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Retroperitoneoscopy-Assisted Cryoablation of Renal Tumors Using Multiple 1.5 mm Ultrathin Cryoprobes: A Preliminary Report

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Abstract

Objectives: Laparoscopic cryoablation has recently been proposed as a minimally invasive nephron-sparing treatment for selected patients. We report on our experience with a retroperitoneoscopic technique using multiple ultrathin cryoprobes.

Methods: Seven patients underwent retroperitoneoscopic renal cryoablation for solid renal masses. Mean tumor size on the CT scan was 2.6 (1.5–3.5) cm. A double freeze-thaw cycle of renal cryoablation was performed under real-time ultrasound monitoring using a total of six 1.5-mm cryoprobes simultaneously.

Results: Cryoablation was technically successful in all patients without any need for conversion. Mean duration of surgery was 161 (130–195) minutes and mean blood loss was 107 (50–250) ml. Perioperative biopsy of the tumor confirmed renal cell carcinoma in four patients and angiomyolipoma in two patients; it was inconclusive in one case. Mean follow-up for 13.6 (4–22) months showed no evidence of residual tumor or recurrence.

Conclusions: Retroperitoneoscopy-assisted cryosurgical ablation using multiple ultrathin 1.5-mm cryoprobes is a minimally invasive treatment that is suitable to treat small renal tumors.

Keywords: Renal tumor; Nephron-sparing surgery; Laparoscopy; Retroperitoneoscopy; Cryotherapy

1. Introduction

The American Cancer Society reported an estimated number of 31,900 new cases and 11,900 deaths from kidney cancer for 2003 [1]. Historically, a large percentage of new renal cell carcinoma (RCC) cases already had metastases at initial diagnosis. However, contemporary series show increased early detection of renal tumors primarily as a result of the widespread use of ultrasound, computed tomography (CT) scanning and magnetic resonance imaging, [2]. Traditionally, renal cancer was controlled surgically by radical nephrectomy. In the meantime, early diagnosis of incidentally discovered small renal masses is becoming more frequent. Surgical treatment of renal tumors has also become more refined.

Nephron-sparing surgery was initially developed for patients with solitary kidney or compromised renal function. It has become the treatment of choice for renal tumor masses smaller than 4 cm, even in patients with normal contralateral kidneys. Long-term cancer control and maintenance of renal function after partial nephrectomy has yielded results comparable to those obtained with radical nephrectomy [3]. Numerous nephron-sparing procedures are available now, includ-

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ing open partial nephrectomy, laparoscopic partial nephrectomy, and a variety of needle or non-invasive techniques for tissue ablation such as cryotherapy, radiofrequency ablation, high intensity focused ultrasound, interstitial laser therapy, and microwave therapy.

Laparoscopic cryoablation has recently been proposed as a minimally invasive nephron-sparing treatment for selected patients with small renal tumors [4]. We report for the first time on the combined use of a retroperitoneoscopic approach and cryotherapy with multiple ultrathin cryoprobes.

2. Materials and methods

2.1. Patient characteristics

Since July 2002, a retroperitoneoscopy-assisted cryoablation has been performed in seven patients with a solid renal tumor without radiological evidence for involvement of the collecting system. All patients gave their informed consent. By CT scan, seven patients were diagnosed as having a solid renal tumor mass (Table 1). Cryoablation was considered to be indicated if the renal lesion had progressed in size compared to previous CT scans, reflecting a suspicion of malignancy. Mean tumor size on the preoperative CT scan was 2.6 (1.5–3.5) cm; none of the tumor masses had extended to the collecting system of the kidney. Three tumors were located on the posterior surface of the kidney, three on the ventral surface, and one was located laterally. Preoperative serum creatinine was 78 (46–122) μmol/l and preoperative hemoglobin 15.2 (14.7–16.7) g/dl. In view of the risk entailed in anesthesia, two patients were considered to be ASA class 1, three subjects ASA class 2, and two patients ASA class 3.

