

REVIEW ARTICLE

Partial nephrectomy for renal cancer: Part I

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INTRODUCTION

The Problem of Kidney Cancer

Kidney Cancer Is The Third Most Common Genitourinary Tumour With 57 760 New Cases And 12 980 Deaths Expected In 2009 [1]. There Are Currently Two Distinct Groups Of Patients With Kidney Cancer. The First Consists Of The Symptomatic, Large, Locally Advanced Tumours Often Presenting With Regional Adenopathy, Adrenal Invasion, And Extension Into The Renal Vein Or Inferior Vena Cava. Despite Radical Nephrectomy (Rn) In Conjunction With Regional Lymphadenectomy And Adrenalectomy, Progression To Distant Metastasis And Death From Disease Occurs In $\approx 30\%$ Of These Patients. For Patients Presenting With Isolated Metastatic Disease, Metastasectomy In Carefully Selected Patients Has Been Associated With Long-term Survival [2]. For Patients With Diffuse Metastatic Disease And An Acceptable Performance Status, Cytoreductive Nephrectomy Might Add Several Additional Months Of Survival, As Opposed To Cytokine Therapy Alone, And Prepare Patients For Integrated Treatment, Now In Neoadjuvant And Adjuvant Clinical Trials, With The New Multitargeted Tyrosine Kinase Inhibitors (Sunitinib, Sorafenib) And Mtor Inhibitors (Temozolimus, Everolimus) [3,4].

A survival rate of $>90\%$, depending on the tumour histology, is expected after partial nephrectomy (PN) or RN'

The second groups of patients with kidney cancer are those with small renal tumours (median tumour size <4 cm, T1a), often incidentally discovered in asymptomatic patients during imaging for nonspecific abdominal or musculoskeletal complaints, or during unrelated cancer care [5]. A survival rate of $>90\%$, depending on the tumour histology, is expected after partial nephrectomy (PN) or RN.

For the last 15 years kidney cancer incidence and mortality rates have been increasing, particularly for patients with tumours of >7 cm, but also in patients with smaller renal tumours of ≤ 7 cm [6]. An analysis of 1618 kidney cancer patients treated at Memorial Sloan Kettering Cancer Center (MSKCC) between 1989 and 2004 showed that despite more patients with T1a tumours (<4 cm), tumour size and stage migration, and increased use of PN, there was no significant improvement in progression-free survival and

overall survival. The explanation for this observation is not clear and could indicate that aggressive surgical treatment of small renal masses in patients not in imminent danger did not counterbalance a population of patients with increasingly virulent larger tumours. Another potential explanation could relate to treatment-related toxicity, with patients earlier in the experience predominantly treated by RN now at greater risk of chronic kidney disease (CKD), cardiovascular toxicity, and worse overall survival, whereas the recent expansion of PN could mitigate against this but has yet to be appreciated in this data set [7].

Historically, PN was used only under the essential conditions of a renal tumour in a solitary kidney, bilateral renal tumours, or tumour in a patient with underlying medical diseases of the kidney and/or renal insufficiency. The transition from essential indications only to *elective or nephron-sparing* indications (i.e. tumour in a patient with a normal contralateral kidney) has developed over the last 15 years and is based on the following major factors: an enhanced

understanding of renal tumour histology and oncological threat, the oncological equivalency of PN and RN for T1 renal cancers, and the emerging critical concerns about CKD and its potential adverse effect on cardiovascular health and worse overall survival. In this review I provide a comprehensive discussion of contemporary PN in the current management of renal tumours.

THE DEVELOPMENT OF PN: A HISTORICAL PERSPECTIVE

In the first half of the 20th century, renal tumours were usually diagnosed as highly symptomatic abdominal masses, with many patients already experiencing metastatic disease. The initial descriptions by Charles Robson of a 'RN', which included the resection of peri-renal fat and regional retroperitoneal lymph nodes using a transthoracic incision, ushered in an approach to *all* kidney tumours

PN was first performed in 1887 when Czerny resected an angiosarcoma from the kidney of a 30-year-old man [9]. Subsequent animal experiments showed that gentle pressure could control bleeding during PN, and that suture approximation of the kidney would ultimately lead to primary healing often with no urinary fistula. Investigators also made important observations of compensatory hypertrophy and described the minimal amount of overall renal tissue required to support life. In the 1930s, pathological studies by Bell [10] indicated that only 7% of renal cancers of <5 cm metastasized, compared to 83% of those >10 cm, and that tumour growth was expansile, rarely invading adjacent organs. Building on this, in 1950 Vermooten [11] provided the rationale for contemporary PN when he operated for a 10-cm renal cancer and proposed a 1-cm margin as adequate to achieve local tumour control. As more surgeons attempted PN, enthusiasm for the operation waned because there were many complications, particularly related to

the kidney, including early vascular control of the renal hilum, complete exposure of the kidney, polar PN, collecting system repair, use of omental pedicle flaps to augment repairs, use of absorbable gelatine sponge bolsters to prevent tearing of the renal capsule during renorrhaphy, and direct vascular repair of injuries to the renal vein and artery [17]. Most of these stone and trauma techniques are fully integrated into modern PN and are used commonly, particularly in the resection of endophytic and peri-hilar renal tumours.

Beginning in the late 1970s and continuing to date, the development of modern radiological imaging techniques of CT, MRI and renal ultrasonography (US), often used to evaluate abdominal and musculoskeletal complaints, created a new class of small, incidentally detected renal masses that were very different from the massive, symptomatic and often metastatic tumours that were common earlier in the 20th century [18]. At the same time, a shift in the principles of surgical oncology was occurring away from a radical Halstedian view toward one of organ preservation in the treatment of such malignancies as breast cancer and extremity sarcoma. Small, incidentally discovered kidney tumours seemed perfectly suitable for similar conservative operations. Concerns about local tumour recurrence and the observation of small satellite tumours seen in RN specimens were voiced by sceptics as major objections to elective PN.

The phrase 'nephron-sparing' was introduced by Licht and Novick [19] from the Cleveland Clinic in 1993, in a report of 241 patients who had renal tumour resection with a normal contralateral kidney, from 1967 to 1991. Although the median follow-up was only 3 years and the median tumour size was 3.5 cm, only two local recurrences were reported and survival was 95%. Similar results were reported by Herr from the MSKCC [20]. A long-term follow-up from the Cleveland

'a shift in the principles of surgical oncology was occurring away from a radical Halstedian view toward one of organ preservation'

that prevailed until the 1990s [8]. This operation, coupled with developing improvements in peri-operative care, blood banking and modern approaches to anaesthesiology, reduced surgical mortality rates to <5%, provided accurate pathological staging of the local extent of disease and regional lymph nodes, and achieved effective local tumour control. RN is currently still used for the same group of patients who present with massive symptomatic renal tumours, and is executed with either curative intent or integrated into a multimodal treatment approach as a cytoreductive nephrectomy for patients with metastatic disease [4].

Progress in open stone surgery, especially in the 1960s and 1970s, enhanced the understanding of renal vascular and collecting system anatomy, use of techniques such as the Gil Vernet extended pyelolithotomy and anatomic nephrolithotomy, and PN for urinary calculus, lead to a resurgence of interest in PN for renal tumours. Techniques to perform elaborate collecting system repairs of the kidney, kidney 'splits' using ice-slush reno-protection, and methods to drain and stent the kidney were also described [14–16]. In the 1980s, trauma surgeons described techniques to control major bleeding from penetrating injuries to

bleeding and urinary fistula, while RN enjoyed increasing success, especially when performed by urologists [12,13].

