Original Article

Results of laparoscopic cryoablation in the treatment of small renal masses

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ABSTRACT

Context: Study of clinical outcome in renal cryoablation.

Aims: Laparoscopic cryoablation (LCA) is emerging as a reliable treatment option for small renal masses (SRMs) particularly in elderly patients. Our aim was to study the results of cryoablation for small renal masses in our cohort of patients.

Settings and Design: We retrospectively studied all patients who underwent LCA for SRMs between September 2005 and July 2008.

Materials and Methods: All patients were discussed in our multidisciplinary meeting prior to cryoablation. Our LCA protocol included two freeze-thaw cycles, achieving a core temperature of –70°C and a peripheral temperature of at least –40°C. Follow-up included serum creatinine measurements and pre- and postcontrast CT scans at 3, 6, 12, 18, and 24 months and yearly thereafter.

Statistical analysis used: Paired samples t-test was used to study statistical difference.

Results: Twenty-two patients underwent LCA with a mean (range) age of 68 (39–81 years) years. The mean (range) tumor size was 29 (19–45 mm) mm. Two patients required blood transfusions, one patient developed pneumonia, and another patient developed a small area of skin necrosis at the cryoneedle entry site. The average (range) hospital stay was 4 (2–14 days) days. Twenty-one patients have had CT follow-up at a mean (range) of 24 (4–42 months) months. Three of the 21 tumors showed central enhancement on follow-up CT scans, consistent with treatment failure.

Conclusions: Laparoscopic cryoablation is a safe treatment option for SRM in a selected group of patients.

Key words: Cryoablation, small renal mass, outcome

INTRODUCTION

Renal cell cancer (RCC) is the third most common urological cancer and accounted for 3777 deaths in 2006 and 7380 new cases in 2005 in the UK.[1] The incidence of renal cancer in the UK was 4.9 per 100,000 population (age-standardized) in 1975 and has risen to 9.7 per 100,000 in 2005.[1] A similar increase in the incidence of incidental small renal masses (SRMs) accounting for up to 60% of the renal tumor incidence has been reported in Europe and USA.[2-4] Much of this dramatic increase has in part been attributed to the advances in imaging techniques and the widespread use of ultrasound scans (USS).[4,5]

Although meta-analysis data are available on small series on the natural history of observed SRMs, their natural history is not fully understood.[6,7] Standard treatment for renal malignancy is surgical and survival following surgery is comparative to that of the normal population, especially with respect to renal tumors measuring less than 40 mm in size.[8] The gold standard treatment for SRMs is open partial nephrectomy; however, laparoscopic partial nephrectomy has recently been shown to provide comparable oncological outcome with the advantage of being minimally invasive.[9] The main drawback with laparoscopic partial nephrectomy is the requirement of high technical skill. Consequently, laparoscopic cryoablation (LCA) has emerged as an alternative minimally invasive nephron-sparing technique for SRMs.[10] Radiofrequency ablation for SRMs is another alternative, although poor radiological correlation and high failure rates (up to 32%) have been reported with RFA for SRMs.[11]

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MATERIALS AND METHODS

All patients who underwent LCA at our institution between September 2005 and July 2008 were retrospectively identified from our hospital database and case notes were reviewed. All enhancing SRMs identified during this study period had been discussed at our multidisciplinary meeting prior to LCA. Renal cryoablation was offered to patients with peripherally situated renal tumors less than 40 mm (occasionally less than 45 mm) in size, who were thought to be at higher risk for open partial nephrectomy or had expressed their preference for cryoablation. Patients under the age of 60 years were actively discouraged from undergoing renal cryoablation.

All procedures were performed by a single surgeon. Patients were placed in the lateral position as for a radical nephrectomy and the transperitoneal approach was used in all cases. Standard Hassan technique was used for primary port insertion and two further ports (10 and 5 mm) were utilized. Occasionally, a further 5-mm port was required for liver retraction in certain right-sided upper pole renal tumors. Tumor was exposed by adequate mobilization of the kidney, dissection of Gerota's fascia and peri-renal fat. The tumor extent was initially assessed by a consultant uroradiologist with laparoscopic ultrasound (Hitachi, EUB-5500 with a dedicated laparoscopic probe) after which Trucut® (18G) biopsies of the tumor were taken. The Seednet™ cryotherapy system (Galil Medical, UK Ltd.) was used for cryoablation. Cryoprobes (17G, Icerods®) were inserted under visual and ultrasound control, 10 mm apart from each other generating an adequate ice ball. The number of cryoprobes varied depending on the tumor size. Tumor core and tumor margin temperatures were monitored throughout the procedure using thermal probes (Galil Medical, UK Ltd.). We used two freeze-thaw cycles. The freezing cycle lasted 10 minutes achieving a core temperature of –70°C and a peripheral temperature of at least –40°C. Our protocol included 5 minutes of passive and 5 minutes of active thawing. The ice-ball was allowed to extend a minimum of 5 mm beyond the tumor margins and this was monitored visually and by real-time USS.

