Conservative vs radical surgery for renal cell carcinoma

HEIN VAN POPPEL
University Hospital Gasthuisberg, Leuven, Belgium

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INTRODUCTION

RCC accounts for ≈3% of all adult malignancies; with the increasing number of incidentally detected kidney tumours there has been a migration to smaller, lower-stage tumours. The TNM classification has recently been adapted [1] to differentiate between tumours measuring ≤4 cm (T1a) and 4–7 cm (T1b). In the management of these small tumours there has been a definite trend away from open radical nephrectomy (ORN) toward nephron-sparing surgery (NSS) and minimally invasive approaches.

RADICAL NEPHRECTOMY

Surgical resection remains the cornerstone of treatment for RCC. ORN was the 'gold standard' of care for localized RCC against which all other forms of surgery for RCC were measured. This standard has been more than challenged by the introduction of elective NSS for small renal tumours and laparoscopic radical nephrectomy (LRN) for lesions not amenable to NSS. Radical nephrectomy consists of the early ligation of the renal artery and vein, removing the kidney outside Gerota's fascia, and removing the ipsilateral adrenal gland and the regional lymph nodes.

Years ago it was suggested and more recently argued again that removing the ipsilateral adrenal gland is not always necessary, in the absence of radiographic adrenal enlargement, unless the malignancy either extensively involves the kidney or is in the upper portion of the kidney [2]. However, adrenalectomy should remain part of radical nephrectomy for RCC of >5 cm, as the risk of unexpected microscopic invasion of the adrenal has been shown to be as high as 7.5% [3,4].

Regional lymph node extension is associated with poor survival. Lymphadenectomy allows for more accurate pathological staging but its therapeutic value remains controversial [5]. Nevertheless, there may be a subset of patients with micrometastatic lymph node involvement who might benefit from prophylactic lymphadenectomy [6,7]. When the lymph nodes are enlarged on imaging, a lymphadenectomy can be useful as up to 30% of patients might have inflammatory nodal enlargement only [8]. The European Organization of Research and Treatment of Cancer (EORTC) trial 30881, comparing the results of radical nephrectomy with or without lymphadenectomy, will be analysed soon and should solve the controversy about the benefit of a 'preventive' lymph node dissection [9].

The surgical approach for radical nephrectomy is determined by the size and location of the tumour, and by patient-related factors. The open procedure is usually done through a transperitoneal (midline or chevron) incision to allow early access to the vessels. Some still prefer an extended subcostal extraperitoneal or transperitoneal incision [10]. Disadvantages of a transperitoneal approach are the longer postoperative ileus and the possible late intra-abdominal adhesions. A thoracoabdominal approach is seldom required but can be used in patients with large upper pole tumours.

LRN (transperitoneal or retroperitoneal) has developed tremendously over the past decade to become a feasible and the best tolerated approach for localized T1-T2 renal tumours that are not amenable to NSS. In these patients LRN is becoming the standard [11]. The benefits of decreased postoperative pain, shortened hospital stay, quicker convalescence and improved cosmesis are clear, and long-term oncological results are equivalent to those of ORN [12].

A follow-up after radical nephrectomy is recommended to detect local recurrence and distant metastases, to permit additional treatment when indicated and if possible. There is no consensus on an optimum follow-up regimen. The risk of postoperative recurrent malignancy is stage-dependent and follow-up should therefore be tailored to the pathological risk factors for recurrence, e.g. stage, size, grade, histological subtype, nodal status and vascular invasion [13,14].

NSS

NSS was initiated and elaborated in Europe; the enthusiasm for its use has been stimulated by advances in renal imaging, improved surgical techniques and methods to prevent ischaemic renal injury, better postoperative management and excellent long-term cancer-free survival data. NSS is now being considered to enable the preservation of renal function with exceptional local recurrences, and high patient satisfaction [15].

The indications for NSS can be categorized as absolute (or imperative), relative or elective. The absolute indications are those where radical nephrectomy would render the patient anephric (either anatomically or functionally) with a subsequent need for dialysis, i.e. bilateral tumours, tumours in a solitary kidney, or significant renal failure.

Relative indications are those in which the contralateral kidney has pre-existing renal disease or is at substantial risk of future compromise, e.g. renal artery stenosis, reflux, stones, diabetes or hypertension.

Currently, smaller tumours, amenable to so-called 'elective' partial nephrectomy, are detected frequently in the presence of a normal contralateral kidney. These indications are still controversial. Although many renal lesions can technically be resected by tumorectomy, such surgery should remain restricted to patients who have easily resectable lesions. These indications become increasingly accepted, although the oncological equivalence of partial and radical nephrectomy has not yet been shown in a controlled randomized trial (Van Poppel H: Prospective randomized Phase III study comparing radical surgery to elective kidney sparing surgery for low stage renal cell carcinoma. EORTC Trial 30904).

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For tumorectomy a simple enucleation, an excavation or enucleo-resection with a rim of healthy parenchyma, a polar nephrectomy or a heminephrectomy can be used [16]. The renal vessels are identified and controlled, and the kidney fully exposed. When a complicated or time-consuming resection is anticipated, temporary clamping of the hilus and cooling can be applied. The renal capsule is incised and blunt/sharp dissection used to remove the tumour, along with a margin of normal parenchyma. Just a few millimetres of normal parenchyma were shown to be enough to guarantee safe resection margins [17]. Arterial or venous bleeding is controlled with suture ligatures, and openings of the pelvi-calyceal system are meticulously closed. When the parenchymal defect cannot be closed, haemostatic agents can be used to fill the defect, to provide additional haemostasis.

Intraoperative ultrasonography to either delineate the intraparenchymal extent of the tumour or to detect secondary tumours, and intraoperative frozen-section analysis for the surgical margins [18], have been proposed but are not routinely applied.