2.2. Surgical technique

All operations were performed with patients under general anesthesia in an overextended flank position. The first incision was made 1 cm below the 12th rib, just above the horizontal lateral line of the erector spinae muscle. The skin and the aponeurosis of the transverse muscle of the abdomen were incised and the retroperitoneal space was reached. An initial small retroperitoneal space to place the dilating balloon was created by finger dissection of the pararenal fatty tissue from the abdominal wall. We instilled 800–1200 ml of saline irrigant and bluntly dissected the retroperitoneal space. This port (10 mm) was used for the camera (25°). A 12-mm port was inserted 2 cm medially away from the anterior iliac spine and one 5-mm port in the middle of both ports under visual control. In obese patients, a fourth 5-mm port can be created at the tip of the 11th rib. The same port placement was employed for anterior and posterior renal tumors. Gerota's fascia was incised and the kidney was completely freed from perirenal fat. A biopsy of the tumor was routinely taken to establish a histological diagnosis. A rigid ultrasonography device was then inserted via the 12-mm port.

For cryoablation, we used the Galil Medical SeedNet™ system. The cryoneedles and the temperature probe were inserted percutaneously under endoscopic and sonographic control. A specially designed template grid was utilized to place cryoneedles circumferentially at the same depth around the central temperature needle. With the template resting on the skin, we placed six 1.5 mm cryoneedles equidistant from one another into the tumor (Fig. 1). We employed high-pressure liquid argon for freezing and helium gas for thawing. Cryolesions were induced with a core temperature of −175 °C to −190 °C at the tip of the cryoprobes. The temperature in the tumor as measured by the temperature probe reached −55 °C to −60 °C. The formation of the ice ball was monitored both visually and by sonography. The ice ball passed beyond the tumor edge by approximately 1 cm to ensure a safety margin (Fig. 2). A cycle included 10–15 minutes of freezing followed by about 10 minutes of thawing. After thawing for the second time, we checked the cryop-

Table 1
Patients characteristics

No.	Sex	Age (years)	Kidney side	Tumor characteristics on CT scanning: Size (cm)	Position	Location	Approach	Histology	Blood loss (ml)	Surgical time (min)	Admission length (days)	Last follow-up (months)	Last imaging finding
1	M	56	L	2.0	lower pole	anterior	retroperitoneal	not conclusive	100	160	5	22	no enhancement lesion shrinking
2[a]	F	75	L	3.0	lower pole	posterior	retroperioneal	angiomyolipoma	50	195	7	[a]	not done
3	M	70	R	3.0	upper pole	anterior	retroperitoneal	RCC grade 2	100	175	9	21	no enhancement lesion shrinking
4	M	49	R	2.5	upper pole	anterior	retroperitoneal	RCC grade 2	50	195	6	13	no enhancement
5	M	69	R	1.5	lower pole	posterior	retroperioneal	RCC grade 1	50	150	5	13	no enhancement
6	M	79	R	2.5	lower pole	posterior	retroperitoneal	RCC grade 2	150	130	7	9	no enhancement
7	F	53	L	3.5	upper pole	lateral	retroperitoneal	angiomyolipoma	250	120	5	4.	no enhancement
Mean		64.4		2.6					107	161	6.3	13.6	

No.: patient's number, M: male, F: female, L: left, R: right, RCC: renal cell carcinoma.
[a] Patient died of heart disease two months after surgery.

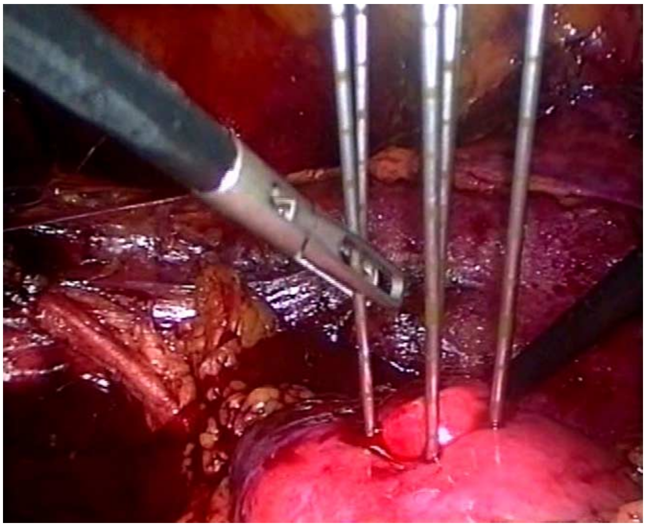

Fig. 1. Six 1.5 mm cryoneedles were placed circumferentially into the tumor around the temperature probe and equidistant from one another.