Clinic indicated that elective PN was both safe and effective [21]. Technical advances including the use of haemostatic agents, argon-beam coagulation for the cut renal surface, and intraoperative US gave renal surgeons more tools to safely approach PN. The introduction of laparoscopic RN (LRN) by Clayman *et al.* [22,23] in 1991 ushered in a new era of minimally invasive kidney surgery. McDougal *et al.* [24] investigated minimally invasive PN in the laboratory setting in the pig model, and in 1993 Winfield *et al.* [25] successfully performed the first laparoscopic PN (LPN), a technically demanding operation being increasingly used with success. Advances in minimally invasive instrumentation, including robotic assistance, dual-teaching counsels, coupled with sophisticated training simulators, might enhance the use of these techniques in the future [26].

RENAL CORTICAL TUMOURS (RCTS): DIVERSE PRESENTATION, TUMOUR HISTOLOGY AND ONCOLOGICAL THREATS

RCTs are members of a complex family with unique histology, cytogenetic defects and variable metastatic potentials, ranging from the benign oncocytoma, to the indolent papillary and chromophobe carcinomas, to the more potentially malignant conventional clear cell carcinoma (CCC) [27,28]. Studies that track the growth of renal tumours under active surveillance, such as a recently pooled analysis of 234 patients from nine centres who were followed for a mean of 34 months, indicated that the mean growth rate was

0.28 cm/year [29].

These results are consistent with other published studies, which also describe that up to 36% of tumours under active surveillance had no

growth, but this feature alone did not predict for benign tumour histology in cases where tissue was obtained [30]. Published surgical series consist predominantly of localized nonmetastatic tumours with all the histological tumour subtypes, including benign oncocytoma, represented, whereas published medical oncology series are replete with the conventional CCC tumour histology which accounts for ≈90% of metastatic renal cancers. However, a certain percentage of small renal tumours have significant metastatic potential and patients with these

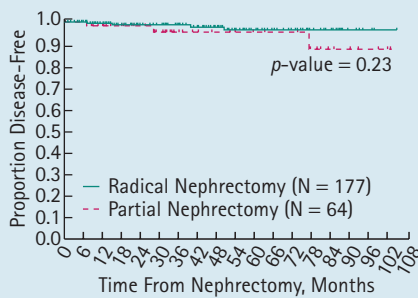
aggressive, albeit small, tumours might present directly to medical oncologists for systemic therapy rather than surgical therapy. Using the Surveillance Epidemiology and End Results (SEER) database, Nguyen and Gill [31] reported a rate of metastases of 5% for tumours of <2 cm. Despite vast improvements in modern CT, US and MRI of the kidney, these imaging studies are not specific. Of patients undergoing renal tumour resection 16.4–23% will ultimately be found to have a benign lesion, including angiomyolipoma, oncocytoma, metanephric adenoma, or haemorrhagic/complex cyst [32–34]. A renal mass with no evidence of macroscopic fat on non-contrast CT, despite an appearance highly suspicious for renal cancer, can still be a benign angiomyolipoma [35].

The role of preoperative renal mass biopsy using CT or US guidance has long been controversial because of issues relating to diagnostic accuracy, dependence upon an adequate biopsy sample for analysis, inability to distinguish tumour histological subtypes and histological grade, and concerns by clinicians of how the biopsy information would alter the ultimate treatment plan. Initial diagnostic renal mass biopsy accuracy rates of 70% [36] have been improved and are now up to 90% in recent reports [37–39]. The role of renal mass biopsy might develop further as immunohistochemical and molecular markers are added to the diagnostic options of the pathologists to more precisely address concerns about tumour histology and grade, and strategies of personalized cancer care are realized in the future. An alternative strategy is to image the more malignant CCC with a specific radiolabelled antibody that reacts to carbonic anhydrase 9, an antigen highly expressed by the conventional CCC. ¹²⁴I-cG250 is under active investigation in a large, phase 2 clinical trial in the USA, and has shown a high sensitivity and specificity in preliminary studies. This specific positron emission tomography scan might be important in surgical planning, active surveillance, evaluating the extent of disease, and as a means to follow either localized or systemic treatments [40]. What is now clear is that the era of diagnostic RN for small renal masses is over and no longer should this be considered acceptable surgical care.

Recent studies of patients referred for surgical intervention have closely correlated

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FIG. 1. Disease-free survival after PN and RN for tumours of ≤ 4 cm across all histologies. Adapted from [47].



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renal tumour size with malignant and metastatic potential. In a series of 2675 tumours treated surgically at MSKCC, 12% were benign and 88% were a form of RCC. The incidence of benign tumours decreased from 38% for tumours of ≤ 1 cm, to 7% for tumours of ≥ 7 cm. The hazard ratio (HR) for the association of malignancy with tumour size was 1.16, indicating that for every 1 cm increase in tumour size there was a 16% increase in the odds of malignancy. For patients with CCC, each 1 cm increase in tumour size increased the odds of high-grade disease (grade 3 or 4) compared to low-grade disease (grade 2 or 3) by 25%. In this subset, the incidence of high-grade CCC increased from 0% for tumours of ≤ 1 cm to 59% for tumours of ≥ 7 cm [41]. The same investigators correlated renal tumour size with metastatic potential. Only one patient in 781 with a tumour of < 3 cm presented to the MSKCC Urology Service with metastatic disease. Of the 2367 patients who did not present with metastatic disease, during a 2.8-year median follow-up, 171 (7.2%) developed metastases. Metastasis-free survival was significantly associated with tumour size, with a HR of 1.24, and hence for each increase in 1 cm tumour growth the odds of metastatic disease increased by 24% [42]. In a review of 1863 surgically treated patients with malignant RCTs (excluding benign tumours such as oncocytoma) at MSKCC between 1989 and 2006, 72% were conventional CCC, 17% were papillary and 12% were chromophobe carcinoma. In that study, 187 patients developed metastasis, 161 (86%) had the conventional CCC, 17 (9.1%) had papillary RCC and nine (4.8%) had chromophobe carcinoma. On a multivariate analysis, chromophobe (HR 0.40) and papillary

carcinomas (HR 0.62) were significantly associated with a better prognosis than CCC [43].

When taken together, the bulk of the clinical evidence suggests that for small renal tumours referred to urologists for a surgical opinion, with no evidence of metastatic disease, particularly those of < 3 cm, the likelihood of a low grade, benign or indolent tumour with limited metastatic potential is extremely high, creating a perfect opportunity to use PN as means of achieving the dual goals of effective local tumour control and maximum organ preservation. A preoperative nomogram (Fig. 1) was constructed using the combined large kidney tumour surgical databases of MSKCC and Mayo Clinic, and is extremely effective in the counselling patients presenting with a renal mass [44]. Alternatively, these data described here linking small renal masses with a generally non-aggressive natural history provides an excellent basis for active surveillance strategies in elderly or comorbidly ill patients [30].

