Surgery in renal cell cancer

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The incidence of renal cancer has increased over the past 30 years, with renal cell carcinoma being the most common form. In this article, the authors discuss the surgical options for treatment of both localised and metastatic renal cell carcinoma.

Renal cancer accounts for approximately 9000 cancer diagnoses and 4000 deaths in the UK each year and represents 2–3% of all cancers. There is a male predominance of 3:2 and the peak incidence is in the 65- to 69-year age group. Renal cell carcinoma (RCC) is the most common form and accounts for 85% of renal cancers. The incidence of renal cancer has increased over the past 30 years, in part as a result of the greater number of incidental tumours detected. In the era of modern imaging, a large proportion of these tumours are classified as small renal masses (<4cm). Small renal masses are believed to have a relatively low malignant potential and rarely metastasise; the typical growth rate of these tumours is approximately 2–3mm per year.

Radiologically guided biopsies have a diagnostic yield of between 85 and 95% and a low complication rate of 1% and are often performed in histologically indeterminate masses. Renal tumour biopsies may also be performed prior to considering patients for active surveillance, prior to ablative therapy or to acquire a histological diagnosis before targeted therapy in metastatic disease.

Active surveillance and ablative techniques such as cryoablation and radiofrequency ablation are alternative treatment options to surgery in carefully selected patients with small renal tumours. Medium-term data suggest these options are safe and are associated with similar cancer-specific and overall survival outcomes to surgery.

Surgery remains the gold-standard curative treatment for localised RCC. The modality implemented may vary according to both tumour and patient characteristics. Where possible, nephron-sparing surgery is recommended to preserve renal function and minimise morbidity. In patients with metastatic disease, cytoreductive surgery may reduce tumour burden and improve performance status prior to treatment with targeted therapies.

SURGERY FOR NON-METASTATIC RENAL CANCER

Tumour stage, complexity and patient performance status are critical when deciding first, if surgery is appropriate, and

Box 1. Tumour stage and characteristics in renal cancer

- Stage T1: Tumour ≤7cm, limited to the kidney
  - T1a: Tumour ≤4cm, limited to the kidney
  - T1b: Tumour >4cm but ≤7cm
- Stage T2: Tumour >7cm, limited to the kidney
  - T2a: Tumour >7cm but ≤10cm
  - T2b: Tumour >10cm, limited to the kidney
- Stage T3: Tumour extends into major veins, adrenals or perinephric tissue, not beyond Gerota’s fascia
  - T3a: Tumour extends into renal vein or its branches, perirenal and/or renal sinus fat
  - T3b: Tumour extends into vena cava below diaphragm
  - T3c: Tumour extends into vena cava above diaphragm or invades wall of vena cava
- Stage T4: Tumour extends beyond Gerota’s fascia
second, which of the surgical modalities should be considered (Box 1). Various patient and tumour characteristics may also influence the decision-making process (Box 2).

T1 Tumours

Historically, open radical nephrectomy (ORN) was the standard surgical treatment for T1 tumours. Current evidence suggests that open partial nephrectomy (OPN) is associated with similar operating times, blood loss and length of hospital stay when compared to ORN (Figure 1).\(^9\) Cancer-specific and recurrence-free survival are statistically equivalent, although quality-of-life data favour OPN.\(^9,10\) Partial nephrectomy is associated with improved postoperative renal function and lower all-cause mortality, regardless of whether open, laparoscopic or robotic-assisted surgery is performed.

The majority of T1 renal tumours are suitable for a nephron-sparing approach (partial nephrectomy; Figure 1). Where technically feasible, the tumour is excised either without clamping the renal vessels (off clamp), clamping the renal vessels (warm ischaemia) or clamping the renal vessels and cooling the kidney with ice for 10 minutes (cold ischaemia). Evidence suggests that an ischaemia time of less than 25 minutes does not lead to significant irreversible renal injury.\(^11\) Cold ischaemia allows 35 minutes on clamp without a significant reduction in postoperative renal function.\(^12,13\) The tumour is excised, defects in the calyces are repaired, haemostasis is achieved and the kidney closed (Figure 2).

Partial nephrectomy may be performed as open (OPN), laparoscopic (LPN), or robotic-assisted procedure (RAPN). Mortality, overall survival and progression-free survival data are comparable for OPN and LPN.\(^14\) OPN is associated with a shorter warm ischaemia time when compared to LPN, although this is not reflected in the long-term renal function data.\(^15\) RAPN has been shown to reduce warm ischaemia time and blood loss when compared to LPN.\(^16\) Long-term oncological outcome data regarding RAPN are not yet available.

