, ipsilateral multiple kidney tumors or patients with bilateral renal tumors. Laparoscopic renal cryoablation appears as an option for the treatment of small kidney masses due to a less invasive procedure with low intraoperative complications, without impairment of normal renal parenchyma, and has good comparable mid-term outcomes on follow-up studies.

The purpose of this report is to analyze our initial clinical experience with laparoscopic cryoablation of kidney tumors and to investigate how effective and safe this method is.

Keywords: renal cell carcinoma, partial nephrectomy, renal cryoablation, laparoscopic cryoablation,

INTRODUCTION:

Renal cell carcinoma (RCC) is the third most common urological carcinoma and accounts for 2-3% of all malignancies in the elderly. The most common histological subtype is adenocarcinoma, which is approximately 85% of the renal tumors. Diagnosis of small kidney masses and renal cell carcinoma (RCC) has increased due to the extensive use of imaging studies [1,2]. Therefore, the size

of new diagnosed kidney tumors has decreased and the incidence of small kidney tumors (less than 4 cm) has increased. Partial nephrectomy is considered a gold standard in the treatment of small kidney masses. Historically, renal cell carcinoma has been known to be a tumor of a variety of clinical manifestations due to several signs and symptoms that can be present and established during diagnosis, such as paraneoplastic syndrome. Minimally invasive techniques, including cryosurgery and radiofrequency ablation, through open, laparoscopic or percutaneous techniques are safe in patients with concomitant diseases. They are associated with faster recovery, less pain, and less cost [3,4,5]. Following the introduction of renal cryoablation at the end of the 1990s, urologists widened the indications as well as the role of cryoablation for the treatment of cT1b-stage tumors in selected patients [6,7]. Renal cryoablation is a recommended therapeutic alternative in specific populations of patients, including elderly patients or with multiple concomitant diseases, single kidneys, ipsilateral multiple kidney tumors or bilateral renal tumors. Cryoablation causes predictable cell death through different types of mechanisms. One mechanism is cellular factors including direct cell damage, intracellular ice formation, and rupture of the cell membrane. Another mechanism involves the initial freezing of the extracellular fluid, which in turn causes osmotic dehydration of the intracellular fluid. Secondary changes from freezing include destruction of microcirculation and subsequent cell hypoxia and necrosis caused by vascular stagnation [8]. In addition, cellular apoptosis occurs everywhere in the renal lesion, especially at the periphery of the renal mass [9,10]. Laparoscopic renal cryoablation appears to be an option for the treatment of small kidney masses due to a less invasive procedure with small intraoperative complications, without impairment of normal renal parenchyma, and with good comparable mid-term outcomes from follow-up studies [11]. The long-term results of the studies are currently expected.

MATERIALS AND METHODS:

For the first time in Bulgaria in March 2017 a laparoscopic cryoablation was performed in our urology clinic at St. Marina University Hospital, Varna.

Patient selection:

The choice of appropriate patients for laparoscopic cryoablation (LCA) is an essential step to ensure satisfactory results. Selection criteria should include both the characteristics of the patient and the characteristics of the tumors. For patients who are elderly or have significant comorbidities not considered good candidates for conventional surgery, cryoablation may be an alternative method of treatment. Patients who also have single kidney, ipsilateral multiple tumors as well as bilateral kidney tumors can also be included. Absolute contraindications for renal cryotherapy are patients who have a history of coagulopathy or who are receiving anticoagulation therapy and are unable to stop treatment. Intra-abdominal infections and ascites remain common contraindications for laparoscopy. Previous abdominal surgery also increases surgical difficulty. The position of each patient should be evaluated taking into account the surgeon's experience.

We present two patients who have been operated in our clinic laparoscopically via transperitoneal approach. The age of the patients was 66 years and 81 years. In both cases, the tumors had a diameter of less than 4 cm - 1.8x1 in one case and 3x2.8 cm in the other. Both tumors were located in the right kidney, one on the lateral side and the other on the medial side of the kidney. Both patients had multiple concomitant diseases, one of which was operated in our clinic for invasive bladder cancer two years ago, laparoscopic cystoprostatectomy was done with ureterocutanestomy (tab. 1).

