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Original Research Article

Outcomes of cryoablation for small renal masses: a single-institution study

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ABSTRACT

Background: The current study reports the clinical outcomes of the efficacy of computerized tomography (CT) guided cryoablation (CA) in the treatment of patients with small renal masses.
Methods: This retrospective single institution study analyses the clinical outcomes of 36 renal tumours that were managed with cryoablation. Patient age, sex, tumour size, complications and recurrences were recorded. These patients were followed up at 3,6- and 12-months interval, they underwent biopsy and abdominal contrast enhanced ultrasound (CEUS) depending upon indications.
Results: 36 patients (63.9% male, 19.4% female) each with a single small renal mass had CA with a follow-up at 3, 6 and 12 months. The mean tumour size was 606.9±31.8 mm^2. Eleven complications occurred in 36 patients, for an overall complication rate of 30.6%. One (2.7%) patient had enhancement at the surgical bed on initial imaging and were considered incomplete ablations. None of the patients showed signs of distant metastases at the 3, 6 and 12-month follow-ups.
Conclusions: Cryoablation of renal masses results in acceptable oncologic efficacy with an acceptable number of complications. Therefore, it remains a viable treatment for renal masses.

Keywords: Cryoablation, Small renal masses, Renal tumours, Cryosurgery

INTRODUCTION

The incidence of renal cell cancer has increased worldwide to around 208,500, which is 2% of all cancers, with a higher incidence in more developed countries.[1] Frank et al found that around 25% of solid kidney tumours are benign, however renal impairment can occur on background of these tumours.[2] Use of imaging modalities such as ultrasound scan (USS), computed tomography (CT) and magnetic resonance imaging (MRI) has led to an increasing number of annually reported cases of renal tumours.[3] The greater risk of end-stage renal disease (ESRD) after radial nephrectomy compared to partial nephrectomy has encouraged the growth of elective nephron-sparing surgery.[4] Minimally invasive nephrectomy methods, such as laparoscopic procedures, cause less postoperative pain and rapid recovery but is associated with more complications than open partial nephrectomy.[5] Cryoablation (CA), microwave ablation (MA), and radiofrequency ablation (RFA) are commonly used methods and have become alternatives to partial nephrectomy. According to Olweny, RFA is the recommended ablative method for renal cell CA, reporting better clinical outcomes than partial nephrectomy.[6] Zondervan et al published a meta-analysis to compare clinical outcomes with CA and RFA; surprisingly, he did

not find any difference among the two treatment groups in terms of clinical efficacy and long-term outcomes. However, the literature lacks large-scale randomised controlled trial (RCTs).[8]

Long-term data has become available regarding the well-known and widely used thermal ablation (TA) technologies; further testing is in progress for these technologies, such as the use of microwaves, irreversible electroporation and high-intensity focal ultrasound. Atwell et al reported encouraging results for a single patient managed with cryoablation; they found the outcomes to be similar to surgical resection for small renal cancers as large as 4 cm.[9] Image-guided percutaneous cryoablation (PCA) offers the latest in nephron-sparing surgery; it has been made possible due to the advent of finer probes and advances in image guidance such as CT scans, ultrasounds and MR imaging. Weld et al reported a primary efficacy rate of 80–100% and a secondary efficacy rate near 100% with the use of cryoablation.[10]

Downsides include technical difficulties and risk of injury to adjacent organs. Conversely, advantages include fewer complications, early recovery and better visualization in real-time with CT and MR imaging.[11]

Extirpative surgery, nephrectomy and partial nephrectomy are considered the gold standard treatment for renal masses; however, it is still a topic of debate, as short-term studies support cryoablation of renal masses as a surgical modality with acceptable oncologic control and morbidity, whereas long-term studies are in favour of nephrectomy.[12,13] The main objective of this study was to present the clinical outcomes and safety of image-guided percutaneous cryoablation for renal masses.

METHODS

This four-year retrospective study which was conducted in the urology department of a tertiary care hospital Kings College Hospital. We retrospectively reviewed patients treated from October 2012 to October 2016. This study was registered and approved by ethical review board. We used cancer tumour registries to identify adult patients undergoing cryoablation for renal cell carcinoma. We only include percutaneous approach in our study. Metastatic renal cell carcinoma or genetical disorders predisposed to renal tumour were excluded. Patients with less than three months of follow-up were excluded from the analysis. Histopathological analysis was performed after taking the core biopsy of the tumours. The number and size of probes vary from patient to patient and depend on individual tumour characteristics. Real-time ultrasonic visualization is used to ensure that the ice ball extends approximately 100 mm beyond the visualized tumour margin. Contrast-enhanced imaging was obtained at three, six- and 12-months post operatively. Recurrence was defined as an area of new contrast enhancement in a completely treated ablation site that appeared three months or more after treatment. Preoperative estimated glomerular filtration rate (eGFR) was calculated with a serum creatinine value obtained within 25 days prior to ablation. Contrast enhancing lesions in the ablation zone found at the first three-month scan were considered an incomplete treatment or early posttreatment changes rather than tumour recurrence. Imaging, laboratory evaluation and physical examination were used to identify metastatic spread. This descriptive analysis was used to report patient demographics, characteristics of tumours and perioperative variables.

