Recent developments in kidney cancer

Michael J. Leveridge, MD, FRCSC;[*] Michael A. S. Jewett, MD FRCSC[†]

[*]Assistant Professor, Department of Urology, Kingston General Hospital, Queen's University, Kingston, ON; [†]Professor, Division of Urology, Department of Surgical Oncology, Princess Margaret Hospital and the University Health Network, University of Toronto, Toronto, ON

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Abstract

Renal cell carcinoma (RCC) diagnosis and management have undergone significant shifts in the recent past. The increasing rate of diagnosis of small renal masses, often in patients at high risk of morbidity with operative treatment, has led to studies, trials and discoveries in renal mass biopsy, active surveillance and minimally invasive thermal ablation. At the other end of the disease spectrum, targeted systemic therapies for metastatic RCC have supplanted cytokine-based treatment, with significant benefits to progression and survival. Recent reviews and trials have also cemented the role of partial nephrectomy as standard surgical management for most low-stage masses, and the roles of regional lymphadenectomy and adrenalectomy concomitant with nephrectomy have been clarified. This review aims to highlight recent evidence that has emerged in the management of this complicated oncologic issue.

Résumé

Le diagnostic d'hypernéphrome et la prise en charge de cette maladie ont fait l'objet d'importants changements au cours des dernières années. Le taux accru de cas de petites masses rénales, souvent chez des patients présentant un risque élevé de morbidité avec le traitement chirurgical, a amené la conduite d'études et d'essais qui ont entraîné des découvertes touchant la biopsie des masses rénales, la surveillance active et l'ablation thermique minimalement invasive. À l'autre bout du spectre pathologique, les traitements généraux ciblés de l'hypernéphrome métastatique ont supplanté le traitement à base de cytokines, ce qui a amené des avantages significatifs sur le plan de la progression et de la survie. Des articles de synthèse et des essais récents ont aussi confirmé le rôle de la néphrectomie partielle en tant que prise en charge chirurgicale standard pour la plupart des masses de faible stade, et les rôles de la lymphadénectomie régionale et de la surrénalectomie en concomitance avec une néphrectomie ont été clarifiés. Le présent article vise à faire ressortir les données récentes dans la prise en charge de ce problème oncologique complexe.

Introduction

The Canadian Cancer Society and the National Cancer Institute of Canada predict 4800 new kidney cancer diagnoses in 2010, and 1650 Canadian deaths from the disease.[1] Kidney cancer is the most lethal genitourinary cancer, but is also among the most interesting cancers due to recent developments exploiting knowledge about known genetic mutations with targeted systemic therapies, better understanding of the extent of associated chronic kidney disease, the utility of nephron-sparing surgery when treating primary tumours and the significant advances in less invasive therapies.

This review is not intended to be an exhaustive assessment of the present state of knowledge of kidney cancer, but is an update on recent clinically relevant developments.

Diagnosis and staging

Overall, about 85% of renal masses, presumed to be kidney cancers on imaging studies, are carcinomas at nephrectomy.[2] Due in part to this high incidence of cancer, biopsy has not been recommended in the routine workup of a patient with a renal mass. Biopsy of renal masses has been recommended in the workup of potentially metastatic disease to the kidney and in the diagnosis of primary lymphoma of the kidney. Concerns surrounding the use of biopsy include technical factors, such as adequate tissue sampling and bleeding complications and tumour factors, such as the heterogeneity of some renal masses, tumours with multiple elements (e.g., angiomyolipoma) and biopsy of cystic lesions.

The University Health Network group has recently published the technique, safety, accuracy and results of small renal mass (SRM) biopsy, typically employing a spring-loaded 18-gauge biopsy needle through a 14-gauge cannula placed adjacent to the mass.[3,4] The first review in 2007 confirms that the accuracy of biopsy is >90% in contemporary series, with very low rates of significant bleeding, as well

as the extreme rarity of tumour seeding with newer biopsy cannulae. In our series of 100 SRM biopsies for a median tumour size of 2.4 cm, we obtained 84 diagnostic biopsies, with 93% ability to determine histologic subtype and 68% ability to determine Fuhrman grade. Histologic concordance between biopsy and surgical specimen was 100% in the 20 patients who proceeded to surgery. There were no serious complications and no tumour seeding of the biopsy tract.

The Cleveland Clinic group has also recently published a review of renal mass biopsy series.[5] Since 2001, the group has shown 88% accuracy in identifying carcinoma and 87% of these with histology. The incidence of significant complications has been less than 1%. Increased experience with local ablative techniques for managing renal masses, as well as advances in the characterization of masses for targeted therapy, provides further rationale for the performance and refinement of renal mass biopsy. Data are also emerging regarding the outcomes of non-diagnostic biopsy. A recent review by Laguna and colleagues noted that 46.4% of non-diagnostic biopsies were followed by repeat biopsy or surgery; cancer was present in 78.5% of all specimens, including 71% of repeat biopsies.[6]

Changes to the American Joint Committee on Cancer (AJCC) staging of renal cell carcinoma (RCC) were recently released in the 7th edition of the AJCC Cancer Staging Manual.[7] T2 lesions are now stratified into T2a (7-10 cm) and T2b (>10 cm). Contiguous ipsilateral adrenal involvement is now defined as T4 disease, while an adrenal lesion separate from the primary mass is defined as M1. Stage T3a now includes renal vein tumour thrombus, and nodal involvement has been grouped together as N1. The staging of RCC is dynamic and retrospective reviews have defined pathological characteristics of prognostic significance within the same stage.[8] These have resulted in proposals for revision of the locally advanced RCC staging system.[9-11] The proposed substaging includes perinephric fat invasion, tumour thrombus of the renal vein or infradiaphragmatic inferior vena cava (IVC) (pT3a); perirenal fat invasion in association with adrenal gland invasion or tumour thrombus limited to the renal vein or infradiaphragmatic IVC (pT3b); tumour thrombus of the renal vein or infradiaphragmatic IVC with concomitant adrenal invasion, supradiaphragmatic tumour thrombus or extension through Gerota's fascia (pT4). Staging systems have not yet incorporated these recommendations, but these characteristics should be recorded and considered in estimating the prognosis in patients after radical nephrectomy (RN).