Tab. 1. Preoperative characteristics of patients

Patients	YI	N.P
Age (y.)	66	81
Tumor volume (cm.)	1,8x1	3x2,8
Charlson comorbidity index	1	2
BMI (kg/m ²)	24	20
ASA score	2	2
Preoperative creatinine (mg / dl)	86	101
Previous operations	No	Yes
Preoperative GFR (ml / min / 1.73 m ²)		

Patient preparation:

Preoperatively, a blood group was assigned to patients, also colon cleansing with laxatives and fasting for 8 hours. Antibiotic prophylaxis and low molecular heparin was done for both patients prior to surgery. The operations were performed under endotracheal general anesthesia. For prophylaxis from thromboembolic events, were used elastic socks in both patients.

Fig. 1. Modified lateral position of the patient



Surgical Technique:

Patients were placed in a modified left lateral lumbar position (Fig. 1). The lower leg is in flexion while the upper leg is in the extension. After creating a pneumoperitoneum with the Véres needle, a 10/11 mm trocar was placed above the umbilicus through which with a 30 degree optic the abdominal cavity was inspected. The remaining trocars were placed under visual control as follows: a 5 mm trocar was placed 7 cm lateral from the umbilicus, another 5 mm trocar was placed 2 cm from the SIAS, and another 12 mm trocar was placed under the rib arc at the intersection of the middle axillar line. After the incision of Told's fascia, the retroperitoneum was open and the ascendance colon was mobilized medially. The kidney fat capsule is also dissected and through 12 mm trocar intraoperatively ultrasonic transducer has been inserted and the kidney was examined and found the tumor formation. The fat tissue surrounding the tumor formation was sent for pathological examination. Followed true-cut biopsy from the tumor and sent samples for pathological verification. Using an intraoperative ultrasound transducer, only one cryoprobe was placed transcutaneously into the patient with the small tumor formation, while three cryoprobes were placed on the patient with the larger tumor. The triangulation of the two additional probes that are placed around the first probe provides for the active formation of a "ice ball" - the ice ball with appropriate surgical edges, which is the basic principle of cryoablation. The effective temperature in the "killing zone" should be -20° C or lower. Cryoprobes can reach a temperature in the tissue at -60° C within a few minutes using the effect of Joule-Thompson with a high pressure circulating gas. Cryoprobes are configured to develop an ice zone for freezing the kidney mass with a minimum temperature of -19.4 ° C or lower to achieve complete homogenous necrosis of the kidney tissue. To ensure adequate freezing temperatures (necrosis) in the peripheral area of †the tumor mass, the ice ball extends 0.5 cm beyond the edge of the tumor, which is achieved by the intraoperative ultrasonic transducer. The resulting freezing (necrosis) is based on the size of the

cryoprobes, the total freezing time and the number of freeze and thaw cycles.

Cryoablation:

Cryoablation of the tumors was performed with the aid of a Cryo S Electric II machine (fifth generation cryomachine). In the first case, with the smaller tumor, we used one cryoprobe and performed 2 times freeze for 10 minutes, followed by thaw for 10 minutes, and in the other case we used three cryoprobes and performed 3 cycles of 10 minutes freeze with 10 minutes of thawing (Fig. 4, 5). We used CO2 for Circulation gas. With an intraoperative ultrasonic transducer of “BK Flex 800”, we observed in real time the appearance of an “ice ball” showing tissue necrosis (Fig. 2, 3).

