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Cryoablation for recurrent renal tumors after primary nephron-sparing surgery using an innovative liquid nitrogen-based cryogenic device

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The growing use and improvement of imaging modalities has resulted in increased detection of renal tumors. The gold standard treatment of small renal masses is nephron-sparing surgery. Such surgical intervention is associated with significant rate of local failure. The currently accepted treatment for local failure after nephron-sparing surgery is radical nephrectomy which is associated with very high complication rate as well as loss of functional renal parenchyma. The aim of the current study was to evaluate the safety, technical feasibility, oncologic success and functional preservation of percutaneous cryoablation using a new liquid nitrogen-based cryogenic device in patients with tumor recurrence after nephron-sparing surgery. We present seven patients with tumor recurrence after nephron-sparing surgery who underwent percutaneous cryoablation using ProSense™ (IceCure Medical Ltd, Caesarea, Israel) under computerized tomography guidance. None of the treated tumor lesions demonstrated contrast enhancement or growth on follow up imaging indicating a 100% oncologic success. Only three adverse events were recorded, all were classified as low grade and resolved spontaneously. In conclusion, percutaneous cryoablation using the novel ProSense™ device for recurrent renal tumors following nephron-sparing surgery is feasible and effective, with excellent renal function preservation and without major complications.

Keywords

Renal tumor; percutaneous cryoablation; liquid nitrogen; nephron-sparing surgery

1. Introduction

The growing use and improvement of imaging modalities has exacerbated the finding of incidental renal masses and improved renal cancer detection [1, 2]. This allowed surgeons to identify lesions at earlier stages of development and consider less invasive treatments. Treatment options for renal tumors include surgical or more conservative approaches. Surgical treatments may include radical nephrectomy or nephron-sparing surgery (NSS), either open or minimally invasive approaches. Less invasive approaches may contain ablative procedures or even active surveillance, depending on the tumor stage [3]. Small renal masses (SRMs) are defined as masses smaller or equal to 4 cm in diameter, and the current gold standard treatment for those masses is NSS [4, 5]. The increased use of this surgical procedures resulted in higher rates of local failure [6, 7]. Currently the accepted treatment for local recurrence after NSS is radical nephrectomy by either open or minimally invasive approach [8, 9]. Such salvage procedures are associated with a very high complication rate as well as loss of functional renal parenchyma [5, 10]. The risk of renal function impairment increases significantly in the presence of medical factors such as age, hypertension, and diabetes mellitus [11]. Cryoablation (CA) represents an alternative approach for treating renal neoplasms, with minimum impact on renal function, excellent functional outcomes and low complication rates [12]. It is important to establish the role of CA in recurrent kidney tumors following NSS.

The aim of the current report was to evaluate the safety, efficacy, and early oncologic outcomes of CA using a new liquid nitrogen-based cryogenic device in patients with recurrent renal cell carcinoma (RCC) lesions after NSS.

2. Patients and Methods

2.1 Patients

The study group included seven patients with tumor recurrence after NSS. The diagnosis was based on a cross sectional imaging (CT or MRI) which demonstrated enhanced solid mass in the kidney. In addition, renal mass biopsy was performed either before or during the procedure. An interventional radiology team performed percutaneous CA in patients under sedation using ProSense™ (IceCure Medical Ltd, Caesarea, Israel) under CT guidance. Two cycles of freezing with intervening passive thaw were applied.

Table 1. Clinical and pathological characteristics of the treated patients

Variable		*Proportion*
Gender: Males/Female (%)		4 (57%) / 3 (43%)
Mean age (years)		63 ± 15.28
Side (R/L)		0/7
Median duration from NSS (months)		60
Mean lesion size (mm)		21 ± 6.07
Mean R.E.N.A.L score		7.42 ± 2.25
Mean follow up time (months)		20.28 ± 16.13
Pathology	Clear Cell RCC	57%
	Papillary type I	14%
	Chromopohobe	28%