Diagnostic imaging of renal tumours

Imaging and blood work are essential for staging the follow up of patients after treatment of the mass. To date, the RCC histological subtype cannot be reliably predicted by imaging. There have been few changes in the role of cross-sectional imaging with computed tomography (CT) or magnetic resonance (MR) scanning of the abdomen. Chest radiographs are generally used in the evaluation of the lungs. The American Urological Association and European Association of Urology have endorsed CT as integral to the workup of a renal mass.[12,13] The Kidney Cancer Research Network of Canada suggests that CT of the chest is reasonable for T2 or greater masses, with little evidence to indicate chest CT as superior in the follow-up setting.[14,15] Bone and intracranial imaging are reserved for symptomatic patients.

The urology and radiology groups from the MD Anderson Cancer Center have recently detailed their protocol for an optimally performed CT of the abdomen in the staging of a renal mass.[16] They recommend unenhanced images in 5 mm increments to establish fat content, calcification and a baseline for comparison in evaluating enhancement. The kidneys are then targeted for arterial, portal venous (wherein the liver is best evaluated) and nephrographic phases; the entire urinary tract is then evaluated in the excretory phase. The role of CT and MR urography was recently investigated and optimized by Silverman and colleagues at Brigham and Women's Hospital in Boston, who detail their protocol for optimal renal imaging.[17] They similarly recommend unenhanced images initially and endorse the nephrographic phase (about 100 seconds post-contrast) as the best time to characterize a renal mass. Excretory phase images allow assessment of the urothelium. These are performed with an empty bladder, 900 cc of oral hydration, intravenous furosemide and maximum collimation of 1.0 mm, 10-15 minutes after contrast injection. The published radiation dose for these techniques however is 14.8 mSv. These imaging protocols are equivalent to 2 full abdominal and pelvic CTs, and a third investigation (nephrographic phase) limited to the kidneys. This raises concerns regarding radiation dose and its long-term effects, particularly in the case of repeated imaging in surveillance or follow up. Brenner and Hall note significant increases in the use of CT in practice, and highlight the mechanisms of DNA damage, as well as its relation to cancer risk.[18] They note that no specific prospective studies exist to detail the risks of CT in the development of cancer, and that the balance of data on the subject is obtained from applying CT radiation dose data to population data from atomic bomb survivors.[19] Attributable lifetime cancer risks from a single scan are age- and dose-related. The authors hypothesize that with current usage rates, radiation from CT could be responsible for 1.5% to 2.0% of all cancers in the United States. They highlight and sanction the use of technological advances to minimize individual exposure during CT, and recommend more judicious and sparing use of the modality when other examination types would suffice. However, there are no prospective data to support these concerns and the "linear no-threshold extrapolation model"

may not account for the body's potential to better repair/protect itself at very low doses.[20]

Magnetic resonance evaluation is also reasonable in patients with renal insufficiency and sensitivity to intravenous contrast agents. Gadolinium-enhanced MR is not without risk. Nephrogenic systemic fibrosis (NSF) is a risk with the use of gadolinium-based MR contrast agents in patients with renal insufficiency. An abnormal proliferation of fibroblasts in skin, liver, lung, heart and muscle can lead to organ dysfunction and immobility.[21] The authors of a recent systematic review of cohort studies suggest an odds ratio of 26.71 for the development of NSF in dialysis patients who received gadolinium-based contrast agents, with an incidence of 5.7% in 1393 patients versus 0.1% in 2953 controls.[21] The newer technology of diffusion-weighted imaging has shown promise in MR imaging of the kidneys without contrast.[22]

The role of positron emission tomography (PET) imaging in RCC is in evolution. A PET assesses tumour metabolic activity through the uptake of (classically) F-fluorodeoxyglucose (^{18}F-FDG). Studies comparing PET to CT in the diagnosis of renal primary tumours have shown excellent specificity but suboptimal sensitivity for PET.[23,24] The PET has shown increased accuracy in identifying metastatic disease in RCC patients, particularly in the setting of equivocal bone lesions on bone scan; improvements in sensitivity from 60% to 87% for bone scan up to 100% for ^{18}F-FDG-PET have been noted.[24,25] Relatively high specificity (75%-100%) and positive predictive value (77%-94%) have also been demonstrated in the assessment of suspected recurrent RCC.[26-29] Results have not been demonstrated to improve on conventional methods of surveillance, although they may mitigate the need for contrast exposure while capturing a whole-body image.

Another emerging technology in the evaluation of renal masses is contrast-enhanced ultrasound, in which microbubbles are used to create enhancement of vascular elements. A recent European study found excellent interobserver reliability and concordance between CT and ultrasound findings in complex cystic renal masses.[30] A recent Japanese study with histopathologic correlation and blinded evaluators found a specificity of 96.4% and a sensitivity of 77.3% for diagnosing RCC in a series of renal masses <5 cm that included a significant proportion of benign lesions.[31]

Choice of surgical technique for localized disease

With localized RCC, the cancer-specific survival rates are excellent with both partial and RN.[32,33] There are now emerging data that RN patients actually have a lower overall survival due to an increased rate of chronic renal insufficiency, and related cardiovascular disease.[33-36] In 2004, Go and colleagues reported the increased risk of cardiovascular events, hospitalization and death in patients with chronic renal insufficiency, with increasing hazard ratios proportional to a decrease in estimated glomerular filtration rate (GFR).[37] This is very relevant to the selection of surgical procedure and partial nephrectomy (PN) is now the procedure of choice for T1a tumours and increasingly for T2. The current focus on minimally invasive laparoscopic surgery is perpetuating radical nephrectomy for these smaller tumours as laparoscopic PN is difficult and cannot easily be done with cooling.