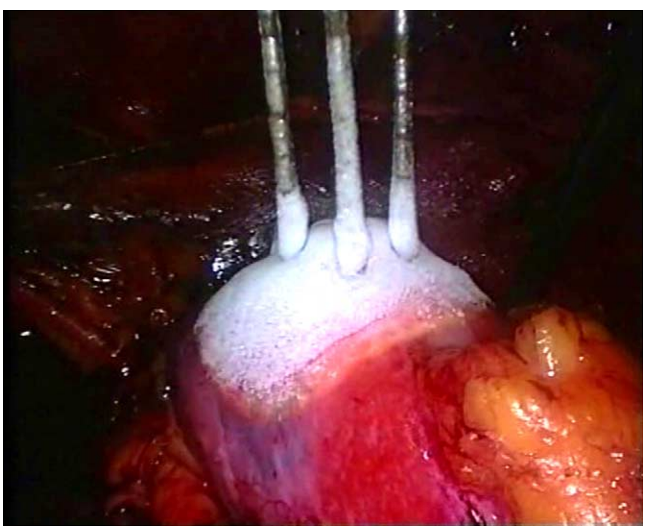

Fig. 2. The ice ball extending beyond the edge of the tumor edge by approximately 1 cm to ensure a safety margin.

robes and brought the hemostasis under control. Usually, no drain was inserted.

2.3. Follow-up

After discharge, follow-up visits were scheduled at three, six, and 12 months and on an annual basis thereafter. Follow-up comprised taking the history, physical examination, and spiral 5 mm slice CT or MRI scans of the abdomen with contrast-enhanced imaging. All patients underwent an additional clinical and sonographic check at the time this manuscript was in preparation.

3. Results

Cryoablation was technically successful in all patients and there was no need for conversion. Mean surgical time was 161 (130–195) minutes and the mean blood loss was 107 ml (50–250) (Table 2). Two patients with angiomyolipoma had minimal arterial bleeding from the tumor when the cryoprobes were pulled out, necessitating one intracorporeal stitch in each. Two patients presented postoperatively with a superficial skin frostbite, which healed with conservative treatment. We did not observe additional complications (particularly urinary fistulae or significant hematuria) and none of the patients needed blood transfusion. On the first postoperative day, the mean postoperative creatinine level was 109 (81–135) μmol/l and the mean hemoglobin level 13.0 (11.1–15.3) g/dl. Histological examination of the biopsy cores revealed clear-cell RCC in four patients, angiomyolipoma in two patients and was inconclusive in one case. Mean admission time was 6.3 (3–7) days.

One patient with known coronary heart disease died of myocardial infarction two months after surgery. Mean follow-up of the remaining patients was 13.6 (4–22) months. All subjects are in good health and without pain or disorder in the treated flank region. The superficial skin frostbites healed without problems.

Table 2
Comparison of various series of laparoscopic renal cryosurgery

References	Mean pt age (years)	No. pts	No. with tumor	Mean tumor size	No. ports	Approach	Mean op. time (min)	Type Freeze cycle	Mean follow-up (months)	Probe size (mm)	Blood loss (ml)	No. days postop. stay	Drain
Bishoff et al.	65.5	8	8	2.2	3 or 4	trans- or retroperitoneal	235	single or double	7.7	4.8[a]	88	3.1	yes
Gill et al.	65.4	32	20	2.3	3	trans- or retroperitoneal	174	double	16.2	4.8	67	1.8	no
Lee et al.	67.9	20	11	2.6	3	trans- or retroperitoneal	306	double	19.2	4.8	92	2.6	yes
Nadler et al.	68.5	15	10	2.1	4	trans- or retroperitoneal	260	14 double/1 triple	15.1	4.8	67	3.5	yes
Current study	64.4	7	4[b]	2.6	3 or 4	retroperitoneal	161	double	13.6	1.5	107	4.3	no

[a] Probe is 4.8 mm if tumor is larger than 2 cm and 3 mm if tumor is smaller than 2 cm.
[b] 1 patient with not conclusive histology, in this table considered as a "non-tumor".

