Management approaches to small renal tumours

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INTRODUCTION

RCC was diagnosed in ≈35 710 individuals in the USA in 2004; 40% of these patients will eventually die from the disease [1]. The incidence of RCC has increased over time [2]; since 1950 there has been a 126% increase in the incidence of RCC, accompanied by a 37% increase in annual mortality [1]. The increase in incidence can be partly explained by the detection of incidental tumours with the widespread use of noninvasive imaging methods.

Radical nephrectomy is the generally accepted surgical technique for treating renal tumours. Nephron-sparing surgery (NSS) was initially used for imperative implications, such as bilateral renal masses or tumour in a functionally or anatomically solitary kidney [3]. NSS has become standard for patients who would be functionally or anatomically anephric after radical nephrectomy. It is also considered mandatory in one or both kidneys in patients with bilateral renal tumours [3]. Presently, NSS is used in patients with a normal contralateral kidney, for smaller renal tumours.

The assurance that RCC does not require the entire kidney to be removed has led to the development of new technology and surgical approaches. The various nephron-sparing methods include open partial nephrectomy (OPN), simple enucleation, laparoscopic partial nephrectomy (LPN), cryoablation, microwave thermal ablation (MT), radiofrequency ablation (RFA) and high-intensity focused ultrasound (HIFU). We review these methods for solid, enhancing renal masses consistent with RCC, and excluding angiomyolipomas.

OPEN PARTIAL NEPHRECTOMY

Currently NSS is an established approach for patients with localized RCC whether or not there is a clinical indication to preserve renal function. OPN is the 'gold standard' for NSS; the wave of new minimally invasive technologies and techniques are compared to the standard created by OPN. The standard accepted indication for elective NSS is a single, localized RCC of <4 cm in diameter on imaging [4]. OPN offers efficacy, morbidity and mortality on a par with radical nephrectomy. The long-term cancer-specific survival of OPN is comparable with that of radical nephrectomy. In a review of nine studies, Novick [4] reported results of open NSS for RCC in 1262 patients; the mean cancer-specific survival for all patients undergoing OPN for localized RCC was 88–97.5%, with a mean follow-up of 5–6 years.

SIMPLE ENUCLEATION

Simple enucleation of small renal tumours, as elective NSS, offers maximum preservation of functional renal tissue and a lower incidence of major bleeding and collecting system damage, thereby theoretically decreasing the incidence of complications such as urinoma and urinary fistula [5]. Despite these advantages, simple enucleation is not widely used because of the questionable adequacy of the thin tumour margin.

In a retrospective analysis of 107 patients who had elective simple enucleation for T1a RCC, Lapini *et al.* [5] reported the incidence of local recurrence, and progression-free and disease-specific survival rates. The 5- and 10-year cancer-specific survival was 99% and 97.8%, respectively, and of progression-free survival was 98.1% and 94.7%, respectively. Two patients had local recurrence of disease and one had distant metastases. In these patients, the tumour was enucleated without excising normal parenchyma. The tissue plane between the pseudocapsule and normal parenchyma was developed with blunt dissection and scissors. Diathermy spray or argon beam coagulation was applied to the tumour bed, providing both haemostasis and a 1-mm margin for oncological control [5]. The authors concluded that simple enucleation is a safe and acceptable approach for elective NSS. Local recurrence rates were comparable with those after OPN.

LAPAROSCOPIC PARTIAL NEPHRECTOMY

Although OPN remains the standard form of NSS, the laparoscopic approach is quickly developing, with both new technology and surgical techniques. In the largest single institutional report of pure LPN, Gill *et al.* [6] reported perioperative outcomes on 100 patients, and compared these results to those from 100 patients who had OPN (Table 1). LPN was reported to have less blood loss and analgesic requirement, shorter hospital stay and convalescence; postoperative creatinin levels were comparable despite increased warm ischaemic time with LPN. Allaf *et al.* [7] recently reported the oncological follow-up of 48 patients treated for RCC with laparoscopic NSS. The mean follow-up was 37.7 months, the mean tumour size 2.4 cm, and the final pathological stage was pT1 in 42 patients (87.5%) and pT3a in six (12.5%). Intraoperative frozen-section biopsies revealed negative margins in all cases. The final surgical margins were positive in one patient (2.1%). The follow-up evaluation consisted of a physical examination and yearly cross-sectional imaging, which revealed no recurrences in 46 of 48 patients (96%). One patient with von Hippel-Lindau disease was found to have local recurrence 18 months after treatment. The second patient had recurrence in the same kidney, in a new location, ≈4 years later. It was concluded that laparoscopic NSS is an effective treatment for clinically localized RCC. Oncological outcomes at a mean follow-up of 3 years are promising, although long-term outcomes are necessary.