A recent retrospective review of 662 patients undergoing RN or PN for renal cortical tumours <4 cm was performed by Huang and colleagues; the review focused on renal functional outcomes.[35] There were no preoperative differences in renal function between the groups, but RN was associated with a significantly increased 3-year risk of development of a GFR <60 mL/min/1.73m^2 (hazard ratio 3.82). The authors estimated that 7% of PN patients and 43% of RN patients developed a GFR of less than 45 mL/min/1.73m^2 over 5 years. The same group created a nomogram to predict the 7-year probability of renal insufficiency after RN, with age, gender, preoperative creatinine and the percent change in renal volume as predictors.[36]

Lane and colleagues recently published results from 1169 patients undergoing PN for solitary tumours less than 7 cm. They found that preoperative GFR, age, gender, solitary kidney and warm ischemia time were significant predictors of the ultimate postoperative GFR in a multivariate analysis. Of these, only warm ischemia time is modifiable.[38] Only 29 patients experienced end-stage renal disease postoperatively, and these patients had a low median preoperative GFR of 23 mL/min/1.73m^2.

Zorn and colleagues found a significant difference in 6-month postoperative creatinine (88.7 vs. 64.2 mL/min/1.73m^2) in their review of 171 patients undergoing laparoscopic RN and 93 undergoing laparoscopic PN, respectively, without imperative indications for PN.[34] Mean operative time was 41 minutes longer in the partial nephrectomy group, with a mean of 37 minutes of warm ischemia; there was no preoperative difference between the groups regarding renal function.

Thompson and colleagues reported on 648 patients with normal antecedent renal function undergoing RN or PN from sporadic, solitary tumours less than 4 cm. They found that RN was associated with a relative risk of 2.16 for all-cause mortality versus PN in patients under age 65.[33] The potential for selection bias has been noted in this study, as those with higher medical risk or those requiring systemic anticoagulation tend to undergo RN, which may bias survival in the intermediate term in favour of the PN cohort A low event rate in the cohort less than age 65 mandated a univariate analysis

only in this study. A recent Surveillance, Epidemiology and End Results (SEER)-Medicare database analysis of patients undergoing RN or PN for masses <4 cm also found a significant increase in mortality in the RN cohort (hazard ratio 1.38), along with a significant increase in cardiovascular events.[39]

The overall survival after nephrectomy for RCC is different from the excellent overall survival in the donor nephrectomy population. A recent long-term analysis of donors revealed no increased mortality versus the general population at 40 years of follow-up.[40] The rate of end-stage renal disease in the donor population was 180 per million persons per year, compared to the population average of 268 per million persons per year. This may be a biased conclusion in that these donors, painstakingly screened to confirm low surgical and medical risk, are not reflective of the population of patients with renal masses.

Recent evidence, however, suggests that the uninvolved renal parenchyma in RCC nephrectomy specimens is abnormal. Bijol and colleagues recently published their findings in 110 nephrectomy specimens, and found that the "non-neoplastic" kidney was completely normal in only 10% of cases.[41] Twenty-eight percent of kidneys showed atherosclerotic changes, and the remaining 62% of kidneys had parenchymal abnormalities, including scarring, microangiopathic changes and diabetic glomerulosclerosis. Severe changes in this group correlated with a larger change in serum creatinine at 6 months than in patients with normal parenchyma adjacent to their tumours.

This recent data regarding intermediate- and long-term functional and survival outcomes in favour of nephron-sparing surgery for localized renal masses highlight the importance of the kidney operation performed (RN vs. PN), rather than the decreased short-term morbidity of the laparoscopic approach.

Thermal ablation therapies in small renal masses

The increased incidence of SRM diagnosis in the elderly and medically unfit patients and the perception of less invasiveness led to an increase in thermal ablative treatments, most commonly radiofrequency ablation (RFA) and cryotherapy, for localized renal tumours. Several recent studies have reported recurrence rates of less than 10% and excellent disease-specific survival rates of 95% to 100% in patients treated with thermal ablation.[42-53] Recent multi-institutional reviews noted recurrent or residual disease in 3.9% to 5.2% of cryoablation patients and 12.9% to 13.4% in RFA patients. These numbers are difficult to compare, as significantly more patients had cryotherapy performed via laparoscopy and RFA was performed percutaneously. There were differences in visualization, patient compliance and management of respiratory motion.[54] Only 2 of these series had a median follow-up of at least 5 years.[45,49] These data must be interpreted in the context of the natural history of SRMs, which have a slow growth rate and low lethality when followed expectantly.[55]

Early studies in patients undergoing PN immediately after RFA found residual viable tumour in 80% to 100% of cases.[56,57] Studies correlating imaging with post-RFA biopsy at later points revealed 35.2% of patients with residual cancer at 6 months (despite 85% having negative imaging studies); no patient was found to have viable tumour in the presence of negative imaging at 12 months.[58,59]

Longer follow-up in future studies, prospective and randomized studies, pre-procedure characterization of tumour biology and standardized follow-up will better define the true role and efficacy of these treatments.

Management of locally advanced disease

Although there has been more attention to the treatment of localized and metastatic kidney cancer, the management of the patient with locally advanced disease is also in evolution. Inferior vena cava thrombus represents a significant challenge to the surgeon, as do decisions regarding the management of regional lymph nodes and the ipsilateral adrenal gland. The original description of the RN by Robson and colleagues included the removal of the ipsilateral adrenal gland, as well as the dissection of the ipsilateral retroperitoneal lymph nodes from the crus of the diaphragm to the bifurcation of the aorta.[60] In the intervening years, evidence has accumulated that adrenalectomy and lymphadenectomy may not be necessary in most cases of RN.[61]

Management of the ipsilateral adrenal gland

The UCLA group has published their experience and opinions regarding the management of the adrenal with a series of 511 patients undergoing RN and ipsilateral adrenalectomy.[62] They noted 5.7% involvement of the adrenal in this series, with both direct local extension and hematogenous metastasis accounting for the adrenal involvement. Multifocality, upper pole lesions and associated renal vein involvement were present in most patients, although it was unclear whether univariate or multivariate statistical analysis was performed. This series highlighted the value of CT in predicting adrenal involvement, showing a 99.4% specificity and a 99.4% negative predictive value. A negative CT is effective in guiding the decision to spare the adrenal in RN. O'Malley and colleagues have recently published a systematic review regarding the need for adrenalectomy as part of RN.[63] Their analysis of 27 studies revealed an incidence of adrenal involvement at nephrectomy of 1.2% to 10%, although this included contralateral involvement in some series. Upper pole lesions, renal vein tumour thrombus, mul-

tifocality and T stage are independent predictors of adrenal gland involvement. They recommend that, in patients with no adrenal abnormality on preoperative imaging, only those with renal vein tumour thrombus or those with tumours 7 cm or greater in diameter located at the upper pole require ipsilateral adrenalectomy at the time of nephrectomy. The role of adrenalectomy has also been explored recently in the setting of PN.[64] Criteria for concomitant adrenalectomy included a suspicious nodule on preoperative imaging, or suggestion of involvement on intraoperative assessment. In this series of 2065 PNs, 48 adrenalectomies were performed. Forty-two (87%) of these were ultimately determined to be benign tissue, including adrenal hyperplasia or adenoma. Metachronous adrenalectomy was undertaken in 15 patients (0.43%), with radiographic suspicion of recurrence, of whom 11 (73%) were determined to have true recurrence of RCC on pathologic analysis. This study highlights both the low incidence of concomitant adrenal involvement in the partial nephrectomy population, as well as the low incidence of metachronous adrenal involvement, both of which bolster the argument against routine adrenal resection in RCC.