Fig. 2. METRUM CryoFlex Cryo S Electric II



Fig. 3. Flex Focus 800

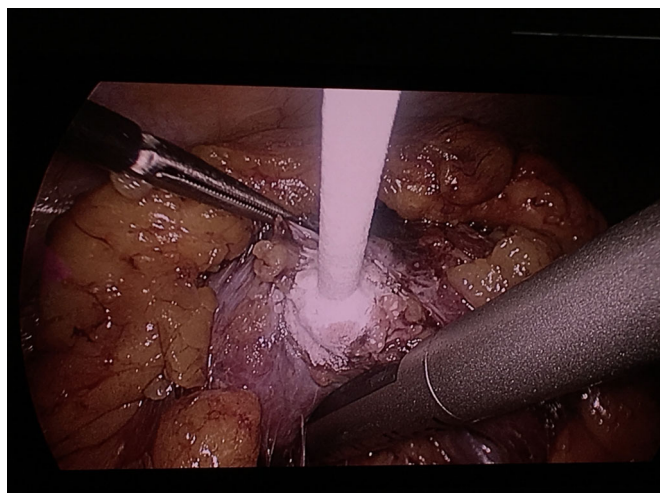
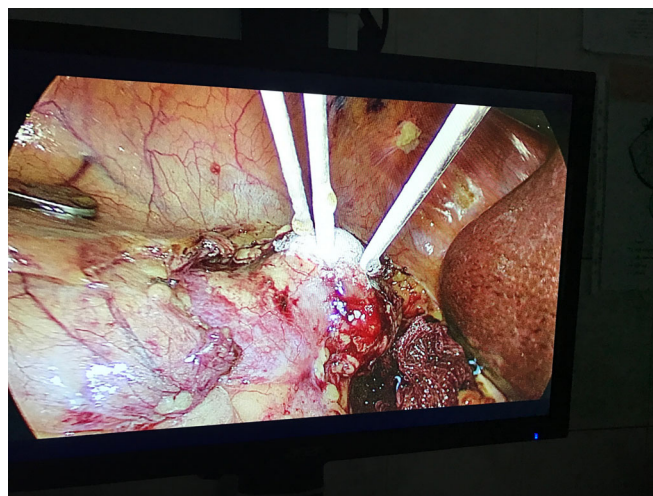


Fig. 4. Laparoscopic cryoablation of the smaller kidney tumor with one cryoprobe for freezing and intraoperative ultrasonic transducer



Fig. 5. Laparoscopic cryoablation of the larger kidney tumor, with three cryoprobes for freezing