RESULTS

The results are summarized in Tables 2 and 3. A total of 36 tumour patients were treated with PCA during the study period. Demographic data can be further reviewed in Table 1. There are 23 (63.88%) male and 13(36.22%) female patient in the present study. Baseline tumour characteristics are also shown in Table 1. The mean size of the tumours was 606.9 mm^2, whereas the largest diameter was 2.58 cm. Of the 36 tumours, 16 were classified as clear cell carcinoma, 2 (5.9%) papillary renal cell carcinoma and 1 (2.9%) as chromophobe carcinoma. Benign lesions included 8 (23.5%) cases of oncocytoma, whereas 2 (5.9%) lesions were unidentifiable and 2 (5.9%) were completely normal. Complications recorded after cryoablations included haemorrhage (6), skin/nerve damage (3) haematuria and renal in 1 patient.

Follow-up

Patients were reviewed at three-month intervals in the clinic, where a brief history and clinical examination were performed, along with blood tests. A repeat dual-phase renal CT or MRI imaging was conducted. We reviewed and tabulated the histopathological results of biopsies.

Table 1: Patient demographics and tumour characteristics.

Sample characteristics	Frequency (%)
Total patient	36
Male sex	23 (63.9)
History of renal cancer	7 (19.4)
Recurrence after cryoablation	9
Tumour characteristics	
Mean size (mm)	606.9 (+7-31.8)
Mean largest diameter	2.58 (±0.07)

Continued.

Sample characteristics	Frequency (%)
Number of lesions	
1 lesion	34 (97.1)
2 lesions	1 (2.9)
Biopsy results	
Normal	2 (5.9)
Interstitial chronic inflammation	3 (8.8)
Oncocytoma	8 (23.5)
Papillary renal cell adenoma	2 (5.9)
Clear cell renal cell carcinoma	16 (47.1)
Chromophobe carcinoma	1 (2.9)
Inconclusive	2 (5.9)
Solid/cystic mass	
Solid	19 (59.4)
Solid and cystic	19 (59.4)
Location	
Side	
Right	22 (62.9)
Left	13 (37.1)
Polar/interpolar	
Upper	12 (34.3)
Mid	1 (2.9)
Lower	11 (31.4)
Interpolar	11 (31.4)
Post/anterior	
Post	20 (58.8)
Anterior	3 (8.8)
Mid	11 (32.4)
Exophytic/central	
Exo	22 (62.9)
Endo	7 (20)
Exo/endo	6 (17.1)
Procedure details	
No. of probes used	
1 probe	22 (62.9)
2 probes	9 (25.7)
3 probes	4 (11.4)
No. of cycles	
1 cycle	29 (93.5)
2 cycles	1 (3.2)
3 cycles	1 (3.2)

Table 2: Complication after cryoablation procedure.

Complication after cryoablation procedure	Frequency (%)
Complications, per procedure	36/8 (22.2)
Haemorrhage (Hb)	36/11 (30.6)
Skin/nerve damage	6
Haematuria	3
Renal failure	1
Pneumothorax	1
Viscera injury	0
AV fistula	0
Wound infection	0
Complication after cryoablation procedures with complications	0

Table 3: 3, 6 and 12 months follow up.

Follow up	Frequency (%)
3 months follow up	27/36 (75)
No. of patient with 3 months follow up	1
No. with enhancement	1
No. of biopsies at the scar	1
No. of CEUS	0
No. of reported distant metastases	27/36 (75)
6 months follow up	
No. of patient with 6 months follow up	26/36 (72.2)
26/36 (72.2%)	1
No. with enhancement	0
No. of biopsies at the scar	0
No. of CEUS	0
No. of reported distant metastases	0
12 months follow up	
No. of patient with 12 months follow up 21/36 (58.3%)	21/36 (58.3)
No. with enhancement	0
No. of biopsies at the scar	0
No. of CEUS	1
No. of reported distant metastases	0

Three months

At three months, 27 (75%) patients had a follow-up. These patients underwent further investigation to determine the metastatic spread. Only 1 patient had biopsies for renal scar, which underwent However, there was no reported distant metastases.