The role of regional lymphadenectomy in RCC

The European Organization for the Research and Treatment of Cancer (EORTC) published the results of EORTC 30881, a multicentre study which randomized 721 clinically node-negative patients with renal masses to undergo RN alone, or RN with complete ipsilateral retroperitoneal lymph node dissection. Median tumour size was 5.5-6 cm. The authors of the study found that only 4% of the latter patients had metastatic disease in the lymph nodes. At a median of 12.6 years of follow-up, there were no differences in time to progression, progression-free survival or overall survival between the 2 groups.[65] This study has been criticized for the low grade and stage of the lesions; it has been described as underpowered to identify a survival benefit to lymphadenectomy.[66] It does, however, suggest that omitting lymphadenectomy in lower stage patients does not adversely affect outcomes. This conclusion has been supported in practice, as it is more difficult to do a lymphadenectomy with laparoscopy.

The EORTC 30881 also shed light on the biology of palpably enlarged lymph nodes encountered at the time of surgery. In the lymphadenectomy cohort, 20% (10 of 51) of patients with palpable nodes harbored metastatic disease in the dissected packet, while in the nephrectomy-alone cohort there were 33 patients with palpably enlarged nodes, which were either biopsied or resected alone without complete lymphadenectomy, and 13% of these nodes were found to harbor disease.[65] Notable also is that the rate of lymph node metastasis in patients without a palpable abnormality at the time of surgery was only 1%.

There is evidence, however, that resection of nodal metastases in RCC can result in survival prolongation. The MD Anderson Cancer Center group published a retrospective look at 40 patients undergoing nephrectomy with complete ipsilateral lymphadenectomy with pathologically positive nodes and no evidence of systemic metastatic disease.[67] Median size of the lesions was 11 cm, and pathologic stage was pT3 and above in 80%. Thirty percent of patients had no evidence of disease at a median follow up of 17 months, while median cancer specific survival was 20.3 months. Pantuck and colleagues found an association between lymph node dissection and survival in their series of 112 patients undergoing nephrectomy with or without lymphadenectomy in the setting of clinically positive nodes.[68] Median survival was improved by 5 months in the lymphadenectomy group. No such survival benefit was found in patients with clinically negative nodes who underwent lymphadenectomy.

A recent series from the Mayo Clinic examined outcomes in resection of metachronous metastatic disease in the retroperitoneal lymph nodes in 15 patients previously treated with radical nephrectomy for RCC.[69] These recurrences were discovered at a median time from nephrectomy of 10.3 months. Ten patients experienced recurrence at a median of 6 months post-resection, and 6 patients died at a median of 18 months follow-up.

The data would therefore suggest that for most renal tumours with clinically negative regional nodes, lymphadenectomy does not improve survival. In those with clinically enlarged nodes and no evidence of distant metastatic disease, however, resection of disease confirmed pathologically may confer a survival advantage.

Renal vein and inferior vena cava tumour thrombus

Tumour thrombus extending into the renal vein and IVC presents a surgical challenge to the urologist and a markedly increased risk to the patient.

The group from Heidelberg, Germany reported survival data in 134 patients with IVC involvement with tumour thrombus.[70] The group found that patients undergoing nephrectomy for clinically localized tumours had the potential for prolonged survival (median 51.7 months) as compared to patients with nodal metastasis (10.7 months) or distant metastatic disease (6.9 months), or to those not undergoing surgery (6.9 months). It should be noted that immune therapy was used in some patients, and that this cohort was managed in the era before the use of targeted molecular inhibitors for treatment of advanced disease.

A multi-institutional review of 1192 such cases who underwent RN has recently been published.[71] The authors found that median survival was 52 months for patients with renal vein thrombus, 25.8 months for those with IVC thrombus median survival for infradiaphragmatic disease 25.8 months and 18 months for patients with supradiaphrag-

matic disease. They were however unable to show a difference in survival based on the level of IVC involvement. Prognostic variables elucidated on multivariate analysis in patients with tumour thrombus included IVC involvement, tumour size, perirenal fat invasion, lymph node metastasis and distant metastasis.

The Mayo group has further analyzed the subset of patients undergoing surgery for RCC with caval thrombus who require vascular bypass or IVC interruption.[72,73] They report that 25.6% of their IVC thrombus patients require bypass, and that among that group, venovenous bypass (VVB) can be selectively employed instead of cardiopulmonary bypass (CPB) in patients without infrarenal bland thrombus or hepatic vein involvement who were deemed unable to tolerate IVC clamping.[72] The VVB did not confer a survival advantage over CPB, but was associated with significant decreases in bypass time and surgical time, with trends toward decreased blood loss (1200 mL vs. 2725 mL) and transfusion volume. Vena cava interruption was employed in 25% of patients with IVC thrombus, via Greenfield filter (2.5%), ligation (14.4%) or segmental resection (8.1%), based on the degree of occlusion and bland thrombus.[73] The IVC interruption was tolerated without significant disability in all cases, and there was no cancer-specific survival difference between patients with or without IVC interruption.