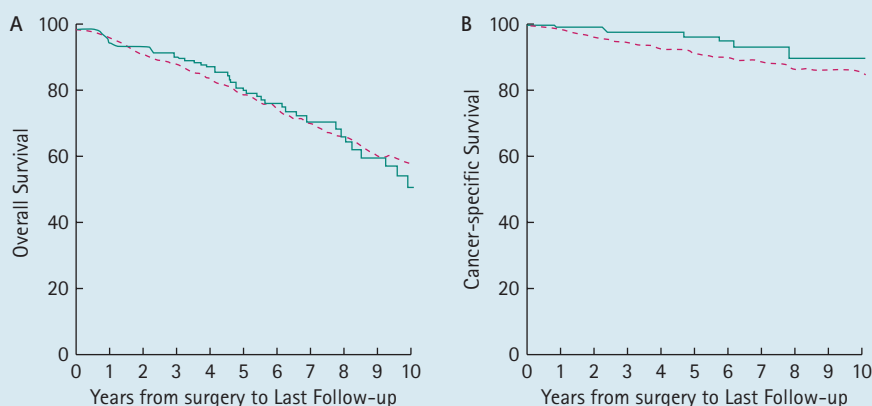
PN IS AS EFFECTIVE AS RN FOR T1A, T1B TUMOURS

For > 50 years the urological oncology community accepted the occasional PN for the essential indications of tumour in a functional or anatomical solitary kidney, yet widely applied RN to *all* renal masses, even the developing population of small renal masses, based on a fundamental belief that a normal contralateral kidney was sufficient to support a healthy life, similar to that of a living kidney transplant donor. The movement away from radical resection of all tumours was ongoing in contemporary surgical oncology (i.e. breast cancer, soft tissue sarcoma) which used limb and organ preservation operations whenever possible, resulting in equivalent local tumour control and survival rates, often in conjunction with adjuvant therapies, to their more radical counterparts. The application of similar surgical strategies for treating small renal mass were sceptically received by the urological oncology community for several reasons, including; concerns that PN was an inferior cancer operation to RN, the belief that local tumour recurrence in the resection margin of PN could lead to disease progression, that technical complications of PN, particularly relating to postoperative

bleeding and urinary fistula, would be exorbitant, and that a patient had sufficient renal reserve to sacrifice the tumour-bearing kidney [45,46]. Initial descriptions of elective PN ('nephron-sparing') inspired more surgeons to consider this approach. Tumour resection using reno-protective measures such as ice-slush and mannitol infusion, precise repair of collecting system entries and intrarenal arteries and veins, and adequate peri-nephric drainage, lead to favourable initial reports [20,45].

Reports from the USA and elsewhere indicated that PN was not compromising the local tumour control or survival when compared to RN for patients with T1a renal tumours (≤ 4 cm) [47,48] (Fig. 1). The expanding experience of PN was happening in parallel to the above-described enhanced understanding of the diverse nature of RCTs and the smaller risk in general associated with small renal tumours than previously thought. The rationale for expanding the indications for PN to larger RCTs of 4–7 cm was articulated [49] and initial reports were met with similarly favourable results both in the USA and Europe [50–52]. A recently published report which combined the Mayo Clinic and MSKCC databases evaluated 1159 patients with renal tumours of 4–7 cm treated with RN (873, 75%) and PN (286, 25%), showed no significant difference in survival between the groups [53] (Fig. 2). Expert laparoscopic surgical teams reported similar renal functional and oncological results favouring LPN over LRN for renal tumours of > 4 cm [54]. We recently reported a series of PN for even larger tumours, with T2 disease in 34 patients. Interestingly, six patients (16%) had benign and 12 (35%) had indolent (papillary or chromophobe) pathology. After 17 months of follow-up, 71% of patients with a malignant diagnosis are alive with no evidence of disease. Although the resection of massive renal tumours (in this series, up to 18 cm in diameter) is largely a function of favourable tumour location and careful case selection, this study indicates that local tumour control can be achieved effectively with results similar to those found in series of tumours of ≤ 7 cm [55]. The ultimate oncological threat of a given tumour depends upon biological factors of the tumour, including histological subtype, the presence or absence of symptoms, tumour grade and tumour size, with prognostic nomograms and algorithms available to predict outcomes with reasonable accuracy [56,57].

FIG. 2. **A**, Overall survival in 873 patients treated with RN (red line) and 286 treated with PN (green line); $P = 0.81$. **B**, Cancer-specific survival in 704 patients treated with RN (red line) and 239 treated with PN (green line); $P = 0.039$. Adapted from [53].



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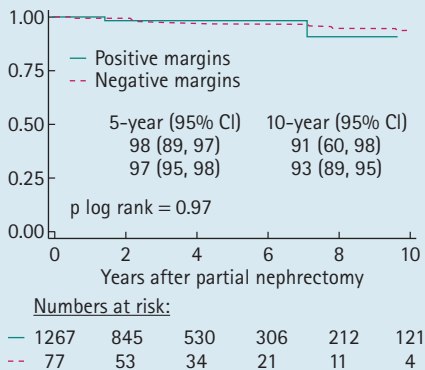
Isolated clinical local recurrence after PN is an uncommon event (<3–5%), with studies often including in the definition of local recurrence both new tumour formation and true local recurrence in the previous resection bed. Barring an overt surgical event or accident which leaves gross tumour behind, risk factors for true local tumour recurrences include tumour in a solitary kidney, large tumour size, multifocal tumours, and positive surgical margins (PSMs). New tumour formation in the operated kidney is an uncommon event, occurring with a lifetime risk, in the absence of familial or hereditary syndromes, in <5% of patients. After either PN or RN, the contralateral kidney also retains a lifetime risk of ≈5% for the development of new tumour formation, necessitating lifelong surveillance [58]. At some finite point, probably measured in years, the risk of a new ipsilateral or contralateral tumour formation probably exceeds the risk of metastatic disease development from the index tumour. In any case, long-term surveillance with a yearly renal imaging study (CT, US or MRI) and chest X-ray (for CCC, chromophobe, papillary renal cancer but not benign oncocytoma or metanephric adenoma) to assess local or systemic recurrence, is recommended. With this approach, disease-free survival rates of >90% are achieved using PN for T1 RCTs across all histological subtypes [56,57]. Although these and other non-randomized studies like them are subject to a variety of selection biases, the weight of these studies indicates that the kidney preservation associated with PN has not adversely affected oncological goals. The current sense at our

centre is that achieving local tumour control with a PN is more a function of tumour location than adherence to a strict size limitation, and metastatic disease potential is more a function of tumour histology and biology than the surgical procedure used.