Six and twelve months

Follow up at 6 and 12 months are recorded in Table 3. Twenty-six patients (72.2%) were followed up at six months. Only 1 patient underwent enhancement, whereas there were no signs of distant metastasis and renal scar. At twelve months follow-up, there were 21 (58.3%) patients reviewed at our out-patient clinics. We did not find any complications such as distant metastasis in followed up patient.

DISCUSSION

Complete surgical excision of renal masses with partial nephrectomy is a standard treatment; however, cryotherapy is also a reasonable surgical option for patients who are required to undergo nephron-sparing surgery. Surgical resection is a standard provision of care for patients with localized renal cell cancer (RCC) due to favourable outcomes associated with surgery. Cryosurgery refers to tissue destruction using extremely cold temperatures. The complex mechanism of action involves direct cellular damage, extracellular damage and microvascular damage.[13] This can be done either laparoscopically or percutaneously, which is typically CT-guided. The laparoscopic technique includes transperitoneal or retroperitoneal approaches.

The purpose of this study is to analyse the outcomes of cryotherapy, as the literature lacks reports on the outcomes of this technique.

Gill and Cowerkers reported 51 patients undergoing cryotherapy with an average tumour size of 2.3 cm.[14] Similarly, another published cryoablation series of 31 patients with a follow-up period of three years reported a lower complication rate (9.8%) with a mean tumour size of 2.1 cm. The current study reports a series of 36 patients with a mean tumour size of 2.5 cm. The hallmark of successful renal cryoablation is to decrease lesion size with or without contrast enhancement on a CT scan or MRI. If enhancement or growth occurs, we advise biopsy and retreatment. In the current study, we performed extensive postoperative imaging to describe the impact of cryoablation lesions. As part of our study protocol, patients underwent contrast-enhanced CT or MRI at three, six and 12 months of CA. We proposed that initial post-operative imaging should be performed six months after cryoablation. Kyle et al recorded that one patient showed enhancement within the cryolesion during follow-up, suggesting tumour reoccurrence. The findings reported in the current study are similar; at the three- and six-month follow-ups, we also find one patient with enhancement.[15]

A literature review reveals that the majority of laparoscopic renal cryoablations have had patients with exophytic lesions; the current series include patients with endophytic, exophytic lesions and some combined exophytic/endophytic lesions dealt with the percutaneous approach.

Tsvivian et al reported that the average decrease in eGFR after a laparoscopic CA procedure was 4.2 and 8.8 mg/ml

among patients with chronic renal insufficiency and normal renal function, respectively.[16] With our percutaneous approach, we recorded the eGFR to decrease by 5.8 mg/ml; only one patient had acute kidney injury, which recovered through conservative management.

Kunkle and Uzzo found that cryoablation has a lower rate of reoccurrence; they also reported that development of metastatic disease has been as low as 1%.[17] The current study finds that no patients were reported to have distant metastases at the three-, six- and twelve-month follow-ups. Kunkle and his associate further reported in another meta-analysis that there was no difference in the development of metastatic disease between partial nephrectomy and a cryoablation procedure.[18] Cryoablation is a safe treatment option with acceptable morbidity for patients with renal masses. Lehman et al found the complication rates for percutaneous and laparoscopic procedures to range from 10% to 62%.[19] The present study reports the complication rate after percutaneous cryoablation to be up to 30.6%. Laguna et al reported a lower complication rate (15.5%) after undergoing cryoablation; additionally, all of the reported complications were minor, such as haematuria, renal failure and low haemoglobin.[20]

The present study is subject to the limitations of a retrospective analysis. Including operations performed by multiple surgeons can be considered both a weakness and a strength of the study due to differences in technique and a confounding variable which could affect the outcome. Furthermore, the study being limited to single centre makes it more prone to limitations. Despite the variations in practice, however, encouraging results have been recorded for patients undergoing cryotherapy that successfully prevents the development of metastatic disease or re-occurrence.

CONCLUSION

This study has reported clinical outcomes for patients undergoing primary cryoablation for the treatment of renal cell cancers. It can either be done with radiological guidance or laparoscopically. CA has a limited effect on kidney function and is therefore an effective option for patients with a solitary kidney or chronic kidney disease. Its therapeutic effect is clear from its low rate of reoccurrence or metastasis following the procedure. It is a minimally invasive technique with a very low rate of complications. Based on our findings, cryoablation is a preferable treatment option for small renal masses.

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