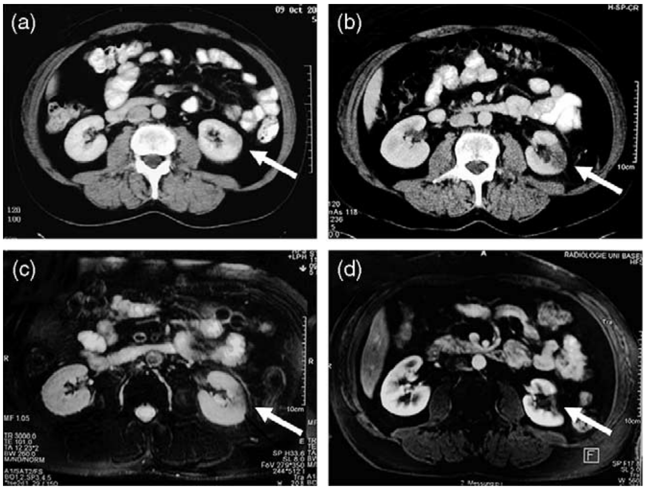

Fig. 3. (a–d) Preoperative CT appearance of a lower renal pole tumor (a). CT follow-up at 3 months shows no decrease of tumor size; however, there is no enlargement in the renal lesion (b). MRI follow-up at 12 months demonstrates a decrease of lesion site (c). Finally, a significant tissue defect is discernible at 18 months after cryoablation (d).

The last follow-up examination did not reveal evidence of residual tumor or recurrence in any patient. The renal lesions were shown to have decreased significantly in size (Fig. 3a–d) in CT/MRI scan after one year (patients #1 and #2).

4. Discussion

Of the energy based ablative treatments, cryoablation provides the most satisfactory results and remains the best-studied and clinically tested method for small RCC. Freezing creates cell death by formation of intracellular and extracellular ice crystals, which in turn creates a hyperosmolar environment. This environment causes cell dehydration and shrinkage, enzyme denaturation, and dysfunction of the cytoskeleton and membrane. Rapid freezing followed by gradual thawing, known as the double freeze-thaw cycle, is employed to maximize these effects [5]. A liquid nitrogen or liquid argon system is applied during the freeze part of the treatment cycle, while thawing is usually carried out with helium gas [6]. Experiments in a porcine model utilizing thermocouples indicate that a temperature of −19.4 °C must be attained to ensure complete tissue necrosis [7].

Cryoablation can be performed with an open, percutaneous or laparoscopic approach. Rukstalis et al. treated 29 patients (17 of them with RCC) using an open procedure to maximize mobilization and exposure of the kidney and to facilitate ultrasound monitoring [8]. At the three-month follow-up, 21 out of 23 patients checked had a complete resolution as evidenced by non-enhancement of the lesion [8]. The few reports on laparoscopic renal cryoablation have mainly been published by Gill and coworkers [4,9,10]. This group approached anterior tumors transperitoneally and approached posterior tumors retroperitoneally [9]. They reported no differences between the two approaches with regard to their side effects or outcome [9]. According to our experience, the retroperitoneoscopic approach enables a quick access to the renal surface in posteriorly located renal lesions because the kidney is fixed anterior-medially by the peritoneum. In anteriorly located renal lesions, the kidney is easily freed from the anterior-medially peritoneal fixation and the ventral surface is readily imaged.

In the Cleveland series, all cases evaluated had a negative histology at six-month follow-up [9]. In patients who underwent MRI after one year, the mean lesion size had continuously fallen with time [9]. Of 31 patients with follow-up over more than six months, 30 had a negative biopsy and one had contrast-enhancing lesions that were positive for cancer [10]. This data appears to confirm the oncological efficacy of cryotherapy, although a long-term follow-up is needed.

The mean size of the tumors treated in our series was comparable to or even greater than that reported in other series [9,11–13]. In our series, cryoablation was indicated in all small tumors (<4 cm) qualifying for tumor enucleation. We routinely perform a retroperitoneoscopic or open partial nephrectomy in tumors >4 cm with close proximity to the renal pelvis. We are convinced that even in small non-exophytic renal lesions cryoablation provides a suitable alternative to partial nephrectomy with a significantly lower perioperative morbidity. To obtain effective tumor control, the ice ball has to extend at least 10 mm beyond the tumor margin [9]. To be killed, cancer cells may need temperatures as low as −40 °C. It is therefore of utmost importance to position the cryoneedle correctly [14]. Accordingly, we employed up to seven ultrathin cryoprobes in contrast to just one probe in the other series. One probe is inserted in the middle of the tumor and the others are aligned near the macroscopic tumor margin and the sonographic contours of the tumor. Insertion and ice ball formation are imaged in real-time using endoscopic ultrasound. The lowest cumulative temperature reached and the hold time at subzero temperatures must be assumed to be closely linked to the number of cryoprobes employed and the number of freeze-thaw cycles. This is because the lowest temperature is reached at the probe (−175 °C to −190 °C). After freezing, the cells are primarily sublethal, secondary reperfusion injury during the thaw period ultimately results in cell death [7]. Besides the number of freeze-thaw cycles, the number of cryoprobes might therefore entail a benefit in terms of tumor destruction. To our knowledge, there is no clinical data available that compares the use of one or multiple cryoprobes for treatment of renal tumor masses. We found only one report on the application of multiple 1.5 mm ultrathin cryoprobes in an open procedure [15]. The imaging at three-month follow-up revealed shrunken nonviable tumor, suggesting that ultrathin probes are effective [15]. A possible drawback of using ultrathin cryoprobes could be the smaller ablation zone. In our limited experience, however, the application of multiple ultrathin cryoprobes was safe and did not compromise oncological results during our 13.6-month follow-up.