PN: CONCERNS FOR SMS AND MANAGEMENT OF DIFFICULT RENAL MASSES (HILAR, BILATERAL SYNCHRONOUS, MULTIFOCAL TUMOURS, TUMOUR IN A SOLITARY KIDNEY, RE-OPERATIVE PN)

A criticism of those advocating the expansion of the indications for PN relates to the need for a 1-cm surgical margin of healthy tissue surrounding the resected tumour. Although this belief is felt to be founded on the basic principles of surgical oncology, there are no firm data to support this view. In fact, in the resection of massive soft-tissue sarcoma, complete gross surgical resection, as defined by the operating surgeon at the end of the procedure and not the pathologist, is the principle goal of the operation, particularly when a large retroperitoneal tumour rests along the aorta or inferior vena cava, where resection of additional benign tissue is impossible and microscopic tumour margins are usually positive. This issue is germane particularly when urological oncologists are pursuing endophytic tumours, peri-hilar renal tumours, or renal tumours abutting the collecting system, that would all be effectively excluded from PN if there was strict adherence to a 1-cm margin rule. Also,

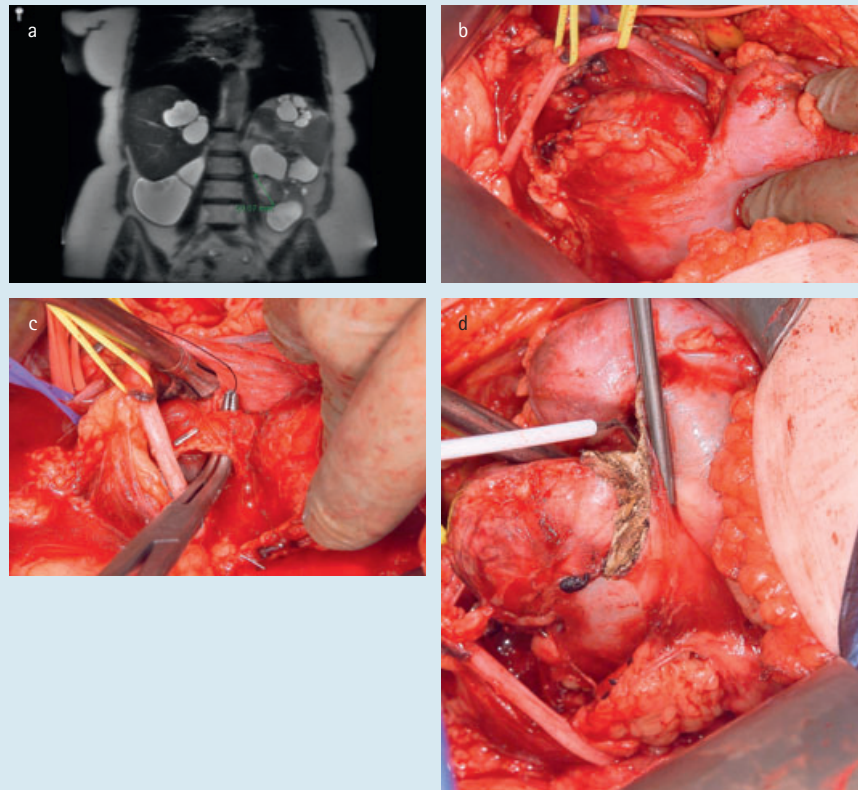
FIG. 3. Recurrence-free and metastasis-free survival based on PSM or negative SMs. Adapted from [59].



uncertain factors in pathology, relating to the handling of the tumour specimen and iatrogenic fractures in the tumour specimen, could also lead to a 'positive' inked margin. Care should be taken to orientate the specimen for the pathologist after a PN. (I place a suture at the parenchymal 'deepest surgical margin').

MSKCC and Mayo Clinic investigators provided some insight into this issue of PSMs by pooling their PN data in 1344 patients undergoing 1390 PN from 1972 to 2005. PSMs were documented in 77 cases (5.5%) and were significantly associated with decreasing tumour size and the presence of a solitary kidney. Interestingly, experienced surgeons from both centres describe small endophytic tumours as challenging because many are not palpable and can be located only by using intraoperative US. Dissection too close to such small tumours can lead to close or even PSMs. In this study, all patients with PSMs were managed expectantly, with an overall 10-year probability of freedom from local disease and metastatic recurrence of 93%. There was no significant difference in either local recurrence or metastatic recurrence in the patients with PSMs or negative SMs (Fig. 3). Although the authors encourage a completion resection in every case, the argument for a complete nephrectomy when a PSM is encountered on final pathology, as well as a 1-cm surgical margin in all cases, is unfounded [59]. With less concern for achieving this traditional 1-cm margin, current surgeons can pursue peri-hilar, endophytic and renal sinus tumours more aggressively and thus increase the number of patients eligible for a PN.

FIG. 4. **a**, A 53-year-old woman with polycystic kidney disease with 5 cm peri-hilar renal mass in left kidney which contributes 80% of her overall renal function. Her eGFR was 36 mL/min/1.73m². **b**, a perihilar renal tumour with suspension of the UPJ. **c**, Ligation and division of lower pole renal vein branch facilitates exposure of the lower pole renal tumour; **d**, Resection of renal hilar tumour following ligation of lower pole renal vein.



During PN for these more challenging tumours, urological oncologists might encounter intraoperative findings that previously would have triggered RN, yet with adherence to fundamental reconstructive and vascular surgical principles, PN can be performed to encompass these challenges. Of RCTs, ≈12% will invade the collecting system, and although this can portend a worse prognosis, complete resection of the tumour and the involved collecting system can be done with suture repair and reconstruction (up to and including dismembered pyeloplasty over an internal stent) as needed. While performing the reconstruction, care must be taken not to exclude a renal papilla from the collecting system, an event which could lead to a urinary fistula with no diversionary options [60]. Most such leaks close spontaneously but might take weeks or even months, with cessation of the leak not facilitated by ureteric stenting. An excluded renal papilla is diagnosed when a retrograde pyelogram before stent placement in a patient

with persistent urinary drainage after a PN shows no evidence of urinary extravasation and a completely intact collecting system.

For tumours close to the renal hilar vessels or projecting into the renal sinus as an endophytic extension from the renal cortex, a troubling preoperative image (Fig. 4a) might look far worse than what is encountered in the operating room (Fig. 4b). Surgeons at Fox Chase reported a series of 36 patients with central renal tumours who had a successful PN. In their series, six patients had benign tumours (17%), all tumours were pT1, and 34 (94%) were considered 'low oncological risk' [61]. The complete mobilization of the kidney on the renal artery, renal vein and ureter, ligation and division of restraining polar vessels (Fig. 4c), coupled with the use of the renal parenchymal-elevating Gil Vernet-type manoeuvre might allow ready access to the renal mass and its complete resection with minimal loss of kidney (Fig. 4d). Also during a PN, an intra-renal vein tumour thrombus

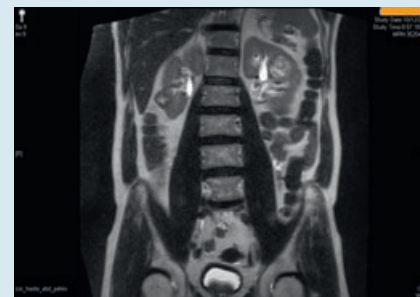
in a branched renal (T3b) vein might be encountered. If the thrombus does not extend to the main renal vein or inferior vena cava, complete resection can be achieved by adhering to the principles of vascular surgery, by obtaining proximal and distal control with care to be certain that thrombus extraction is complete. The ultimate prognoses for these more complicated central tumours after complete resection will depend upon tumour histology, size and grade. Important aids to the surgeon performing a difficult open PN include the use optical loupes to assist in fine-suture repair and reconstruction, and intraoperative US [62] to assist in endophytic tumour localization, to exclude a branched renal vein thrombus, and to search for satellite tumours.

Bilateral renal tumours are reported in 1–5% of patients [63]. In a study of 1082 nonmetastatic renal tumours managed from 1989 to 2001, MSKCC investigators identified 46 patients with bilateral tumours (4%) of which 33 (72%) were synchronous and 13 (28%) were asynchronous. The median (range) tumour size for the synchronous group was 3.9 (1.0–12.5) cm. The first tumour in the asynchronous group had a median tumour size of 4.75 (2.5–12.5) cm and the second asynchronous tumour of 2.25 (1–4.0) cm, occurring at a median time of 84.5 (28–240) months from the contralateral tumour. In all, 92 tumours were identified, with a histological concordance rate of 76% between kidneys. Surgical management in this series was 42% RN and 58% PN, with seven patients undergoing bilateral PN. The most common histological subtypes were conventional CCC in 66% and papillary in 14%. With a median follow-up of 74 months, 72% of patients were disease-free and seven had a recurrence (two local, five metastatic).