2.2 The cryosurgical system

The Prosense Cryosurgical system® uses liquid nitrogen as a cryogen, which reaches temperatures as low as -196ºC. This cryosurgical system utilizes the cryogen under low pressure that causes the cryoprobe to reach a very low temperature, thereby freezing the malignant tissue, which causes irreversible membrane damage and cell death [13]. The cryoprobe achieves rapid freezing by means of an active freeze zone at its distal tip and a warm regulated zone proximal to the freeze zone area, hence preventing undesired freezing along the cryoprobe shaft [14]. The killing of the tumor cells results from the direct i.e. intracellular ice formation and osmotic dehydration as well as indirect damage namely ischemia [15]. The killing of tumor cells is also suggested to have an immunologic response which is still a subject of further investigation.

The endothelial cells of the microvasculature are also damaged through the direct injury mechanisms, resulting in vascular stasis. In the hours and days following the CA procedure, ischemic damage occurs throughout the previously frozen volume which results in uniform necrosis; this necrotic tissue disappears over time. The main advantages of the new cryotherapy system include lower procedure temperatures with better safety profile due to lower working pressure. Lower cryotherapy temperatures are assumed to be more effective in treating SRM. Using liquid nitrogen allows a lower cost procedure. By modulating the temperature in a freeze-thaw-freeze pattern, the cryoprobe produces an ice ball, which, if it spreads 1 to 5 mm beyond the tissue margin, it will ensure that cytocidal temperatures are reached throughout the tumor lesion.

2.3 Follow-up protocol

Follow up protocol included outpatient clinic visits every 3 months during the first year, and annually thereafter. Follow up includes clinical evaluation, laboratory analysis (CBC, renal and liver function tests as well as urinalysis) and imaging: US at first follow up visit, CT/MRI at second visit. Additional imaging according to physician decision, at least annually with CT/MRI and chest X-Ray.

2.4 Endpoints

The study endpoints included the following: Safety (number and severity of adverse events), technical feasibility (localization of the cryoprobe, in the lesion and visualization of ice ball with a diameter larger than the tumor), oncologic success (was indicated by a reduction in tumor lesion size and absence of enhancement on imaging) and functional preservation (extent of serum creatinine decrease after the CA procedure).

3. Results

The study group included seven patients with renal tumor recurrence after NSS. There were 4 (57%) males and 3 females (43%) with a mean age of 63 years, mean lesion size of 21.00 ± 6.07 mm, mean R.E.N.A.L score of 7.42 ± 2.25 and mean follow up time of 20.28 ± 16.13 months. None of the treated lesions demonstrated contrast enhancement or growth on follow up imaging indicating 100% oncologic success. Only three adverse events (AE) were recorded: one patient had small perinephric hematoma and two patients experienced transient macroscopic hematuria. These AEs were classified as low grade side effects and resolved spontaneously. The average decreases in serum hemoglobin and serum creatinine were 0.14 ± 0.10 gr/dL and 0.04 ± 0.01 mg/dL, respectively. Regarding the CA process, the overall mean procedure time was 49 min, of which the mean duration of the freezing cycles was 23 min. The average diameter of the ice ball was 32.7 mm, being significantly larger than the mean size of the tumors (Tables 1-3).