Our departmental follow-up protocol for post-LCA included pre- and postcontrast CT abdomen at 3, 6, 12, 18, and 24 months and yearly thereafter. Clinical examination and serum creatinine were routinely performed at each clinical visit. Paired samples *t*-test was used to study statistical difference between pre- and postoperative creatinine levels.

RESULTS

In the study period, 10 men and 12 women with an average (range) age of 68 (39–81 years) years underwent LCA. The mean (range) tumor size was 29 (19–45 mm) mm. Tumor sizes were larger than 40 mm in three patients measuring 42, 43, and 45 mm in 78-, 81-, and 77-year-old patients, respectively. The position of the 22 tumors was variable, including anterior (*n*=2), anterolateral (*n*=5), lateral (*n*=9), posterolateral (*n*=1), posterior (*n*=4), and medial (*n*=1).

The procedure was successfully completed laparoscopically in all patients in the study. The mean operating time (range) was 166 (90–224 minutes) minutes, the mean (range) number of cryoprobes used was five (3–6), and the mean blood loss was 50 ml. No intraoperative complications occurred. The mean (range) duration of hospital stay was 5 (2–14 days) days. Postoperative complications were graded according to modified Clavien classification.[12] There were three grade II complications (blood transfusions in two and pneumonia in one patient), one of the patients needing a blood transfusion subsequently underwent super selective renal vessel embolization (grade III), and another patient was noted to have a grade I complication (7 mm area of skin necrosis developed at the cryotherapy needle site which did not require any treatment).

The mean (range) number of biopsies taken was two (one to three) and the mean (range) total length of biopsy material obtained was 16 (1–34 mm) mm. Overall, adequate histological samples were obtained in 20 patients (91%), which included neoplasia in 17 patients and normal tissue in 3 patients. Necrotic tissue was obtained in one patient and in another patient biopsies were indeterminable on histological assessment [Table 1]. One of the patients confirmed to have an oncocytoma on histology and did not wish to have any CT follow-up. At a mean (range) follow-up of 24 (4–42 months) months, mean (range) tumor size was 23 (0–58 mm) mm on CT. Three tumors have shown complete dissolution at 7, 20, and 23 months, respectively [Figure 1]. Central enhancement was noted in three patients on follow-up CT scans. The preoperative tumor sizes of these enhancing tumors were 22, 38, and 40 mm and their time to appearance of enhancement on CT scan were 14, 6, and 3 months, respectively. One of these three patients also showed features of inferior vena cava

Table 1: Histopathological analysis of Trucut® biopsies of the SRMs prior to cryoablation and their size and central enhancement on follow-up CT scans

Diagnosis	Number (n=22)	Mean size (mm)	Central enhancement
Clear cell RCC	11	27.3	1
Papillary RCC	3	35	
Oncocytoma	2	35.5	
Transitional cell carcinoma	1	36	
Normal renal tissue	3	26.7	2
Necrotic tissue	1	32	
Indeterminable	1	23	