‘For patients with bilateral synchronous tumours there is controversy amongst urological oncologists about what operation to use and in what sequence’

When this series of bilateral tumours, either synchronous or asynchronous, was compared to patients with unilateral disease, there was no difference in disease-specific survival [58]. For patients with bilateral synchronous tumours there is controversy amongst urological oncologists about what operation to use and in what sequence. In a follow-up study from MSKCC which focused only upon bilateral synchronous tumours, MSKCC investigators identified 73 (3%) of 2777 patients with

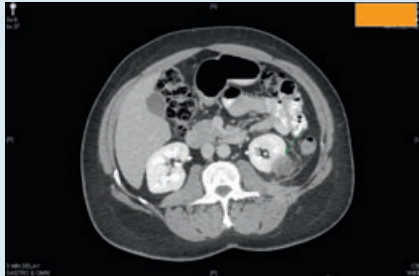
FIG. 5. Bilateral renal tumours in 62-year-old man. Right tumour 2.5 cm, left tumour 4.8 cm but endophytic in location. A left PN was performed first, which revealed a conventional CCC (pT1aNxM0); ≈70% of the left kidney was preserved. 6 months later, a right PN was performed, also revealing a pT1aNxM0 conventional CCC.



bilateral synchronous tumours, from 1989 to 2008. Three patients had bilateral RN (all before 2003), 28 (38%) had a RN followed by a PN, and 32 (44%) at bilateral PN. As this team became increasingly committed to maximally preserving renal function using PN, the use of bilateral PN increased (34% from 1995 to 2004, to 92% from 2004 to 2008). Forty-five patients (62%) had the larger tumour removed first, with a histological concordance rate between the kidneys of 70% [63]. In that study also, there was no difference in survival between patients with unilateral vs bilateral synchronous tumours. It is my preference to pursue the larger tumour first, as it is associated with greater metastatic potential, as described above [64] (Fig. 5).

Although multifocal and bilateral tumours are part of hereditary and familial tumour syndromes such as von Hippel-Lindau disease, hereditary papillary renal cancer, and the Birt-Hogg-Dube syndrome, and can account for 3–5% of all renal cancers [65], multifocal RCTs can also occur in patients with sporadic renal tumours. MSKCC investigators evaluated 1071 RN specimens from 1989 to 2002, and found 57 (5.3%) with pathological evidence of tumour multifocality, including six (11%) that occurred in the bilateral synchronous setting. Preoperative imaging detected tumour multifocality in 19 patients (33%) and therefore occult tumour multifocality was detected in the operating room in 38/1071 RN specimens (3.5%). Primary tumours in the multifocal group were conventional CCC (51%) followed by papillary (37%), and 74%

FIG. 6. A 58-year-old woman with a growing and enhancing left renal mass 13 months after percutaneous cryoablation. There was a perinephric reaction after ablation. The patient was referred for PN.



had the same tumour histology in all lesions. Multivariate analysis showed that bilaterality, papillary histology, advanced tumour stage, and lymph node metastases were associated with multifocal tumours. After a median follow-up of 40.5 months, the disease-free survival rate was not significantly different between multifocal and unifocal renal tumours [66]. When faced with an index renal tumour and surrounding minute satellite tumours detected visually or with the aid of intraoperative US, it is my practice to resect the smaller tumours first, without the use of cold ischaemia, by using a #15 blade on a long knife handle, followed by argon-beam coagulation of the renal cortical resection

nephrectomy for tumour, stone disease, donor transplantation, or infection. When performed by experienced surgeons, PN in this setting can be safe, with a low rate of temporary or permanent dialysis [67,68]. The largest experience with tumour in a solitary kidney is from the Cleveland Clinic, which reported 400 cases from 1980 to 2002. In 323 patients (81%) the contralateral kidney had been surgically removed and 77 had a congenital solitary kidney. In 46% of these patients, evidence of renal insufficiency was present before surgery. The authors used hilar clamping in 96% of the cases, with a mean tumour size of 4.18 cm, of which 92% were renal cancers. Interestingly, 36% of the patients had multifocal disease resected. Only 13 of the 82 patients who had disease recurrence had a local kidney recurrence. After resection, 95% of patients had satisfactory long-term renal function, with only two patients requiring immediate dialysis and 18 others progressing to end-stage renal disease requiring dialysis at a mean of 3.6 years after PN [69]. The same group compared LPN (30) and open PN (169) in renal tumours in a solitary kidney from 1999 to 2006, and reported that the LPN cases had a significantly greater need for postoperative dialysis, longer ischaemic times, and twice the complication rate than the open approach. This expert team of laparoscopic surgeons concluded that open PN might be the preferred approach in these patients at high

risk of CKD [70]. It is hoped that with the increasing use of PN for T1 tumours, a good prognostic category in general with patients likely to survive a long time but remain at

risk for a contralateral renal tumour, the need to perform PN in the solitary kidney will lessen.

Repeat PN for new tumour formation is a difficult operation due to scar tissue from previous renal mobilization and peri-renal adhesions often involving the great vessels of the renal hilum. The group with the most experience with repeat PN is from the National Cancer Institute (NCI), who manage many patients with hereditary and familial cancer syndromes. They reported a series of 51 attempted PN in 47 such patients from 1992 to 2006. There were major complications or re-operations in 10 patients

(20%), one perioperative death, and a significant increase in serum creatinine level and decrease in creatinine clearance. An additional operation was required in 10 patients (20%). Two patients required long-term dialysis. Of the 46 surviving patients, the median follow-up was 56 months [71].

Increasingly, urological oncologists are being asked to operate on renal masses with imaging evidence of viability after radiofrequency ablation (RFA) or cryoablation (Fig. 6). In a recent report from the Cleveland Clinic, which has a substantial experience in both RFA and cryoablation, documented recurrence rates for cryoablation were 13/175 cases (7.4%) and 26 of 104 (25%) for RFA, the mean pre-ablation tumour size of which were 3.0 and 2.8 cm, respectively. Repeat ablations were performed in 26 patients but 12 were not candidates for repeat ablation due to large tumours, disease progression, or failure of repeat ablation. Of these, 10 patients had an attempted resection and only two were able to undergo a PN (open), with seven requiring RN. One operation was aborted. From these data it appears that a failed ablative procedure in a patient originally eligible for a PN creates a difficult challenge for surgical salvage, and will most likely lead to a RN [72]. The NCI team recently reported their experience with 13 patients previously treated with RFA at a median of 2.75 years before using salvage PN. No tumours were converted to RN but the salvage operations were very difficult due to extensive fibrosis and scarring. The median (range) operative duration was 7.8 (5–10.7) h and the median blood loss was 1500 (500–3500) mL [73]. When ablative procedures are discussed with patients as an alternative to PN, patients need counselling about difficult surgical salvage in the case of tumour persistence, and the likely loss of the renal unit.

