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Title

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Permalink

<https://escholarship.org/uc/item/96f4b58v>

Journal

Nature Reviews Nephrology, 14(4)

ISSN

1759-5061

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Publication Date

2018-04-01

DOI

10.1038/nrneph.2018.10

Peer reviewed

The role of nephrologists in the management of small renal masses

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Renal cell carcinoma (RCC) is the most common malignancy seen in the nephrology clinic, yet most nephrologists have inadequate knowledge of current treatment options. Here we discuss RCC presentation and therapies, including potential renal adverse effects, and highlight the need for involvement of nephrologists in the multidisciplinary management of this disease.

The biology and clinical behaviour of kidney cancer — the most common malignancy seen in nephrology practice — is generally missing from the education of nephrologists. This state of affairs is all the more puzzling because of the interesting biology of kidney cancer and the opportunities for cutting-edge research. The field of onconeurology has now been recognized by the nephrology community, but the main focus is on the renal responses and adverse events that occur as a result of the treatment of non-renal malignancies, rather than on kidney cancer. With this Comment, we hope to promote the concept that nephrologists should be aware of the biology of renal cell carcinoma (RCC) and understand the effects of its presence in the setting of chronic kidney disease (CKD) and of its treatment on the incidence and progression of CKD.

The need for nephrology input

Most nephrologists have found a renal mass during the standard work-up of acute kidney injury (AKI) or asymptomatic haematuria, generally occurring consequent to renal ultrasound to rule out obstruction. The usual reaction in this situation is to consult urology and, once the AKI is resolved, the patient is lost to nephrology follow-up. This approach is ill-advised because approximately one-quarter of patients with RCC have CKD on presentation and RCC treatment is associated with AKI, hypertension and CKD progression. Many targeted and immune checkpoint inhibitor therapies for RCC are associated with complications as diverse as acute tubular necrosis, tubulointerstitial nephritis and hypertension. Moreover, AKI in patients with RCC is strongly associated with new onset of CKD. All of these issues require the input of a nephrologist for diagnostic and therapeutic advice and management, both before and after treatment.

RCC in patients with kidney disease

Patients with CKD have a markedly high incidence of RCC. In particular, the risk of RCC among patients with end-stage renal disease (ESRD) is 100-fold greater than that of the general population, resulting in an

incidence of up to 7%, which has been attributed to the high burden of acquired cystic kidney disease (ACKD) in patients on dialysis. Shared risk factors for RCC and CKD, including hypertension and diabetes mellitus, seem not only to contribute to CKD progression but also to promote an inflammatory milieu that is conducive to cancer induction. The risk of RCC might also be related to glomerular filtration rate (GFR) as this risk seems to increase with CKD stage among patients who are not on dialysis¹. Albuminuria, an early presentation of a variety of renal diseases, has also been linked to RCC.

The association of RCC with poor kidney function was elegantly demonstrated in transplant recipients, among whom the incidence of RCC rose with graft failure and fell with re-transplantation². Given these compelling data, the question arises as to whether nephrologists should screen for renal cancers in the CKD and ESRD populations. At present, routine screening of patients on dialysis is not regularly performed. Current practice is supported by an analysis that showed no clear survival benefit of ACKD screening in the ESRD population³. In our opinion, however, yearly screening with computed tomography for young patients with ESRD, in whom the benefits of RCC treatment would outweigh the risks of surgery, would be prudent. Screening of transplant candidates for RCC is more widely accepted, even though transplant recipients who develop RCC have a more favourable prognosis than their dialysis-dependent peers or the general population. The issue of screening for kidney cancer remains controversial and requires the attention of nephrologists as well as further deliberations in the light of continually accruing data.