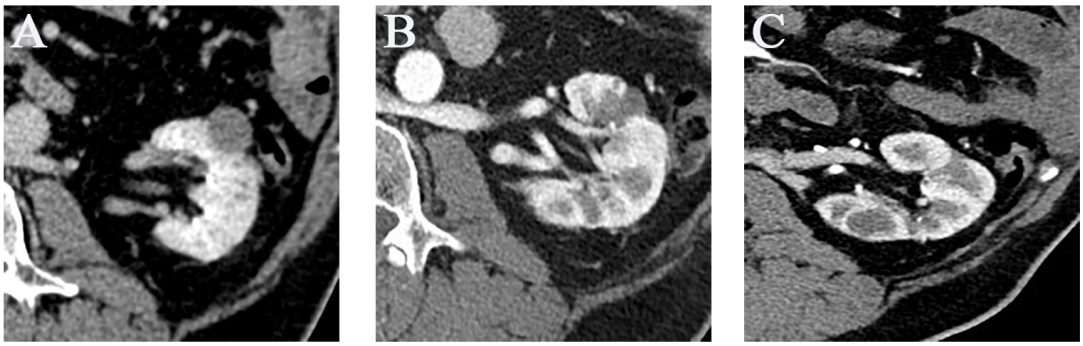

Figure 1. CT images of renal tumor recurrence after NSS, treated with cryoablation. A – Baseline CT demonstrating local recurrence tumor in the left kidney, B – Follow-up study 22 months after the procedure, C – Follow-up study 37 months post procedure, demonstrating gradual disappearance of the tumor.

Table 2. Detailed description of the patients treated by Cryoablation

	Age (years)	Time since NSS (months)	Lesion size (mm)	Tumor location	Renal score	Follow up duration (months)	enhancement	Lesion size decrese	success
case 1	65	468	22	Cortical (anterlolaterla)	4	42	−	+	+
case 2	70	60	24	Intraparenchymal (middle)	9	48	−	+	+
case 3	78	12	31	Cortical (upper pole)	10	16	−	+	+
case 4	36	120	11	Cortical (lower pole)	6	13	−	+	+
case 5	80	48	17	Hillary	10	10	−	+	+
case 6	45	17	17	Cortical (lower pole)	8	10	−	+	+
case 7	67	123	25	Cortical (upper pole)	5	3	−	+	+

Table 3. Results of renal mass cryoablation procedure

Variable		*Proportion*
Mean duration of procedure time (min)		49 ± 7.06
Mean duration of cryoablation cycles (min)		23 ± 5.87
Mean ice ball size (mm)		32.7 ±0.95
Mean decrease in serum Hemoglobin level g/dL		0.14 ± 0.10
Mean decrease in serum Creatinine level mg/dL		0.04 ± 0.01
Procedure related complications	Small perinephric hematoma (%)	1 (14%)
	Hematuria (%)	2 (28%)

4. Discussion

Currently, at the time of diagnosis of renal cancer, nearly half of the patients harbor tumor lesions smaller than 4.0 cm in diameter (Stage T1a) [2]. Hence today, NSS is the standard treatment for these tumors. Such surgical intervention may result in tumor bed recurrence. The currently accepted approach for local failure after NSS is radical nephrectomy [8, 9]. This challenging procedure is associated with high complication rate and loss of renal function16. Herein we presented our preliminary experience with a new conservative approach which is based on a novel cryogenic device. This novel device is based on liquid nitrogen as a cryogenic liquid for tumor CA. In the current report, we demonstrate that this CA procedure is technically feasible, safe, enabling maximal renal function preservation with adequate oncologic outcome. Fig. 1 demonstrates CT images of renal tumor recurrence after NSS, treated with CA. Follow up of 37 months post procedure with gradual disappearance of the tumor. These results are more favorable compared to partial or radical nephrectomy using either open or minimally invasive approaches [8]. Completion nephrectomy for true locoregional recurrence might be a technically demanding procedure associated with significant postoperative morbidity and a high rate of open conversion. Shah et al., recently summarized their experience with 45 patients displaying tumor recurrence after NSS. Of those managed by laparoscopy, 48.5% had complications and 36% were converted to open nephrectomy [8]. A similar rate of complications was also reported by Boris et al., [16]. These unfavorable results emphasize the need for an alternative approach in such a situation.

Our current study has some limitations including: a) a relatively short oncologic follow up time, b) it is a single center experience, c) the study group is small, and d) there is no randomized prospective comparison with other treatment approaches.

In conclusion, we reported the use of a novel cryogenic device, percutaneous CA, for recurrent renal tumors following NSS and conclude that it is oncologically effective with excellent preservation of renal function in the absence of major complications. Longer follow up time and a larger group of patients are required before defining the role of this procedure for the management of local failure after NSS.

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Conflict of Interest

The authors declare no competing interests.

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