Potential tumor-cell spilling during minimally invasive surgical procedures is still under debate. However, examination of the published data shows that laparoscopic procedures are not associated either with increased tumor cell circulation or incidence of port side metastasis [16,17]. To the Authors' knowledge, there is no clinical report to date of tumor cell spilling after minimally invasive surgery of a small renal tumor. An intraoperative biopsy was taken prior to cryoablation in order to obtain an adequate histological diagnosis and to ensure an appropriate oncological follow-up. The core biopsy taken with a scissors was carefully harvested.

Reported complications are mainly associated with the laparoscopic-transperitoneal approach including superficial liver laceration due to trauma from a laparoscopic fan retractor or a postoperative ileus [9,12]. A pancreatic injury requiring surgical re-exploration has been reported after employing the retroperitoneal approach [13]. In contrast to conventional laparoscopy, retroperitoneoscopy is an even less minimally invasive approach that does not pass beyond the peritoneal cavity. Thus, typical complications associated with peritoneal dissection are avoided. In two of our patients with angiomyolipoma, minimal arterial bleeding from the tumor site after pulling out the cryoprobes could be managed easily by suturing. Two of our patients presented postoperatively with a superficial skin frostbite, which healed under conservative treatment. We conclude that the template block may have lacked sufficient insulation on the skin side. During the last four procedures, we therefore avoided direct contact between the template grid and skin which prevented this particular complication.

Percutaneous cryotherapy of renal lesions with magnetic resonance imaging (MRI) has been described as an even "more minimally" invasive treatment than laparoscopy for renal cryoablation. However, we have some concerns regarding the oncological efficacy of this procedure. Shingleton et al. employed an interventional MRI system to guide 2 or 3 mm cryoprobe placement and monitor the progress of the cryolesion [18]. In a cohort of 65 patients with an average follow-up of 18 months, 14% of the patients required repeat treatment [18]. Similar problems are reported by the same group employing MRI-guided cryoablation in patients with solitary kidneys [19]. Of the 14 patients treated with one to four 3.0 mm cryoprobes, two were lost to follow-up. At a mean follow-up of 17 months, the ablation was incomplete after one treatment in four out of 12 patients. In two of these four patients, the tumor was not completely ablated even after the second treatment [19]. We believe that a retroperitoneoscopy-assisted technique for placing the cryoneedles enables an excellent minimally invasive imaging of the kidney, including macroscopic tumor margins that cannot be identified with percutaneous ultrasound, MRT or CT management. Additionally, precise cryoneedle insertion and ice ball formation can be readily controlled by real-time endoscopic ultrasound. As seen in our series, back bleeding after cryoprobe removal can be easily managed, whereas this is not possible with percutaneous procedures. Nevertheless, partial nephrectomy and tumor enucleation have proved to be an effective alternative to the method we have presented [20]. However, taking into account the very much more elaborate technical procedure of endoscopic partial nephrectomy and the potential risk of bleeding, cryoablation seems to be just as efficient and was associated with less intraoperative risk for patients.

5. Conclusions

Cryosurgical ablation of small renal tumors with multiple ultrathin 1.5-mm cryoprobes is an attractive alternative to tumor enucleation with a low rate of intraoperative complications. The minimally invasive retroperitoneoscopy-assisted approach enables optimal imaging of the kidney and endoscopic real-time sonographic control of the tumor freezing-thaw cycles. The use of multiple cryoprobes may improve tumor control. However, long-term oncological data must be obtained to corroborate and verify our experience with this procedure.

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