LAPAROSCOPIC CRYOABLATION

To date, laparoscopic cryoablation is one of the most studied minimally invasive approaches to the small renal tumour [8]. This

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TABLE 1 Perioperative outcome of laparoscopic vs OPN, from Gill et al. *[6]. All patients had sporadic solitary renal tumours of <7 cm*

Variable	LPN (N patients)	OPN (N patients)	P
Mean:			
Tumour size, cm	2.8 (100)	3.3 (100)	0.06
Operative duration, h	3.9 (98)	3 (100)	0.01
Blood loss, mL	125 (100)	250 (100)	<0.001
Warm ischaemia time, min	27.8 (95)	17.5 (92)	<0.001
Median:			
Analgesic required, mg*	20.2 (76)	252.2 (54)	<0.001
Hospital stay, days	2 (97)	5 (98)	<0.001
Convalescence, weeks	4 (66)	6 (62)	<0.001
Serum creatinine, mg/dL			
preoperative	1.0 (100)	1.0 (100)	0.52
postoperative	1.1 (100)	1.2 (100)	0.65
Positive surgical margins, n	3 (100)	0 (100)	0.02

**Morphine sulphate equivalent.*

method uses a liquid nitrogen-cooled cryoprobe to ablate normal and cancerous tissues at temperatures of −40 °C. The cryoprobe is monitored during surgery by the laparoscopic camera and by ultrasonography. A dual freeze-thaw cycle is used. Histological pathology to assure complete tumour destruction is not possible with this method but biopsy offers tissue sampling at lesion borders and may or may not provide an adequate assessment of lesion margins.

Gill *et al.* [8] recently published the 3-year results for 56 patients undergoing laparoscopic renal cryoablation. At 3 years, cryolesions were ≈75% smaller and 17 lesions (38%) completely disappeared. Postoperative needle biopsy identified local recurrence/residual tumour in two patients. The cancer-specific survival in 51 patients who had a unilateral sporadic renal tumour was 98%. These results are encouraging but 5-year data are necessary to further define the role of cryosurgery as an option in NSS for RCC.

RADIO FREQUENCY ABLATION

RFA is another NSS approach to the small renal mass. A needle, through open, laparoscopic or percutaneous technique, is introduced into the lesion. High-frequency electrical current is delivered, through needle electrodes, to the cancerous tissue and returns to the generator through a return pad on the patient. The exposed tissue undergoes cellular protein denaturation and membrane disintegration [9]. RF energy delivered to tissues, in the absence of a saline infusion, is referred to as dry RFA. With dry RFA, rapidly increasing temperatures lead to tissue desiccation and charring, which increases tissue impedance, thereby interfering with the transfer of energy through the tissue. This limits the effective range of the RF probe. To expand the range of the probe and make it possible to treat larger tumours, the electrodes may be cooled with saline infused to the treatment tip, decreasing tissue desiccation [9].

Treatment probes are placed under ultrasonographic or CT guidance. Intraoperative imaging is complicated by RF interference and microbubble formation at the lesion. CT and MRI offer hope in improving the assessment of the lesion immediately after the procedure.

Table 2 [10–15] presents data from six studies reporting outcomes with RFA. As with other novel therapies for the small renal mass, RFA will require larger studies to show equivalent efficacy and decreased morbidity than for OPN. Furthermore, delivery of RF energy, including the method used, number of probes and duration of treatment, need further study to produce uniform results [9].

MICROWAVE THERMAL ABLATION

MT is a promising minimally invasive nephron-sparing method because the microwave tissue coagulator is useful in controlling parenchymal bleeding in solid vascular organs such as liver and spleen [16]. This feature of MT is also useful in both OPN and LPN [17].

Terai *et al.* [17] recently evaluated laparoscopic MT for small renal tumours without renal pedicle clamping. Results were reported from 19 patients, with renal tumours of 1.1–4.5 cm. The mean operative duration was 240 min, with minimal blood loss in 14 patients, and 100–400 mL in four. One case was converted to an open secondary procedure because there were perirenal adhesions. Complications included urine leakage, arteriovenous fistula and almost total loss of renal function. A median follow-up of 19 months was reported, with no patients showing local recurrence or metastasis by CT.

HIFU

HIFU is the least invasive of the tumour ablation methods, the goal of which is 'contact-less' destruction of a defined part of an organ by extracorporeally applied energy. This is achieved by targeting ultrasound energy to a focus within the body. The energy induces 'well-defined thermonecrosis.' [18]. Although HIFU has been used at other anatomical sites for >50 years, its application to the treatment of renal tumours is still experimental. The kidney is imaged well by ultrasonography, but it also has characteristics that make it challenging for therapeutic ultrasound applications. Because the kidney moves during breathing, tumour imaging can be difficult. Also, the overlying ribs absorb HIFU energy and can make certain tumours difficult to ablate.