The resection of a renal tumour in a patient with metastatic renal cancer can be done with PN, particularly if the tumour is in a functional or anatomical solitary kidney. This can be done to achieve complete local tumour control in conjunction with a metastasectomy, or after induction systemic chemotherapy with an excellent response in metastatic sites but persistence in the kidney. In an initial experience with 15 patients, nine of whom were previously treated for metastatic disease with either metastasectomy or systemic agents, excellent local tumour control and renal function

‘Increasingly, urological oncologists are being asked to operate on renal masses with imaging evidence of viability after radiofrequency ablation (RFA) or cryoablation’

bases. In some cases, 15–20 such satellite tumours can be resected before approaching the larger index tumour or tumours. For the larger tumours (>2 cm), formal PN with necessary collecting system or vascular repairs with or without cold ischaemia, depending on the tumour location, is used. Multifocal tumours that can be resected completely should be managed by PN and no longer trigger an automatic RN.

A difficult problem faced by urological oncologists is renal tumour in the solitary kidney, a classical indication for PN, which can be due to a congenital absence of the contralateral kidney or following contralateral

sufficient to avoid dialysis was achieved in 14 [74]. Currently, surgical resection after systemic therapy with targeted therapies (mTOR and tyrosine kinase inhibitors) is often requested by medical oncologists as part of an integrated multi-modal treatment plan [4] which can include the primary tumour (cytoreductive nephrectomy), metastatic sites (metastasectomy) or local recurrences. Depending on the size of the index tumour and its response to systemic therapy, surgeons might plan surgical resection. The Cleveland Clinic group reported a preliminary experience of 21 operations in 19 patients treated with systemic targeted therapies (including sunitinib in 12, sorafenib in three, and bevacizumab/interleukin-2 in four) followed by subsequent surgical resections in patients with either stable disease or a partial clinical response. Operations included nine RN, three PN, six local tumour recurrence resections and three metastasectomies. Surgery was open in 18 cases and laparoscopic in three. Only one patient had a complete pathological response to the systemic therapy, and 80% had conventional CCC in the resected specimen. Three patients had major complications (16%) including two major postoperative bleeds leading to one death, and an anastomotic bowel leak. At a median follow-up of 8 months, 16 patients (84%) were alive, eight of whom had disease progression. Nine patients with metastatic disease or later disease progression were

continued on systemic targeted therapy. Decisions concerning the resumption of systemic therapies or active surveillance after complete

resection are currently made based on the patient's overall performance status and level of drug toxicity. Clinical trials using these same agents in the neoadjuvant and adjuvant setting have been initiated in the USA and Europe. I expect that the role of the surgeon in metastatic renal cancer will continue to expand, particularly as the likelihood of a complete pathological remission with this generation of targeted agents remains low, as shown by this and other studies [75].

PATIENTS WITH RENAL TUMOUR AND UNRECOGNIZED MEDICAL RENAL DISEASE

A historical misconception is that RN, although likely to cause a detectable and permanent rise in serum creatinine level due

to the sacrifice of normal renal parenchyma not involved by tumour, will not cause serious long-term side-effects as long as the patient has a normal contralateral kidney. The renal transplant reports were often cited as the clinical evidence to support this view, as patients undergoing donor nephrectomy have not been reported to have higher rates of kidney failure requiring dialysis, or death [76]. However, there are distinct differences between renal donors and renal tumour patients. Donors tend to be carefully selected, screened for medical comorbidities, and are generally young (aged ≤ 40 years) [77,78]. By contrast, patients with renal tumour are not screened, are older (mean age 61 years), and often have significant comorbidities that can affect kidney function, including metabolic syndromes, hypertension, coronary artery disease, obesity, vascular disease, and diabetes, alone or in combination. As patients age, particularly beyond the age of 60 years, nephrons atrophy and the GFR progressively decreases [79]. A clinical and pathological study from the Harvard Medical School examined the non-tumour-bearing kidney of patients undergoing resection of RCTs, and reported a far greater degree of unsuspected underlying renal disease in these patients than previously appreciated [80]. The non-neoplastic renal tissue in 110 nephrectomy specimens, including 67 CCCs, of which 39 were ≤ 5 cm, were correlated with the patient's clinical history. Only 10% of patients had completely normal adjacent renal tissue and 28% were found to have vascular sclerotic changes. In the remaining 62% of cases, there was evidence of significant intrinsic renal abnormalities, including diabetic nephropathy, glomerular hypertrophy, mesangial expansion, and diffuse glomerulosclerosis. In that study, 91 patients (83%) had RN to treat their tumours. This study indicates that the loss of functional nephrons during RN, coupled with pre-existing intrinsic renal abnormalities, which might or might not be clinically apparent but present at the pathological level in the vast majority of patients, causes worsening of overall renal function.

CKD IS AN INDEPENDENT RISK FACTOR FOR CARDIOVASCULAR DISEASE

CKD is increasingly viewed as a major public health problem in the USA. Currently it is estimated that there are 19 million adults in the USA in the early stages of CKD and that by

‘Currently it is estimated that there are 19 million adults in the USA in the early stages of CKD’

2030, 2 million will be in need of chronic dialysis or renal transplantation [81]. CKD is defined as a GFR of $<60 \text{ mL/min/1.73 m}^2$. Traditional risk factors for CKD include age >60 years, hypertension, diabetes, cardiovascular disease, and family history of renal disease. The prevalence and incidence of kidney failure requiring either dialysis or renal transplantation increased from 1988 to 2004. Also of great importance has been the increased prevalence of the earlier stages of CKD, decreased GFR and/or proteinuria, by 10% as determined by the National Health and Nutrition Examination Surveys, which compared 15 488 adults from 1988 to 1994, with 13 233 adults from 1999 to 2004. A higher rate of diabetes and hypertension during the later time frame in the United States is thought to be responsible for the increase in earlier stages of CKD.

Recommendations for assessing patients at increased risk of CKD include measurement of urine albumin and estimated GFR (eGFR) using equations based on the level of serum creatinine, age, sex and race [82]. In 2003, the National Kidney Foundation, American Heart Association, and the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure classified CKD as an independent cardiovascular risk factor [83–87]. Certain serum factors, including elevated inflammatory and prothrombotic factors (C-reactive protein), fibrinogen, interleukin-6 and factor 8, decreased haemoglobin levels, and lipoprotein A might mechanistically contribute to the elevated cardiovascular risk. Therefore, medical interventions designed to modify well-known traditional risk factors, such as systolic blood pressure $>140 \text{ mmHg}$, diabetes, cigarette smoking, high-density lipoprotein <40 , low-density lipoprotein >130 , body mass index $>30 \text{ kg/m}^2$, physical inactivity, and left ventricular hypertrophy, might be effective in reducing the cardiovascular mortality risk in CKD. Two widely used formulae, the Modification in Diet and Renal Disease (MDRD) equation and the Cockcroft-Gault equation, which incorporate sex, age, race and serum creatinine level, are superior to serum creatinine level alone for the eGFR [82]. These formulae have been extensively evaluated in populations of patients with and without diabetes, including blacks, whites, Asians, patients with kidney disease, and transplant donors. Both equations are more accurate for evaluating kidney function in patients with CKD, as

opposed to younger patients or those with type 1 diabetes without microalbuminuria, or healthy potential kidney donors [88]. Investigators from Tufts University Medical Center and the CKD Epidemiology Collaboration team have modified the MDRD equation, which performs best for patients with CKD, to address relative inaccuracies reported in patients with a higher GFR, by introducing a new equation termed 'CKD-epi'. This equation will require further validation in elderly and non-white patients before its widespread application [89].