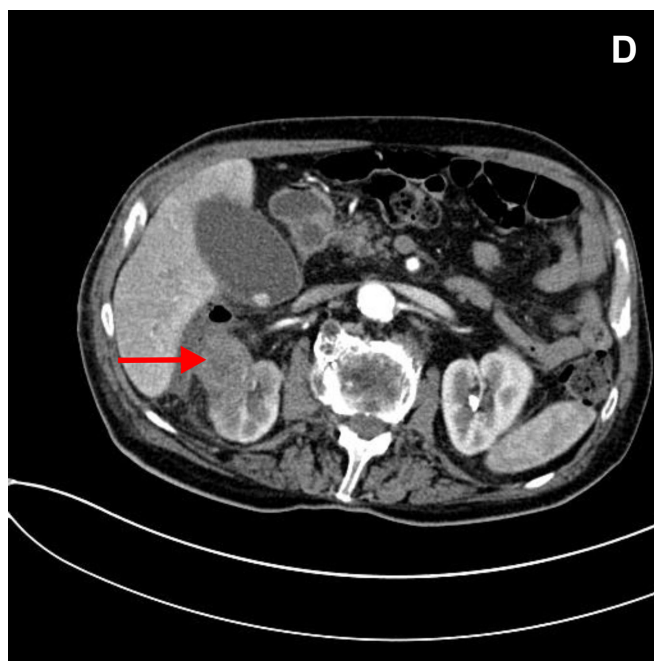
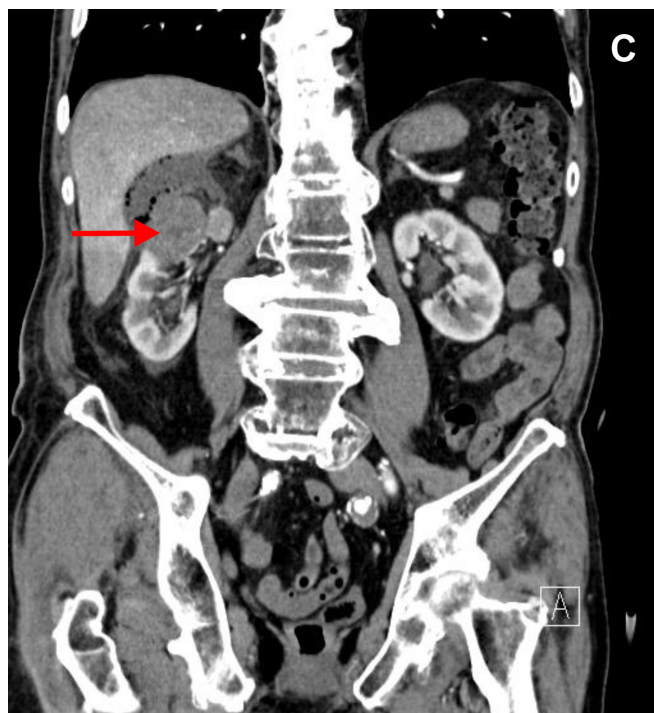
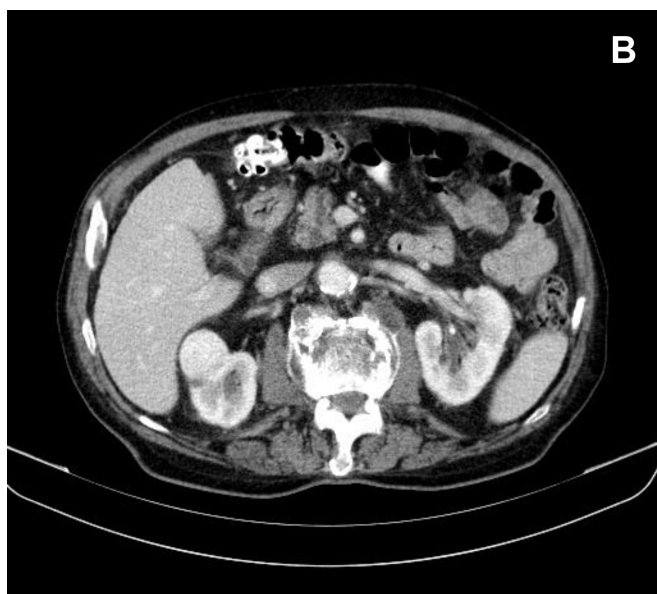
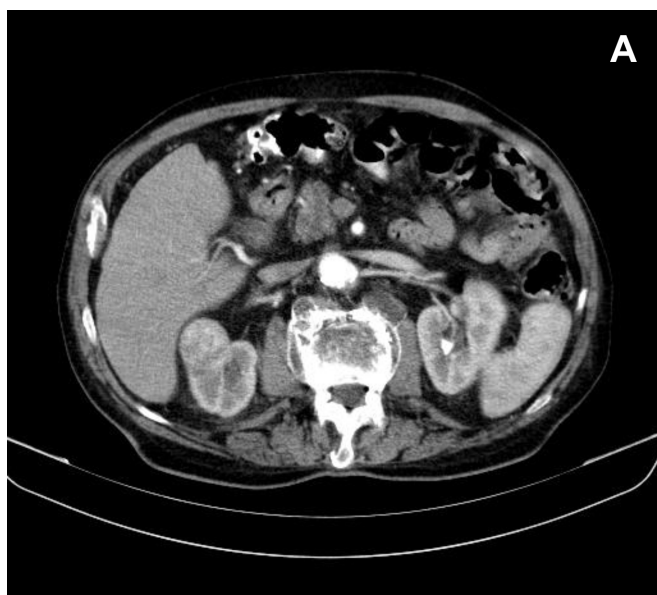
RESULTS:

The operations were performed with minimal blood loss, with an operating time of 50 minutes in one case and 90 minutes for the other. There were no postoperative complications. The early postoperative period passed smoothly and without complications. The patients were discharged clinically healthy on the 4th day of surgery. On the first day after the operation, CT with i.v contrast was done that established necrosis of the tumor formations (Fig. 6).