As mentioned above, one large group has highlighted survival differences within groups currently assigned the same AJCC stage, and recommended a new grouping within T3 to reflect these changes, which often involve renal vein or IVC involvement alone or in convert with perirenal fat or adrenal involvement.[9-11]

Follow-up after surgical treatment of localized disease

Numerous investigators have undertaken retrospective reviews to elucidate those factors that influence recurrence of RCC after surgical management by RN or PN. Of these, pathologic tumour stage has been the most reliable predictor of recurrence risk, including time to recurrence and location of recurrence. Other parameters used have included tumour grade, tumour histology, necrosis, microvascular invasion and performance status.[74-77]

These investigations have led to the development of numerous follow-up schemes, detailing the timing of assessment by various means.[15,77-81] Signs, symptoms and performance status can be gleaned from the history and physical examination; serological tests can assess renal function, as well as provide information on the status of bone health via

	Months Post-op									
	3	6	12	18	24	30	36	48	60	72
pT1										
Hx & PE			x		x		x	x	x	x
Blood test			x		x		x	x	x	x
CXR			x		x		x	x	x	x
CT or U/S abd					x				x	
pT2										
Hx & PE		x	x	x	x	x	x	x	x	x
Blood test		x	x	x	x	x	x	x	x	x
CXR		x	x	x	x	x	x	x	x	x
CT or U/S abd			x				x		x	
pT3										
Hx & PE		x	x	x	x	x	x	x	x	x
Blood test		x	x	x	x	x	x	x	x	x
CXR		x	x	x	x	x	x	x	x	x
CT abd		x	x	x	x		x		x	
pTxN+										
Hx & PE	x	x	x	x	x	x	x	x	x	x
Blood test	x	x	x	x	x	x	x	x	x	x
CXR	x	x	x	x	x	x	x	x	x	x
CT abd	x	x	x	x	x	x	x	x	x	x

Hx & PE: history and physical examination
Blood test: include complete blood count, serum chemistries, and liver function tests
CXR: can be alternated with chest CT
CT abd: can be alternated with abdominal ultrasound in pT1-2N0 patients
* -if patient is symptomatic or abnormal blood test, earlier radiologic investigations may be indicated
-follow-up beyond 72 months, refer to text for more details

Fig. 1. Canadian Urological Association (CUA) recommendations for the follow up of patients after radical or partial nephrectomy. Reprinted from reference 15 with permission of the CUA.

alkaline phosphatase (ALP). Radiologic examination of the chest and abdomen are used to identify recurrences there, and imaging of the bones and brain are used as symptomatically indicated.

The Canadian Urological Association (CUA) has approved guidelines on the follow-up of patients following RN or PN for RCC (Fig. 1).[15] The CUA has adopted a stage-based follow-up protocol, acknowledging the merit of, but also the lack of, prospective validation of protocols based on other patient and tumour parameters. It is recommended that patients with PN be followed similarly to pT1 patients after RN, though a CT of the abdomen to assess the operative site at 3 months could be considered. Beyond 6 years, CT of the abdomen is recommended at 7 and 9 years postoperatively for pT2 disease, every 2 years for pT3 disease and yearly for patients with node-positive disease. History, physical examination, blood work and chest x-ray are recommended yearly beyond 6 years in all patients. Participants at the Canadian Kidney Cancer Forum have committed to using the guidelines, which will hopefully be validated by the Canadian Kidney Cancer Information System now being developed.

Advanced (metastatic) kidney cancer

Recent multicentre randomized, controlled clinical trials have established a new class of small molecule inhibitors as the first-line treatment of metastatic RCC.[82-84] Immune cytokine therapy with interferon-gamma or interleukin-2 is no longer the standard of care.[14] While this represents a significant shift in the treatment of advanced disease, it comes with an adverse effect profile that the treating physician must appreciate.[85] The Kidney Cancer Research Network of Canada recommends that these treatments be undertaken only under the guidance of oncology specialists with expertise in the toxicity, interactions and monitoring of patients on treatment.[14] Bhojani and colleagues recently published a systematic review of the toxicities associated with sorafenib, sunitinib and temsirolimus use.[85] This extensive review compiles adverse signs, symptoms and laboratory abnormalities data from Phase I through III studies. Importantly, they resist direct comparisons between the profiles of the agents, as they have not been directly compared in the same study, and have been used in patient populations with different performance statuses and at different stages in the treatment of their metastatic disease.

The European Association of Urology and The Canadian Kidney Cancer forums have recently published guidelines and a consensus statement based on the major Phase III studies of these 3 agents.[14,61,86] Sunitinib remains the first-line therapy in patients with metastatic RCC. Temsirolimus is the first-line therapy in poor prognosis patients with everolimus as an alternative, and sorafenib is the second-line therapy in patients who have failed prior cytokine immunotherapy. Benefit in progression-free survival can be seen when using a second agent in the event of failure on an initial agent. This is a changing field as new agents are introduced, usually with supporting randomized controlled trials, but there is little comparative data of the newer versus the more established agents.

The important role of cytoreductive nephrectomy in patients receiving systemic therapy was established by the Southwest Oncology Group and EORTC trials published in 2001, which demonstrated a survival advantage of 3 to 10 months in the group receiving interferon and nephrectomy compared to interferon alone.[87,88] In the era of targeted therapy, we do not know if there is still a benefit from cytoreductive nephrectomy. To date, no randomized prospective trials have been undertaken to specifically address this question. However, the large majority of patients in the major sunitinib and sorafenib trials underwent nephrectomy as part of their treatment.[82,89] The UCLA group has recently published that despite this dearth of direct evidence, "cytoreductive nephrectomy should be considered to have shown a survival benefit and should be used in appropriately selected patients with metastatic RCC receiving postsurgical systemic therapies."[90] The Kidney Cancer Research Network of Canada stated that cytoreductive nephrectomy is not likely to be harmful, and that the decision to perform it is "to be made based on clinical indications." The surgical feasibility of operating on patients who have received tyrosine kinase inhibitor therapy has been established, with no differences in surgical parameters and complications between those receiving systemic therapy and those undergoing nephrectomy alone.[91]