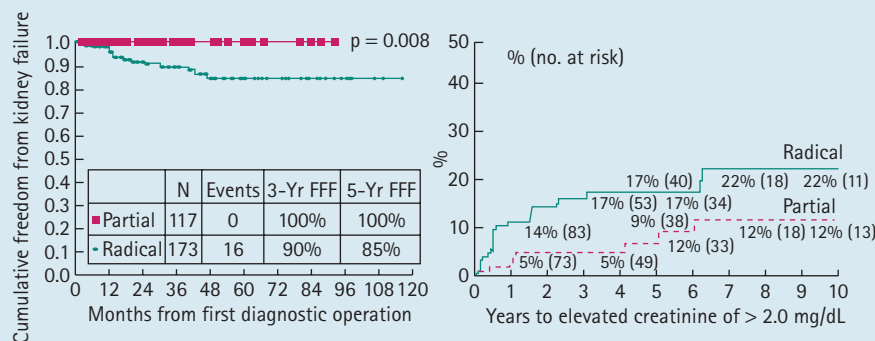
An eGFR of $<60 \text{ mL/min/1.73 m}^2$, or stage 3 CKD, is associated with a graded increase in the risk of progression to end-stage kidney disease and premature death caused by cardiovascular disease. A clinician can quickly calculate the eGFR using a website which only requires patient age, sex, race, and serum creatinine level (http://www.nephron.com/MDRD_GFR.cgi). In our practice, the routine use of the MDRD equation to estimate eGFR has become an essential part of the initial office evaluation of the patient with a renal tumour, and is critical for surgical planning and counselling [90]. The adverse clinical effects of a decline in eGFR was reported by investigators at Kaiser Permanente in California, who estimated the longitudinal GFR in 1 120 295 patients between 1996 and 2000 who had not undergone dialysis or kidney transplantation. The investigators examined the multivariable association between eGFR and the risks of death, cardiovascular events and hospitalization. The median patient age was 52 years, 55% of them were women, and the median follow-up was 2.84 years. The risk of death increased as the eGFR decreased below $60 \text{ mL/min/1.73 m}^2$ with adjusted HR of 1.2 (GFR 45–59), 1.8 (GFR 30–44), 3.2 (GFR 15–29) and 5.9 (GFR <15), respectively. The adjusted risk of hospitalization and cardiovascular events followed a similar pattern [91]. The link between CKD and cardiovascular risk factors was also reported by Foley *et al.* [92], who analysed data from 15 837 non-institutionalized adults between 1988 and 1994 in the Third National Health and Nutrition Examination Survey. Data were gathered on nine cardiovascular risk factors (smoking, obesity, hypertension, high total cholesterol, C-reactive protein, glycosylated haemoglobin, homocysteine levels, low haemoglobin, high urinary albumin to creatinine ratio) and eGFR. The eGFR was $>60 \text{ mL/min/1.73 m}^2$ in 93.3% of patients,

30–59 (stage 3 CKD) in 6.2% and <30 (stage 4 and 5 CKD) in 0.5%. As kidney function deteriorated, the percentage of subjects with two associated cardiovascular risk factors increased from 34.7% (stage 1 and 2 CKD) to 83.6% (for stage 3), to 100% for stage 4 and 5. Patients with CKD were far more likely to require medical interventions to treat cardiovascular disease than those with normal renal function. The low prevalence of patients with stage 4 or 5 CKD is attributable to their 5-year survival rates of only 30% [92].

ELECTIVE PN PRESERVES RENAL FUNCTION

Data comparing late renal functional and oncological results in >450 patients undergoing PN or RN for tumours of $<4 \text{ cm}$ were first reported from the Mayo Clinic (2000) and MSKCC (2002). Patients undergoing RN were more likely to have elevated serum creatinine levels to $>2.0 \text{ mg/dL}$ and proteinuria (Mayo Study) [93], a persistent finding even when study patients were carefully matched for associated risk factors (MSKCC study) including diabetes, smoking history, preoperative serum creatinine level and American Society of Anesthesiologists (ASA) score [94]. In both studies, oncological outcomes were highly favourable ($>90\%$ survival rates) whether PN or RN was used (Fig. 7). Investigators from MSKCC later created a postoperative prognostic nomogram for renal insufficiency which used the percentage change in kidney volume as calculated from CT scans, preoperative serum creatinine level, ASA score, patient age, and sex. In that study, a serum creatinine level of $>2 \text{ mg/dL}$ was described as renal insufficiency. The investigators studied 161 patients undergoing PN and 857 undergoing RN; 111 (10.9%), of which 105 underwent RN (95%), had renal insufficiency at a median of 14.4 months after surgery. Using a multivariate analysis, patient age, sex, preoperative creatinine level, and percentage change in kidney volume were all significant factors associated with freedom from renal insufficiency, with preoperative serum creatinine level of $>1.0 \text{ mg/dL}$ contributing nearly 70 points to the nomogram [95]. Sceptics pointed out that these studies failed to show an increased risk of dialysis in the RN patients but their criticism failed to mention the cardiovascular morbidity and mortality associated with CKD for patients not yet requiring dialysis.

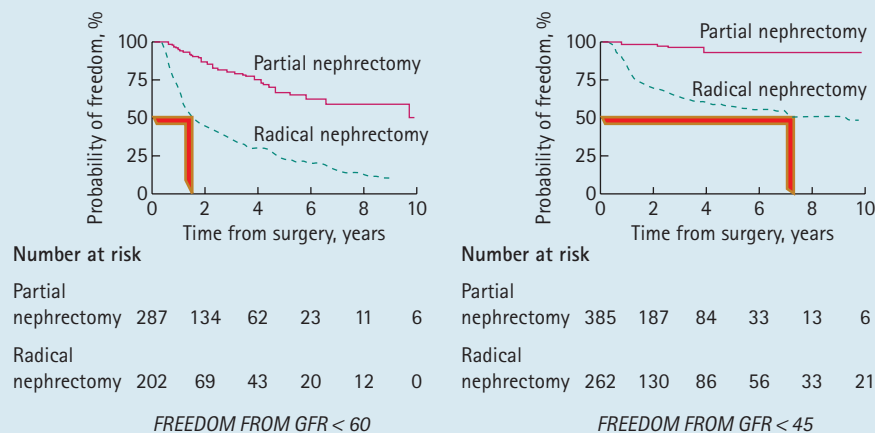
FIG. 7. Adverse effects on renal functional of RN vs PN for renal tumours of ≤ 4 cm (MSKCC, Mayo Clinic). From [93] and [94].



McKiernan J, Simmons R, Katz J, Russo P. Natural history of chronic renal insufficiency after partial and radical nephrectomy. *Urology* 2002; 59(6):816-20

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FIG. 8. Adverse effects on eGFR of RN vs PN, leading to CKD. Adapted from [96].