Kohrmann *et al.* [18] reported the results of HIFU application to three renal tumours, in three sessions, followed by clinical examination and MRI over the following 6 months. Within 17 and 48 days, MRI indicated necrosis in the two lower pole tumours. One tumour, in the upper pole, was inadequately treated by HIFU. The position of the tumour, in relation to the overlying ribs, made it difficult to deliver the ultrasound energy to the target area.

Determining successful tumour ablation and appropriate follow-up are challenges with

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TABLE 2 Percutaneous RFA: initial outcomes

Study	N tumours	Mean tumour size, cm	Complete tumour ablation, n/N (%)	Mean follow-up, months	Complications
Mc Dougal *et al.* [10]	20	3.2	19/20 (95) with 1 session	55.2	1 perinephric haematoma.
Merkle *et al.* [11]	18	5.3 cm^2	16/18 (89)	16.1	Information not available
Gervais *et al.* [12]	42	3.2	36/42 (86)	13.2	1 minor haemorrhage, 2 major haemorrhages +1 ureteric stricture
Su *et al.* [13]	35	2.2	33/35 (94); 2 patients required re-treatment for residual enhancement on follow-up CT	9	Burn injury to liver. Resolved w/o furthers sequelae. Small asymptomatic perirenal haematomas identified in 8 patients by CT immediately after RFA; none required blood transfusion.
Pavlovich *et al.* [14]	24	2.4	24/24	2	No major complications.
Ogan *et al.* [15]	13	2.4	12/13; 1 tumour with persistent enhancing rim on CT	4.9	No major complications. One patient developed small perinephric haematoma that resolved w/o intervention

TABLE 3 Guidelines for surveillance of localized RCC after partial nephrectomy. Adapted from Evans [20].

Pathological stage	Guidelines for surveillance
pT1–2 N0M0	Annual history, physical, systems review, chest radiograph, chem-20, complete blood count and urine analysis. Abdominal CT or renal ultrasonography every 2 years.
pT3N0M0	History, physical, systems review, chest radiograph, chem-20, complete blood count and urine analysis every 6 months for 2 years, then every 2 years. Abdominal CT or renal ultrasonography every 6 months for 2 years, then every 2 years.

HIFU; this method provides no tissue for pathological staging and grading. Another feature of the noninvasive nature of HIFU is its reliance on intraoperative imaging to monitor tumour ablation. Ultrasonography, the current method in use, is limited in its resolution and two-dimensional imaging. Duplex Doppler ultrasonography, CT and MRI are other methods currently under development for this application.

HIFU offers a minimal procedure time, morbidity and time to full recovery. However, if HIFU is to gain acceptance as a standard approach, then equivalent efficacy, compared with OPN needs to be confirmed. Visualization of the kidney/lesion, control of lesion size, complete ablation of the tumour and reduction in side-effects are problems with HIFU that need to be addressed [18].

FOLLOW-UP

NSS allows for excision of cancerous tissue while preserving functional renal tissue, thereby leaving the patient with maximum renal function. The preservation of functional tissue carries with it the theoretical risk of leaving cancerous tissue behind. The local tumour recurrence rates after partial nephrectomy for pathological stages T1, T2, T3a and T3bN0M0 were reported to be 0%, 2%, 8.3% and 10.6%, respectively, and the respective metastatic tumour recurrence rates were 4.4%, 5.3%, 11.5% and 14.9%, respectively [19]. Reasonable surveillance guidelines are essential so that patients with a favourable prognosis avoid bothersome, expensive and unnecessary testing, while those at high risk of recurrence may be followed more closely. Table 3 [20] presents guidelines for the surveillance of localized RCC after partial nephrectomy.

Among nephron-sparing methods only OPN, simple enucleation and LPN allow the tumour to be excised with margins that can be clearly reviewed by a pathologist. Laparoscopic cryoablation, RFA, laparoscopic MT and HIFU either provide tissue with ablated margins or provide no tissue. CT, MRI and ultrasonography are used for the follow-up and the lack of enhancement or growth would suggest that the tumour is successfully ablated. Newer data suggest that MRI is more sensitive, but there is as yet no direct trial that compares these two methods in the patient who has had NSS and requires surveillance for recurrence.

Hallscheidt *et al.* [21] reported that MRI and multidetector-row CT achieve similar accuracy in tumour staging of RCC when compared to histopathological staging after surgery. In a prospective study, 82 RCCs were assessed for tumour staging before surgery with CT and MRI. The results were then correlated with histopathological findings after surgery. Overall, the accuracy for CT was 80–83% and for MRI was 78–87%. Suspicious imaging can be validated with a tissue biopsy, which may or may not provide more information.