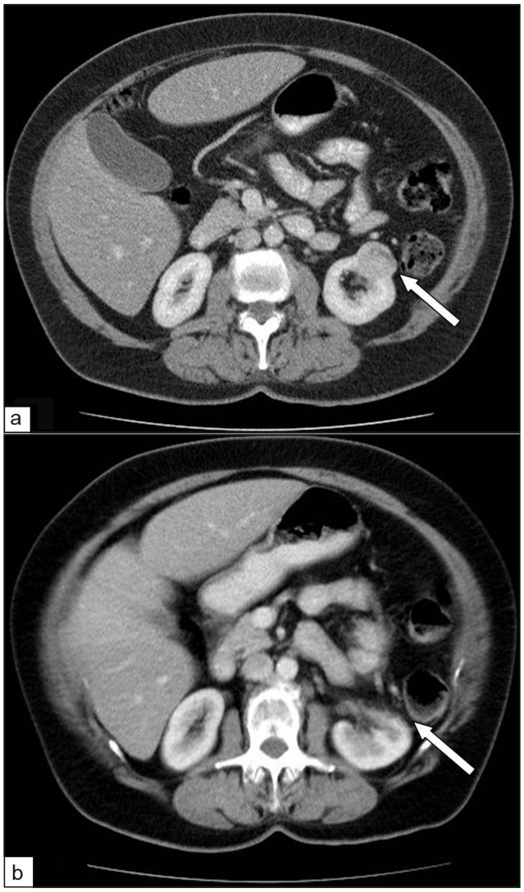

Figure 1: A small left renal mass is seen on a pre-LCA CT scan (a, white arrow). The post LCA CT scan of the same patient shows complete dissolution of the tumor at seven months following cryoablation (b).

thrombus with an increase in the tumor size by 20 mm on the 3 months follow-up CT scan was subsequently treated with open radical nephrectomy. Retrospective review of the precryoablation CT for this patient revealed that the tumor had actually invaded renal segmental veins, which would have precluded renal cryoablation as a treatment option. Another patient with central enhancement also underwent nephrectomy at 12 months. Histological assessment of these two nephrectomy specimens confirmed RCC. The third patient with central enhancement is being monitored as the patient did not wish to undergo an invasive surgical procedure.

Biopsy of the three tumors which were larger than 4 cm in size on precryoablation CT confirmed oncocytoma in one and clear cell RCC in the other two. None of these tumors showed progression in terms of size or enhancement characteristics on the follow up CT scans.

The mean (range) pre-operative serum creatinine level was 107 (68–167 μmol/L) μmol/L and the mean level at discharge was at 111 (75–197 μmol/L) μmol/L. The slightly raised postoperative creatinine was not statistically significant (paired samples t-test, $P > 0.2$).

DISCUSSION

SRMs form a distinct group of pathology where a number of treatment options are available that can be tailored to the individual patient. It is well understood that surgical extirpation of stage T1a renal tumors provides up to 97% 5-year cancer-specific survival rates.[13] Open partial nephrectomy has been established as the gold standard for the treatment of SRMs, although excellent 5-year cancer-specific survival has also been achieved by laparoscopic partial nephrectomy (LPN) in certain centers.[14,15] The main drawback with LPN is the demanding technical ability. The other drawbacks of LPN include higher morbidity and a possible impact on renal function secondary to warm ischemia.[16] The option of minimally invasive thermal ablation, such as LCA, in place of LPN could be utilized by all laparoscopic surgeons who are familiar with radical nephrectomy.[10] Furthermore, SRMs are often found in patients with significant comorbidities in whom LCA is often a suitable option. In the series by Gill *et al.*, the mean ASA score of the patients who underwent LCA was three, reiterating the value of minimally invasive surgery in this population.[17]

Gill *et al.*, first described renal cryoablation in a series of 32 patients demonstrating the feasibility of LCA.[10] More recently, the Cleveland group published their cryoablation series with a minimum of 5 years follow-up demonstrating a 5-year cancer disease specific survival rate of up to 92% and disease-free survival up to 81%.[18] Similarly, a promising recurrence-free survival rate of 97% has been quoted by Cestari *et al.*, in the short- term follow-up.[19]

In our institution, renal cryoablation has been offered to patients with peripherally situated renal tumors that are less than 40 mm in size and who are thought to be at higher risk for open partial nephrectomy or have expressed their preference for cryoablation. Considering the lack of long-term data, patients younger than 60 years were actively discouraged from undergoing renal cryoablation. LCA was only performed on two patients under the age of 60 years, one who was a diabetic and had expressed his preference to be considered for LCA and the other had Von-Hippel-Landau disease which necessitates maximum preservation of renal function. The three patients with tumor sizes greater than 40 mm were older than 75 years. All the alternative treatment options had been discussed both with the patients and at the multidisciplinary meeting and LCA was thought to be the safest option in these patients. Although Lehman *et al.*, have shown that LCA of larger tumors (> 30 mm) increases the risk of both operative complications and the recurrence rates, in our series the larger tumors (>40 mm) have not shown any progression at a mean of 22 months follow-up.[20]