➤ *Lancet Oncology* 7:735-740, 2006

‘Multivariable analysis indicated that RN remained an independent risk factor for the development of new onset CKD’

A basic principle in nephrology is that serum creatinine levels alone are a poor indicator of overall renal function (GFR) which is more a function of sex, race, serum creatinine level and age. Although the precise measurement of GFRs using inulin clearance, radionuclide EDTA or renal scintigraphy using ^{99m}Tc -MAG3 is possible, the use of the formulae described above to estimate renal function avoid these more complex measurements and procedures, as well as the difficulties associated with outpatient urinary collections. MSKCC investigators analysed their PN and RN

experience using the MDRD equation to estimate GFR in a retrospective cohort study of 662 patients with a normal serum creatinine level and two healthy kidneys, who underwent either elective PN or RN for a RCT of ≤ 4 cm in diameter. Data were analysed using two threshold definitions of CKD, a GFR of < 60 or a GFR of $< 45 \text{ mL/min/1.73 m}^2$. To their surprise, 171 patients (26%) had pre-existing CKD (GFR < 60) before surgery, despite two intact, normal-appearing kidneys and a serum creatinine level within normal limits. After surgery, the 3-year probability of freedom from a new onset of a GFR of < 60 was 80% after PN, but only 35% after RN. Corresponding values for the 3-year probability of a GFR of < 45 , a more severe

level of CKD, was 95% for PN and 64% for RN. Multivariable analysis indicated that RN remained an independent risk factor for the development of new onset CKD [96] (Fig. 8). Importantly, a detectable decline in renal function also occurred in the patients undergoing PN. A recent study from the Mayo Clinic queried their nephrectomy registry from 1989 to 2003, and identified 648 patients treated with RN or PN for a solitary renal tumour of ≤ 4 cm (excluding perinephric fat, nodal and distant metastases patients) and a normal contralateral kidney. Overall survival was calculated in 327 patients aged < 65 years at the time of surgery, and it was found that RN was significantly associated with an increased risk of death which persisted after adjusting for year of surgery, diabetes at presentation, Charlson-Romano index, and tumour histology [97]. Using the SEER cancer registry data linked with Medicare claims, MSKCC investigators studied 2991 patients aged > 66 years and surgically treated for renal tumours of ≤ 4 cm from 1995 to 2002. In all, 2435 patients (81%) underwent RN and 556 underwent PN. After a median follow-up of 4 years, 609 patients had a cardiovascular event and 892 died. After adjusting for preoperative demographic and comorbidity variables, RN was associated with a 1.38 times greater risk of overall mortality and a 1.4 times greater number of cardiovascular events after surgery [98]. Similar results were reported in patients undergoing LRN and LPN [99].

These important data, when taken together, strongly suggest that routine RN for small renal tumours is unjustified, particularly for patients with small RCTs at low risk of developing metastatic disease, with a long anticipated survival, and who remain at risk for the common aforementioned medical diseases. Urologists are now increasingly aware that CKD status can be created or pre-existing CKD significantly worsened by the overzealous use of RN [100]. Short-term endpoints stressed by some authors, particularly of late in laparoscopic reports, including length of hospital stay, analgesic requirements and cosmetic elements, while advocating LRN for small renal masses, must now be tempered by these new concerns that RN for treating small renal tumours, whether by open or laparoscopic techniques, causes CKD and decreases overall patient survival. The most recent AUA guidelines for the management of the small renal tumour emphasize these points and strongly support

the use of PN whenever technically feasible [101].

CONCLUSION

PN, once an operation performed only for the essential indications of tumour in an anatomical or functional solitary kidney, has emerged as the preferred means of treating T1 renal masses. We now have an enhanced understanding of the biology of RCTs, which indicates that $\approx 45\%$ of renal tumours are benign and indolent. Due to abdominal imaging for non-specific abdominal complaints, incidental renal tumours are detected in 70% of cases, leading to a tumour size and stage migration to small tumours at the time of presentation. Well conducted studies show that PN provides equivalent oncological control to RN for tumours of ≤ 7 cm. PN, whether approached by open, laparoscopic or the newly introduced robotic-assisted approaches, is now considered the treatment of choice for small renal masses. A new appreciation of CKD, impaired renal function before end-stage renal disease which requires renal-replacement therapy in the form of transplantation or dialysis, and its associated cardiovascular morbidity and mortality, now provides an added incentive for kidney-sparing surgery. RN is associated with the causation or worsening of preexisting CKD, cardiovascular events, and worse overall survival. Despite these compelling arguments for the PN, there is gross under-use in the USA and Europe, largely due to the overzealous use of RN, a practice which now must be considered as detrimental to the long-term health of a patients with kidney tumours. Widespread training in PN and enhanced use, whether by open or laparoscopic approaches, is clearly indicated in the USA and elsewhere.

CONFLICT OF INTEREST

None declared.

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Abbreviations: (L)PN, (laparoscopic) partial nephrectomy; (L)RN, (laparoscopic) radical nephrectomy; PSM, (positive) surgical margin; RCT, renal cortical tumour; CCC, clear cell carcinoma; CKD, chronic kidney disease; MSKCC, Memorial Sloan Kettering Cancer Center; US, ultrasonography; SEER, Surveillance Epidemiology and End Results; HR, hazard ratio; NCI, National Cancer Institute; RFA, radiofrequency ablation; eGFR, estimated GFR; MDRD, Modification in Diet and Renal Disease; ASA, American Society of Anesthesiologists.

APPENDIX

Questions

- 1 Which of the major types of renal cortical tumours has the greatest malignant potential?
(a) chromophobe RCC
(b) papillary RCC
(c) renal oncocytoma
(d) conventional CCC
Answer: d
- 2 Approximately what percentage of suspicious renal masses undergoing surgical resection will be found to be benign upon final pathology?
(a) 5%
(b) 20%
(c) 40%
(d) 60%
Answer: b
- 3 True or false: PN provides equivalent local tumour control, progression-free survival and overall survival for T1 (<7 cm) renal tumours when compared with RN
Answer: True
- 4 True or false: PN for a small endophytic renal tumour which is completed with a complete gross resection but a microscopic PSM is associated with a worse overall prognosis.
Answer: False
- 5 A 3-cm renal tumour involving a branched renal vein represents what clinical stage?
(a) pT1
(b) pT2
(c) pT3b
(d) pT3a
Answer: c
- 6 For patients with bilateral synchronous or asynchronous tumours, renal cortical

tumour histological concordance between each kidney is about:

- (a) 10%
- (b) 30%
- (c) 50%
- (d) 70%

Answer: d

7 Surgical salvage to resect a renal tumour previously treated with either cryoablation or RFA is associated with:

- (a) A decreased likelihood of completing a PN
- (b) Extensive peri-tumoral fibrosis
- (c) Greater operative time and blood loss
- (d) All of the above

Answer: d

8 Patients with a renal tumour differ from renal transplant donors in which of the following ways?

- (a) Patients with a renal tumour are older
- (b) Patients with a renal tumour might have significant comorbid diseases
- (c) The non-tumour-bearing kidney in renal tumour patients might have significant intrinsic abnormalities
- (d) All of the above.

Answer: d

9 CKD is defined as an eGFR (in mL/min/1.73 m²) of:

- (a) <60
- (b) <100
- (c) <80
- (d) <120

Answer: a

10 CKD is associated with:

- (a) cardiovascular disease
- (b) hospitalization
- (c) worse overall survival
- (d) all of the above.

Answer: d

11 For a renal tumour of ≤4 cm treated by RN and not PN, after surgery one would expect:

- (a) lower serum creatinine level
- (b) less protein in the urine
- (c) enhanced overall survival
- (d) a lower eGFR

Answer: d

12 True or false: eGFR is a more accurate assessment of renal function than serum creatinine alone.

Answer: True