CONCLUSION

Partial nephrectomy, open or laparoscopic, remains the generally accepted standard

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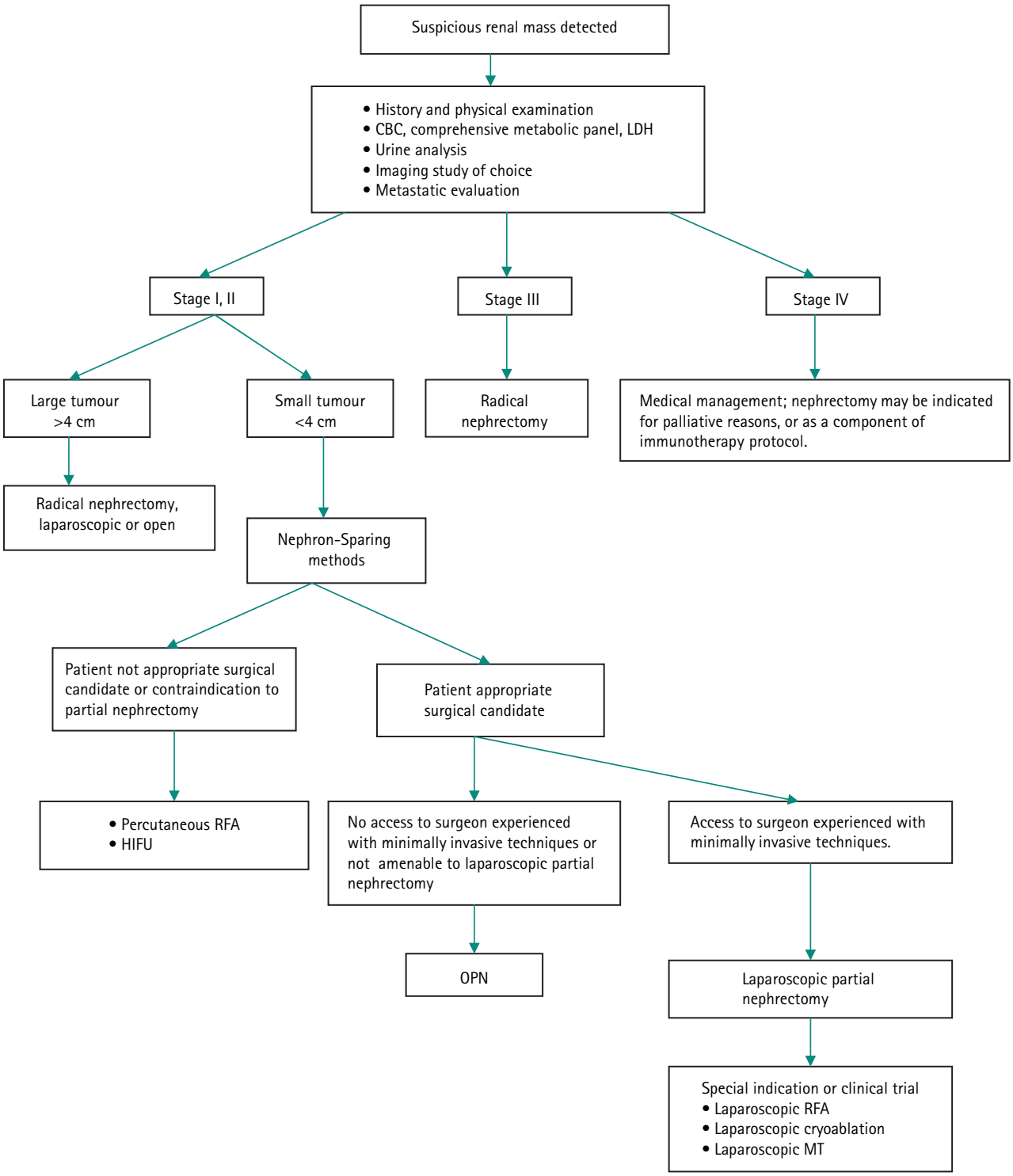
FIG. 1. Decision tree for managing small renal tumours, assuming normal contralateral kidney.



intervention for small (<4 cm), single, localized renal tumours. Minimally invasive techniques are emerging and most are reserved for poor surgical candidates, or as part of a clinical study. Developing technologies aspiring to produce outcomes comparable to that of OPN, while decreasing morbidity, will require large, uniform trials with a long-term follow-up to validate their place in the approach to the small renal tumour. Figure 1 shows a decision tree, which describes the roles for the various

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treatment methods for managing small renal tumours.

CONFLICT OF INTEREST

None declared.

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Abbreviations: **NSS**, nephron-sparing surgery; **O(L)PN**, open (laparoscopic) partial nephrectomy; **RFA**, radiofrequency ablation; **MT**, microwave thermotherapy; **HIFU**, high-intensity focused ultrasound.

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