The most important complications of partial nephrectomy are haemorrhage, urinary fistula and renal insufficiency. Complications are obviously more frequent in imperative resections. Bleeding can occur in the perirenal space and is recognized by an adequately placed suction drain. Intrarenal haemorrhage, and severe haematuria, result from arteriocalyceal or arteriovenous fistula, or pseudo-aneurysm formation. Both types of postoperative bleeding can be efficiently treated by superselective embolization. When urinary leakage is excessive the most important factor in solving the problem is adequate suction drainage to avoid urinoma formation. Placing a JJ ureteric stent or a nephrostomy can be helpful.

Prolonged clamping of the hilus with no cooling can result in tubular necrosis, necessitating temporary haemodialysis. Damage to the intima of the renal artery by an inappropriate clamp in an atherosclerotic patient can also be responsible for infarction of the renal remnant, with definitive renal insufficiency [19].

The technical success rate with NSS is excellent, and long-term patient survival rates are comparable to those obtained after radical nephrectomy, particularly for low-stage RCC. The major disadvantage of NSS is the risk of postoperative local tumour recurrence in the remnant kidney, which has occurred in up to 10% of patients. This can be a result of incomplete resection (local recurrence) after simple enucleation, or when the surgical margin was not clear of tumour, or to multifocality (kidney recurrence). In both situations a second operation, mostly radical nephrectomy, can still offer cure.

NSS provides effective long-term treatment for patients with localized RCC when preserving renal function is clinically important. It is becoming an increasingly accepted approach in patients who have a single, small (<4 cm) and easily resectable RCC and a normal contralateral kidney [20]. Whether elective NSS should be proposed in larger and more centrally located tumours remains highly questionable, and the feasibility of difficult NSS reported by some expert centres cannot be an argument to advocate this approach in current urological practice.

After partial nephrectomy the follow-up should mainly be focused on the remnant kidney, to detect any local or kidney recurrence in the early stages. Local recurrence should be sought after pure enucleation (as in imperative cases) and kidney recurrence after resection of a clear cell RCC in genetic syndromes like Von Hippel-Lindau, or of a papillary RCC, both being more often multifocal or bilateral. Patients who develop a recurrence with no signs of metastases will be considered for salvage surgical treatment. Surveillance for recurrence must be tailored according to the initial pathological tumour type and stage, and to the surgical technique applied, with ultrasonography and abdominal CT. As long as NSS is not the unequivocal 'standard' treatment for RCC, a regular follow-up remains warranted [19].

MINIMALLY INVASIVE NSS

Open partial nephrectomy, with its excellent 5- and 10-year oncological follow-up results, is the reference standard against which all other NSS alternatives must be compared. The new minimally invasive nephron-sparing alternatives can essentially be divided into three categories: excision (laparoscopic partial nephrectomy, LPN), probe ablation (e.g. cryotherapy and radiofrequency ablation, RFA), and noninvasive ablation (high-intensity focused ultrasound, HIFU).

The technique of LPN for treating RCC is still under development. Although both intra- and retroperitoneal LPN have been successful it has been difficult to reproduce the essential elements of open partial nephrectomy using contemporary laparoscopic instrumentation. Despite advanced techniques, including the use of a harmonic scalpel and biological tissue adhesives such as fibrin glue, LPN has resulted in longer operations and higher complication rates than open partial nephrectomy.

The initial experience suggests that LPN can be used for small exophytic renal tumours, with adherence to established principles and techniques of the open surgical approach. Although both the instrumentation and technique are being refined, it is too early to consider LPN a reproducible operation for cancer that is appropriate outside a specialized centre [21].

Laparoscopic cryoablation could represent a reasonable alternative as the kidney is an anatomically favoured site for cryoablative therapy, because it can readily be dissected from adjacent organs and usually gives rise to a unifocal malignancy. During cryoablation the tumour is supercooled to a core temperature of <–40 °C using a liquid nitrogen-based cryoprobe. Normal and neoplastic renal tissues are ablated and rendered necrotic at –20 °C. To assure complete tumour destruction the advancing ice-ball is monitored laparoscopically and ultrasonographically [22]. A major criticism of the technique is that histological documentation of complete tumour destruction is not currently available. Long-term clinical and radiographic follow-up of these patients is ultimately needed to validate the efficacy of this minimally invasive approach for treating renal malignancy; 5-year follow-up data should be available in the near future.

Newer energy sources for tumour ablation include HIFU, interstitial RFA, and laser and microwave coagulators. These methods may eventually permit tumour destruction by minimally invasive techniques and completely extracorporeal methods. Theoretical and experimental evidence indicate that the primary mechanism of tissue destruction by both RFA and HIFU is thermonecrosis. These

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methods induce cavitary defects in animal and human renal tissues, safely and reproducibly, while limiting collateral injury to the unaffected parenchyma [22].

To gain a place among the options of nephron-sparing approaches, HIFU and RFA must give clinical and pathological success rates approaching that of open partial nephrectomy. Although renal RFA has the potential to further minimize morbidity, serious concerns remain about the completeness of cancer cell death and the reliability of intraoperative monitoring. Non-invasive technological advances like HIFU could have considerable potential for the future [23].

CONFLICT OF INTEREST

None declared.

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Correspondence: Prof Dr Hein Van Poppel, Department of Urology, University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium.
e-mail: hendrik.vanpoppel@uz.kuleuven.ac.be

Abbreviations: **EORTC**, European Organization of Research and Treatment of Cancer; **HIFU**, high-intensity focused ultrasound; **NSS**, nephron-sparing surgery; **RFA**, radiofrequency ablation; **ORN**, **LRN**, open, laparoscopic, radical nephrectomy; **LPN**, laparoscopic partial nephrectomy.

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