Conclusions

Renal cell carcinoma is a lethal, but interesting, urologic malignancy whose management has seen significant evolution in recent years. Needle core biopsy of SRM for diagnosis and of metastatic RCC for selection of therapy is becoming established with diffusion of necessary expertise. It is safe and uncomplicated in centres with experience. The staging system for RCC is changing gradually with substaging of T1 and T2 disease. Several pathological features, including invasion of perinephric fat, extent of venous thrombus, adrenal involvement, should be noted at the time of nephrectomy as they may be incorporated in future staging modifications. The technique and potential side effects of triphasic CT scan and MR imaging are better recognized and need to be considered when ordering these axial images. It is now clear that overall survival after RN is lower than after PN for localized disease, due to complications of chronic kidney disease in the remaining kidney. Open PN is preferable to laparoscopic nephrectomy, if laparoscopic PN is not available or suitable. Thermal ablation with RFA or cryotherapy

is an alternative to surgery but has increased rates of local recurrence which may or may not need further treatment in elderly/infirm patients. In clinically localized disease, adrenalectomy and lymphadenectomy do not need to be performed routinely at the time of nephrectomy. A follow-up protocol has been defined by the CUA as a guideline which should be considered after nephrectomy. Future database and prospective studies will further refine these findings and their impact, and will uncover new opportunities for further study and improvement of patient management.

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References

1. Canadian Cancer Society. *Canadian Cancer Statistics 2010*. Canadian Cancer Society; 2010.
2. Silver DA, Morash C, Brenner P, et al. Pathologic findings at the time of nephrectomy for renal mass. *Ann Surg Oncol* 1997;4:570-4.
3. Volpe A, Kachura JR, Geddie WR, et al. Techniques, safety and accuracy of sampling of renal tumours by fine needle aspiration and core biopsy. *J Urol* 2007;178:379-86.
4. Volpe A, Mattar K, Finelli A, et al. Contemporary results of percutaneous biopsy of 100 small renal masses: A single center experience. *J Urol* 2008;180:2333-7.
5. Lane BR, Samplaski MK, Herts BR, et al. Renal mass biopsy–a renaissance? *J Urol* 2008;179:20-7.
6. Laguna MP, Kummerlin I, Rioja J, et al. Biopsy of a renal mass: Where are we now? *Curr Opin Urol* 2009;19:447-53.
7. Edge SB, Byrd DR, Compton CC, et al., editors. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010.
8. Greene FL, Page DL, Fleming ID, et al., editors. *AJCC Cancer Staging Manual*. 6th ed. 6th ed. New York, NY: Lippincott Raven Publishers; 2002.
9. Ficarra V, Galfano A, Guille F, et al. A new staging system for locally advanced (pT3-4) renal cell carcinoma: A multicenter European study including 2,000 patients. *J Urol* 2007;178:418-24; discussion 423-4.
10. Ficarra V, Galfano A, Mancini M, et al. TNM staging system for renal-cell carcinoma: Current status and future perspectives. *Lancet Oncol* 2007;8:554-8.
11. Ficarra V, Novara G, Iafrate M, et al. Proposal for reclassification of the TNM staging system in patients with locally advanced (pT3-4) renal cell carcinoma according to the cancer-related outcome. *Eur Urol* 2007;51:722,9; discussion 729-31.
12. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. *J Urol* 2009;182:1271-9.
13. Ljungberg B, Hanbury DC, Kuczyk MA, Merseburger AS, Mulders PFA, Patard J, et al. Guidelines on renal cell carcinoma. European Association of Urology. http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Full/RCC.pdf. Accessed April 18, 2011.
14. Canadian Kidney Cancer Forum 2008. Management of kidney cancer: Canadian kidney cancer forum consensus statement. *Can Urol Assoc J* 2008;2:175-82.
15. Kassouf W, Siemens R, Morash C, et al. Follow-up guidelines after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma. *Can Urol Assoc J* 2009;3:73-6
16. Ng CS, Wood CG, Silverman PM, et al. Renal cell carcinoma: Diagnosis, staging, and surveillance. *AJR Am J Roentgenol* 2008;191:1220-32.
17. Silverman SG, Leyendecker JR, Amis ES Jr. What is the current role of CT urography and MR urography in the evaluation of the urinary tract? *Radiology* 2009;250:309-23.
18. Brenner DJ, Hall EJ. Computed tomography–an increasing source of radiation exposure. *N Engl J Med* 2007;357:2277-84.
19. Hall EJ, Brenner DJ. Cancer risks from diagnostic radiology. *Br J Radiol* 2008;81:362-78.
20. Tubiana M. Computed tomography and radiation exposure. *N Engl J Med* 2008;358:850; discussion 852-3.
21. Agarwal R, Brunelli SM, Williams K, et al. Gadolinium-based contrast agents and nephrogenic systemic fibrosis: A systematic review and meta-analysis. *Nephrol Dial Transplant* 2009;24:856-63. Epub 2008 Oct 24.
22. Kim S, Naik M, Sigmund E, et al. Diffusion-weighted MR imaging of the kidneys and the urinary tract. *Magn Reson Imaging Clin N Am* 2008;16:585-96.