Tab. 2. Perioperative characteristics

Patients	Y.I	N.P
Operating time (min)	50	90
Blood loss (ml)	-	-
Hospital stay (day)	4	4
Patology:		
Onkocitoma		
Angiomyolipoma		
RCC	1	1
Complications	-	Fever

Fig. 6. - **A)** Preoperative native CT image in which a tumor formation in the upper pole of the kidney is located medially 2.8 x 3 cm in size; **B)** Preoperative contrast CT image of the same formation; **C)** and **D)** Post-operative contrast CT on day one postoperation, red arrows indicate necrosis of the tumor formation



DISCUSSION:

At present, up to 40% of renal tumors are accidentally detected due to the widespread use of imaging technologies, leading to an apparent increase in the incidence of small kidney tumors. Minimally invasive therapies, including cryosurgery through open, laparoscopic or percutaneous techniques, are safe in patients with concomitant diseases. Partial nephrectomy has replaced radical nephrectomy and is the gold standard for the treatment of small kidney tumors up to 4 cm. As a result of minimal invasiveness and promising oncological results, laparoscopic partial resection of renal tumors is the first line of treatment but is associated with a longer learning curve, presence of technique than partial open nephrectomy. On the other side

ablation as minimal invasive surgery using cryoprobe or radio frequency probes and offers advantages in patients with concomitant diseases and has a significantly lower incidence of complications than open or laparoscopic partial resection [12, 13].

In the systematic review of the literature we have found that laparoscopic kidney cryoablation has acceptable average oncological results with low recurrence rates (3-5 years) and is a safe procedure with a low level of complications. Most often is an alternative treatment method and is used in elderly patients with comorbidities that are usually categorized at high surgical risk. The purpose of the cryoablative procedure is to cause deadly freezing of the entire tumor volume, while not damaging surrounding normal healthy tissues. Although studies on kidney cryosurgery in animals have been reported since 1974, reports of clinical use in human kidney tumors have been relatively recent. For the first time in 1995, Uchida et al reported percutaneous cryosurgery [14], immediately after it in 1996. Delworth et al reported open cryoablation and in 1998 Gill et al reported laparoscopic cryoablation of small kidney tumors [15, 16].

Following these promising initial reports, more and more reports on this new topic are being published and explored. With regard to safety, clinical trials and animal studies of low incidence of post-operative complications [16] have been reported so far. Most commonly, renal cryosurgery is performed by open, laparoscopic and percutaneous techniques using cryoprobe with different diameters ranging from 1.4 mm to 5.0 mm. Laparoscopic renal cryosurgery has different advantages over the open, one of which is the ability to identify the exact location of cryoprobes and tumors by using an intraoperative ultrasound transducer as well as real-time monitoring of the freezing process itself, if necessary, change the parameters as well as the probes themselves. Furthermore, another advantage of the laparoscopic method is that it allows the

displacement of adjacent organs from the freezing site, thereby reducing the possibility of iatrogenic injuries.

Two published laparoscopic cryoablation studies of small kidney tumors with a minimal mean follow-up of 3 years demonstrated radiographically documented success rates of 97% and 96%, respectively. Moinzadeh et al reported tumor recurrence in 3 of 56 tumors (5.4%) after laparoscopic cryoablation with an average follow-up period of 36 months [17]. Schwartz et al reported recurrences in 2 patients in 50 tumors (4%) after laparoscopic cryoablation with mean follow-up of 10 months [18]. Interestingly, blood loss and the incidence of post-operative complications were higher in patients operated by laparoscopic partial resection than in patients who had laparoscopic cryoablation (211 ml versus 110 ml and 11.1% vs. 3.3%, respectively). Radiographic follow-up most often CT with intravenous contrast after cryoablation is the main tool of assessing the effect of treatment if contrast enhancement is found it is evidence of incomplete tumor necrosis, that mean recurrence of the disease. In some centers, a biopsy after ablation was performed to evaluate tissue necrosis, while other centers count only on radiographic assessment. Wright et al demonstrated an excellent correlation between post-cryoradiographic data and the subsequent percutaneous biopsy of the treated lesions, and reported that no lesion that showed no contrast enhancement during treatment showed evidence of recurrence of the tumor [19].

CONCLUSION:

Laparoscopic cryoablation is a mini-invasive, safe and effective method and can be used as an alternative to partial kidney resection in selected patients and patients with severe concomitant diseases. It is associated with a low level of complications and has a very low effect on renal function.

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