T2 Tumours

Laparoscopic radical nephrectomy (LRN) is the recommended surgical treatment for T2 tumours. LRN is associated with a significantly shorter hospital stay and reduced analgesia requirements when compared to ORN; however, oncological outcomes are generally agreed to be similar.\(^17\) Where technically feasible, partial nephrectomy may be performed. In less complex T2 tumours, partial nephrectomy has been shown to have similar oncological and perioperative outcomes to those of radical nephrectomy. In certain circumstances, such as a patient with a complex tumour in a single functioning kidney or bilateral tumours, preserving functioning renal tissue may be imperative to prevent rendering the patient dialysis-dependent. In this situation it is possible to perform a nephrectomy and bench dissection of the tumour (ex-vivo dissection) followed by transplanting the same kidney back into the patient (autotransplantation) (Figure 3).

T3 Tumours

Tumour thrombus extending into the renal vein or the inferior vena cava is an adverse prognostic indicator, although the level of tumour thrombus is not thought to be directly linked to lymph node or distant metastasis.\(^18\) Nephrectomy and excision of the tumour thrombus in non-metastatic renal cancer is recommended as a treatment option; again, this is dependent on the patient’s condition.

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**Box 2. Characteristics that influence surgical modality**

**PATIENT**
- Obesity
- Diabetes
- Hypertension
- Performance status
- Single kidney/poorly functioning contralateral kidney
- Genetic conditions, eg von Hippel-Lindau syndrome

**TUMOUR**
- Size
- Location within kidney/complexity
- Endophytic/exophytic
- Bilateral tumours
- Stage
- Extent of inferior vena cava involvement

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**Figure 1. Flow chart for surgical management of T1 renal tumours**

[Diagram showing flow chart with T1a and T1b branches leading to various treatment options such as active surveillance or ablative therapy, partial nephrectomy open, laparoscopic or robotic assisted, and laparoscopic radical nephrectomy open if not technically feasible.]
on both tumour and patient characteristics (Figure 4). The surgical method adopted depends on the level of the tumour thrombus and the degree of occlusion. In most T3a and T3b tumours the tumour can either be ‘milked’ back into the renal vein or the inferior vena cava can be clamped and opened to excise the tumour (Figure 4). In T3c tumours, venovenous bypass or cardiopulmonary bypass and deep hypothermic circulatory arrest may be required to facilitate tumour excision.

SURGERY IN PATIENTS WITH METASTATIC RENAL CANCER

Surgery on the primary tumour

Surgery on the primary tumour (cytoreductive nephrectomy, CRN) is a palliative procedure and an adjunct to targeted therapies in metastatic renal cancer. CRN is associated with improved overall survival if combined with immunotherapy when compared to immunotherapy alone.19 CRN in combination with targeted therapies such as tyrosine kinase inhibitors has been shown to improve overall survival from 9.6 to 20.6 months when compared with patients treated with targeted therapies alone.20 Progression-free survival increased from 4.5 to 7.6 months and risk of death was lower in the CRN plus targeted therapy group.20,21

Surgery following systemic therapy is, however, associated with a higher incidence of wound complications, and tumour progression in ‘non-responders’ may increase the complexity of surgery.22 Overall grade 3 or 4 complication rates are not significantly increased as a result of pre-CRN systemic therapy; however, adverse effects may make CRN more surgically and anaesthetically challenging.22,24

Renal cell carcinoma has been shown to produce high levels of proinflammatory and T-cell inhibitory cytokines, which may actively suppress immunological responses. Removal of the tumour may benefit the patient by removing a source of growth factors, immunosuppressant cytokines, and molecules that underlie paraneoplastic...
Symptoms such as cachexia. RCC has been associated with the phenomenon of spontaneous regression of metastatic disease. Surgical mortality remains low in these patients and laparoscopic CRN is a safe option in carefully selected patients.

Metastasectomy
Renal cancer most commonly metastasises to the liver, bone, brain or lung. The role of metastasectomy remains controversial and its success varies depending on the number of metastases and the specific organ affected. Overall survival can be increased in patients who have had complete surgical resection of liver, lung and pancreatic metastases. This finding has also been shown in bone metastases, where a significantly higher 5-year cancer-specific survival was found in patients following excision of metastases. There are no agreed guidelines regarding the surgical treatment of metastases, partly because of the lack of high-level evidence. The decision to proceed to surgery in metastatic disease is therefore made on a case-by-case basis.

COMPLICATIONS IN RENAL SURGERY
Perioperative complications
Patients with significant comorbidities and advanced tumour stage are at increased risk of complications at the time of nephrectomy. Recent data from UK nephrectomies report a 3.9% risk of major complications (Clavien-Dindo grade 3, 4 or 5) and a 30-day mortality of 0.55%. The transfusion rate associated with nephrectomy is 8.4% and the conversion rate (minimally invasive to open procedure) is 6%. Conversion is common in prolonged procedures as a result of difficult dissection; cases where significant bleeding is encountered or the bowel is injured.

Postoperative complications
The risk of urinary leak following partial nephrectomy is reported as approximately 10%; this risk is associated with the complexity of the tumour and is usually managed by inserting a ureteric stent. The risks of pseudoaneurysm formation requiring embolisation, abscess formation requiring drainage or the need for dialysis are all less than 5%.

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REFERENCES