23. Kang DE, White RL Jr, Zuger JH, et al. Clinical use of fluorodeoxyglucose F 18 positron emission tomography for detection of renal cell carcinoma. *J Urol* 2004;171:1806-9.
24. Aide N, Cappele O, Bottet P, et al. Efficiency of [^{18}F]FDG PET in characterizing renal cancer and detecting distant metastases: a comparison with CT. *Eur J Nucl Med Mol Imaging* 2003;30:1236-45.
25. Wu H, Yen R, Shen Y, et al. Comparing whole body ^{18}F-2-deoxyglucose positron emission tomography and technetium-99m methylene diphosphate bone scan to detect bone metastases in patients with renal cell carcinomas—a preliminary report. *J Cancer Res Clin Oncol* 2002;128:503-6.
26. Ramdave S, Thomas GW, Berlangieri SU, et al. Clinical role of F-18 fluorodeoxyglucose positron emission tomography for detection and management of renal cell carcinoma. *J Urol* 2001;166:825-30.
27. Jadvar H, Kherbache HM, Pinski JK, et al. Diagnostic role of [F-18]-FDG positron emission tomography in restaging renal cell carcinoma. *Clin Nephrol* 2003;60:395-400.
28. Dilhuydy MS, Durieux A, Pariente A, et al. PET scans for decision-making in metastatic renal cell carcinoma: a single-institution evaluation. *Oncology* 2006;70:339-44.
29. Park JW, Jo MK, Lee HM. Significance of 18F-fluorodeoxyglucose positron-emission tomography/computed tomography for the postoperative surveillance of advanced renal cell carcinoma. *BJU Int* 2009;103:615-9.
30. Ascenti G, Mazziotti S, Zimbaro G, et al. Complex cystic renal masses: Characterization with contrast-enhanced US. *Radiology* 2007;243:158-65.
31. Fan L, Lianfang D, Jinfang X, et al. Diagnostic efficacy of contrast-enhanced ultrasonography in solid renal parenchymal lesions with maximum diameters of 5 cm. *J Ultrasound Med* 2008;27:875-85.
32. Leibovich BC, Blute ML, Cheville JC, et al. Nephron sparing surgery for appropriately selected renal cell carcinoma between 4 and 7 cm results in outcome similar to radical nephrectomy. *J Urol* 2004;171:1066-70.
33. Thompson RH, Boorjian SA, Lohse CM, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. *J Urol* 2008;179:468-71; discussion 472-3.
34. Zorn KC, Gong EM, Orvieto MA, et al. Comparison of laparoscopic radical and partial nephrectomy: Effects on long-term serum creatinine. *Urology* 2007;69:1035-40.
35. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: A retrospective cohort study. *Lancet Oncol* 2006;7:735-40.
36. Sorbellini M, Kattan MW, Snyder ME, et al. Prognostic nomogram for renal insufficiency after radical or partial nephrectomy. *J Urol* 2006;176:472-6; discussion 476.
37. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351:1296-305.
38. Lane BR, Babineau DC, Poggio ED, et al. Factors predicting renal functional outcome after partial nephrectomy. *J Urol* 2008;180:2363-8; discussion 2368-9.
39. Huang WC, Elkin EB, Levey AS, et al. Partial nephrectomy versus radical nephrectomy in patients with small renal tumours–is there a difference in mortality and cardiovascular outcomes? *J Urol* 2009;181:55-61; discussion 61-2.
40. Ibrahim HN, Foley R, Tan L, et al. Long-term consequences of kidney donation. *N Engl J Med* 2009;360:459-69.
41. Bijol V, Mendez GP, Hurwitz S, et al. Evaluation of the nonneoplastic pathology in tumour nephrectomy specimens: Predicting the risk of progressive renal failure. *Am J Surg Pathol* 2006;30:575-84.
42. Gervais DA, McGovern FJ, Arellano RS, et al. Radiofrequency ablation of renal cell carcinoma: Part 1, indications, results, and role in patient management over a 6-year period and ablation of 100 tumours. *AJR Am J Roentgenol* 2005;185:64-71.
43. Park S, Anderson JK, Matsumoto ED, et al. Radiofrequency ablation of renal tumours: Intermediate-term results. *J Endourol* 2006;20:569-73.
44. Zagoria RJ, Traver MA, Werle DM, et al. Oncologic efficacy of CT-guided percutaneous radiofrequency ablation of renal cell carcinomas. *AJR Am J Roentgenol* 2007;189:429-36.
45. Levinson AW, Su LM, Agarwal D, et al. Long-term oncological and overall outcomes of percutaneous radio frequency ablation in high risk surgical patients with a solitary small renal mass. *J Urol* 2008;180:499-504; discussion 504.
46. Wyler SF, Sulser T, Ruszat R, et al. Intermediate-term results of retroperitoneoscopy-assisted cryotherapy for small renal tumours using multiple ultrathin cryoprobes. *Eur Urol* 2007;51:971-9.
47. Weld KJ, Figenshau RS, Venkatesh R, et al. Laparoscopic cryoablation for small renal masses: Three-year follow-up. *Urology* 2007;69:448-51.
48. Lehman DS, Hruby GW, Phillips CK, et al. First prize (tie): Laparoscopic renal cryoablation: Efficacy and complications for larger renal masses. *J Endourol* 2008;22:1123-7.
49. Aron M, Kazumi K, Haber G, et al. Laparoscopic renal cryoablation long-term oncologic outcomes with minimum 5-year follow-up. *J Urol* 2008;179(4S):209-10.
50. Atwell TD, Farrell MA, Leibovich BC, et al. Percutaneous renal cryoablation: Experience treating 115 tumours. *J Urol* 2008;179:2136-40; discussion 2140-1.