In our series, a 18G Trucut® needle was used to biopsy the tumor under laparoscopic ultrasound guidance prior to cryoablation. An adequate histological sample was obtained in 20 patients (91%) from the biopsies taken immediately prior to LCA. Although a final, complete surgical specimen for pathological analysis could not be obtained due to the nature of cryoablation, reports from the literature have shown concordance rates of up to 100% between the histology of preoperative biopsies and the excised tumor.[21] The majority of SRMs in our study were confirmed to be RCCs; however, two SRMs were confirmed to be oncocytomas and one lesion a TCC. It has been reported that some oncocytic tumors identified on core biopsy prior to extirpative surgery can be associated with tumor heterogeneity and can harbor RCC.[22] Hence we applied the same follow-up protocol for RCCs as well as oncocytomas in this study. We recognize that TCC is an unusual diagnosis in a renal cryoablation series. The preoperative CT scan in this patient had shown a peripherally situated, well-circumscribed, enhancing tumor that measured 29 mm in maximum diameter, consistent with an RCC. Even on retrospective review, it was difficult to identify the tumor as a TCC.

In our series, three tumors demonstrated central enhancement on postcryoablation CT. The preoperative sizes of these tumors were 40 mm or less and the abnormal enhancement appeared on early CT follow-up (3–14 months). One of these three patients developed inferior vena cava thrombus with a 20-mm increase in tumor size on the follow-up CT scan; this patient was subsequently treated with open radical nephrectomy. In this case, retrospective review of the precryoablation CT revealed that the tumor had actually invaded renal segmental veins which would have precluded renal cryoablation as a treatment option. Although our LCA failure rate as demonstrated on CT follow-up is 14% (3/21) if we exclude the patient with segmental vein invasion who would not have been a suitable candidate for cryoablation, our failure rate of 10% (2/20) is comparable to other studies.[17,18] In addition, in a study of the longest available renal LCA follow-up (8 years), a local recurrence rate of 14% has been reported.[18]

The mean (range) postablation cryolesion size was 23 mm (0–58), which includes three tumors that have undergone complete dissolution. Furthermore, two lesions initially increased in size following LCA at 3 months but subsequent CT scans demonstrated that these lesions are decreasing in size but have not yet returned to their pre-LCA size. This is a recognized phenomenon as reported in other series.[17,19] In a series by Gill *et al*., the mean cryolesion size at day one post-LCA was 36 mm compared to the preoperative mean tumor size of 21 mm. The cryolesions subsequently returned to their preoperative size at a mean of 6 months.[17] Similarly, Cestari *et al*., demonstrated that following an initial increase in cryolesion size post-LCA, a 85% reduction in cryolesion size was achievable by 24 months post-LCA.[19] Interestingly, we had used five cryoprobes to achieve a peripheral tumoral temperature of at least –40°C in the two patients with cryolesions which initially increased in size post-LCA but are now slowly reducing in size. The number of cryoprobes used may have an influence on the post-LCA cryolesion size. The rationale behind using many cryoprobes was to ensure a wide margin (approximately 10 mm) of ice ball around the tumor.

The complications in our series include a case of serious bleeding requiring blood transfusion and another requiring embolization. We believe that these may have been caused by unnoticed movement of the cryoprobes during cryoablation. We have since ensured that the thermocouple and the cryoprobes are protected from movement during the freeze-thaw cycles.

The lack of significant deterioration in serum creatinine post-LCA is reassuring; however, we understand that a more formal measure of renal function in the form of glomerular filtration rate (GFR) would provide a more objective assessment of nephron loss secondary to cryoablation.

In our institution, we have reliably identified three recurrent tumors on CT follow-up, two of which were treated appropriately. If we exclude the patient with preoperative CT features of segmental vein invasion who would not have been a suitable candidate for cryoabation, our local recurrence rate is 10% (2/20). Apart from two bleeding-related complications and a postoperative pneumonia, we have observed that renal cryoablation is a safe procedure. Although size and enhancement characteristics on postcontrast CT scan are used as surrogate markers for recurrent/residual tumor, long-term follow-up studies are required to establish oncological outcome and also to consolidate the indications for renal cryoablation.

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