51. Caviezel A, Terraz S, Schmidlin F, et al. Percutaneous cryoablation of small kidney tumours under magnetic resonance imaging guidance: Medium-term follow-up. *Scand J Urol Nephrol* 2008;42:412-6.
52. Finley DS, Beck S, Box G, et al. Percutaneous and laparoscopic cryoablation of small renal masses. *J Urol* 2008;180:492-8; discussion 498.
53. Leveridge MJ, Mattar K, Kachura J, et al. Assessing outcomes in probe ablative therapies for small renal masses. *J Endourol* 2010;24:759-64.
54. Cadeddu JA, Raman JD. Renal tumour ablation is a function of patient selection and technique–not the ablation technology. *Cancer* 2008;113:2623-6.
55. Chawla SN, Crispen PL, Hanlon AL, et al. The natural history of observed enhancing renal masses: Meta-analysis and review of the world literature. *J Urol* 2006;175:425-31.
56. Michaels MJ, Rhee HK, Mourtzinos AP, et al. Incomplete renal tumour destruction using radio frequency interstitial ablation. *J Urol* 2002;168:2406-9; discussion 2409-10.
57. Rendon RA, Kachura JR, Sweet JM, et al. The uncertainty of radio frequency treatment of renal cell carcinoma: Findings at immediate and delayed nephrectomy. *J Urol* 2002;167:1587-92.
58. Weight CJ, Kaouk JH, Hegarty NJ, et al. Correlation of radiographic imaging and histopathology following cryoablation and radio frequency ablation for renal tumours. *J Urol* 2008;179(4):1277,81; discussion 1281-3.
59. Raman JD, Stern JM, Zeltser I, et al. Absence of viable renal carcinoma in biopsies performed more than 1 year following radio frequency ablation confirms reliability of axial imaging. *J Urol* 2008;179:2142-5.
60. Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. *J Urol* 1969;101:297-301.
61. Canadian Kidney Cancer Forum 2009. Management of kidney cancer: Canadian Kidney Cancer Forum Consensus Update. *Can Urol Assoc J* 2009;3:200-4.
62. Tsui KH, Shvarts O, Barbaric Z, et al. Is adrenalectomy a necessary component of radical nephrectomy? UCLA experience with 511 radical nephrectomies. *J Urol* 2000;163:437-41.
63. O'Malley RL, Godoy G, Kanofsky JA, et al. The necessity of adrenalectomy at the time of radical nephrectomy: A systematic review. *J Urol* 2009;181:2009-17. Epub 2009 Mar 14.
64. Lane BR, Tiong HY, Campbell SC, et al. Management of the adrenal gland during partial nephrectomy. *J Urol* 2009;181:2430-6; discussion 2436-7.
65. Blom JH, van Poppel H, Marechal JM, et al. Radical nephrectomy with and without lymph-node dissection: Final results of european organization for research and treatment of cancer (EORTC) randomized phase 3 trial 30881. *Eur Urol* 2009;55:28-34. Epub 2008 Oct 1.
66. Margulis V, Wood CG. The role of lymph node dissection in renal cell carcinoma: The pendulum swings back. *Cancer J* 2008;14:308-14.
67. Canfield SE, Kamat AM, Sanchez-Ortiz RF, et al. Renal cell carcinoma with nodal metastases in the absence of distant metastatic disease (clinical stage TxN1-2M0): The impact of aggressive surgical resection on patient outcome. *J Urol* 2006;175(3 Pt 1):864-9.
68. Pantuck AJ, Zisman A, Dorey F, et al. Renal cell carcinoma with retroperitoneal lymph nodes: Role of lymph node dissection. *J Urol* 2003;169:2076-83.
69. Boorjian SA, Crispen PL, Lohse CM, et al. Surgical resection of isolated retroperitoneal lymph node recurrence of renal cell carcinoma following nephrectomy. *J Urol* 2008;180:99-103; discussion 103.
70. Haferkamp A, Bastian PJ, Jakobi H, et al. Renal cell carcinoma with tumour thrombus extension into the vena cava: Prospective long-term followup. *J Urol* 2007;177:1703-8.
71. Wagner B, Patard JJ, Mejean A, et al. Prognostic value of renal vein and inferior vena cava involvement in renal cell carcinoma. *Eur Urol* 2009;55:460. Epub 2008 Aug 5.
72. Granberg CF, Boorjian SA, Schaff HV, et al. Surgical management, complications, and outcome of radical nephrectomy with inferior vena cava tumour thrombectomy facilitated by vascular bypass. *Urology* 2008;72:148-52.
73. Blute ML, Boorjian SA, Leibovich BC, et al. Results of inferior vena caval interruption by greenfield filter, ligation or resection during radical nephrectomy and tumour thrombectomy. *J Urol* 2007;178:440-5; discussion 444.
74. Frank I, Blute ML, Cheville JC, et al. An outcome prediction model for patients with clear cell renal cell carcinoma treated with radical nephrectomy based on tumour stage, size, grade and necrosis: The SSIGN score. *J Urol* 2002;168:2395-400.
75. Kattan MW, Reuter V, Motzer RJ, et al. A postoperative prognostic nomogram for renal cell carcinoma. *J Urol* 2001;166:63-7.
76. Sorbellini M, Kattan MW, Snyder ME, et al. A postoperative prognostic nomogram predicting recurrence for patients with conventional clear cell renal cell carcinoma. *J Urol* 2005;173:48-51.
77. Zisman A, Pantuck AJ, Wieder J, et al. Risk group assessment and clinical outcome algorithm to predict the natural history of patients with surgically resected renal cell carcinoma. *J Clin Oncol* 2002;20:4559-66.
78. Levy DA, Slaton JW, Swanson DA, et al. Stage specific guidelines for surveillance after radical nephrectomy for local renal cell carcinoma. *J Urol* 1998;159:1163-7.
79. Ljungberg B, Alamdari FI, Rasmuson T, et al. Follow-up guidelines for nonmetastatic renal cell carcinoma based on the occurrence of metastases after radical nephrectomy. *BJU Int* 1999;84:405-11.
80. Skolarikos A, Alivizatos G, Laguna P, et al. A review on follow-up strategies for renal cell carcinoma after nephrectomy. *Eur Urol* 2007;51:1490-500; discussion 1501.
81. Stephenson AJ, Chetner MP, Rourke K, et al. Guidelines for the surveillance of localized renal cell carcinoma based on the patterns of relapse after nephrectomy. *J Urol* 2004;172:58-62.
82. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. *N Engl J Med* 2007;356:125-34.
83. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med* 2007;356:2271-81.
84. Motzer RJ, Hutson TE, Tomczak P, et al. Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. *J Clin Oncol* 2009;27:3584-90.
85. Bhojani N, Jeldres C, Patard JJ, et al. Toxicities associated with the administration of sorafenib, sunitinib, and temsirolimus and their management in patients with metastatic renal cell carcinoma. *Eur Urol* 2008;53:917-30.
86. Patard JJ. European association of urology guidelines for systemic therapy in metastatic renal cell carcinoma: What is recommended and why? *Eur Urol Suppl* 2008;7:46-54.
87. Flanigan RC, Salmon SE, Blumenstein BA, et al. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. *N Engl J Med* 2001;345:1655-9.
88. Mickisch GH, Garin A, van Poppel H, et al., European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Group. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: A randomised trial. *Lancet* 2001;358:966-70.
89. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med* 2007;356:115-24.
90. Pantuck AJ, Belldegrun AS, Figlin RA. Cytoreductive nephrectomy for metastatic renal cell carcinoma: Is it still imperative in the era of targeted therapy? *Clin Cancer Res* 2007;13(2 Pt 2):693s-6s.
91. Margulis V, Matin SF, Tannir N, et al. Surgical morbidity associated with administration of targeted molecular therapies before cytoreductive nephrectomy or resection of locally recurrent renal cell carcinoma. *J Urol* 2008;180:94-8.

Correspondence: Dr. Michael A.S. Jewett, Division of Urology, University of Toronto, 610 University Ave, 3-124, Toronto, ON M5G 2C4; fax: 416-598-9997; m.jewett@utoronto.ca