Management of RCC

Currently, the urological community, with oncological consultation, takes primary responsibility for the management of small renal masses. Nephrology involvement is not routine and is often deferred unless complications of AKI or CKD have occurred. The delay in nephrology care is partially related to the lack of consultation but also due

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doi:10.1038/nrneph.2018.10
Published online 5 Feb 2018

Box 1 | Nephrology management of patients with small renal masses

Preoperative evaluation

- CKD screening and staging (KDIGO criteria)
 - Measure serum creatinine for eGFR calculation
 - Check urine for albuminuria and/or proteinuria
- Criteria for nephrology referral
 - eGFR <45 ml/min/1.73 m² or <60 ml/min/1.73 m² with proteinuria, diabetes mellitus or resistant hypertension
 - High risk of AKI indicating avoidance of nephrotoxins
 - Other considerations: tobacco use and obesity

Operative management

- Prioritize partial nephrectomy for patients with the following:
 - CKD or proteinuria (those at highest risk of end-stage renal disease)
 - Solitary kidney or bilateral tumours
 - Familial renal cell carcinoma
- Consider other nephron-sparing procedures (thermal ablation or laparoscopic procedures) for patients with high operative risk
- Evaluate adjacent non-cancerous tissue for kidney disease (discuss with nephropathologist)

Postoperative management

- Kidney function surveillance
 - Monitor serum creatinine and eGFR
 - Check for albuminuria and/or proteinuria
- Optimize blood pressure in patients with hypertension
- Optimize glycaemic control in patients with diabetes
- Treat albuminuria and/or proteinuria
- Address cardiovascular risk factors (tobacco use, hyperlipidaemia and obesity)
- Evaluate and treat concurrent renal disease diagnosed on biopsy
- Manage CKD if present

Recommendations are based on the American Urological Association guideline on renal mass and localized renal cancer⁴. AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes.

to the indifference of nephrologists regarding their role in the treatment of RCC and the increasing specialization and fragmentation of the health-care system.

In May 2017, the American Urological Association (AUA) published a guideline on renal mass and localized renal cancer, with input from the American Society of Nephrology and the College of American Pathologists⁴. This guideline promotes a working relationship between nephrologists, pathologists, oncologists, radiologists and urologists, and emphasizes counselling, diagnosis and management that incorporates kidney disease assessment, GFR preservation and diagnosis of kidney pathology⁴ (BOX 1). Nephrology referral is recommended for patients with CKD, particularly those who have diabetes mellitus or are expected to experience a decline in GFR after surgery. Independent of nephrology referral, the guidelines advocate for CKD risk assessment with preoperative screening to evaluate serum creatinine and proteinuria levels for CKD staging according to the KDIGO classification. Optimal blood pressure and glycaemic control as well as careful attention to medication regimens to minimize nephrotoxicity may help to reduce the risk of AKI.

The historical treatment of renal masses was total nephrectomy, often without first obtaining a biopsy sample to confirm malignancy. This approach occasionally led to unnecessary surgery and resulted in excessive

morbidity and mortality, especially among elderly and extant patients with CKD. The current dogma in the urology community is to consider partial over radical nephrectomy in many cases, and the risk of tumour seeding with RCC biopsy has been largely debunked². Surprisingly, the rate of AKI following nephrectomy increased from 2% to 10.4% over the past decade, possibly owing to an ageing population with a greater prevalence of comorbidities, including more advanced CKD⁵. As AKI can lead to CKD or contribute to CKD progression, minimization of AKI risk is particularly important in patients with loss of nephron mass.

In the EORTC randomized controlled trial, the incidence of moderate renal dysfunction (estimated (e)GFR 30 to <60 ml/min/1.73 m²) following surgery for a small renal mass was significantly lower with partial nephrectomy than with radical nephrectomy⁶. The incidence of more advanced CKD (eGFR <30 ml/min/1.73 m²) was also slightly lower following partial nephrectomy, but this difference was not statistically significant. Oncological survival was similar in both nephrectomy groups but the incidence of renal cancer-related deaths was low. The AUA guidelines, therefore, recommend prioritizing partial nephrectomy for small renal masses⁵. Partial nephrectomy is also recommended for patients with comorbid diseases that are thought to affect kidney function, such as diabetes mellitus, severe hypertension, recurrent urolithiasis and morbid obesity⁴. Non-surgical, nephron-sparing procedures including thermal ablation offer greater GFR preservation for individuals with high surgical risk. Active surveillance has similar oncologic outcomes to nephrectomy and is associated with lower CKD risk in select groups, particularly in the elderly population².

Future perspectives

The traditional lack of a role for nephrologists in the diagnosis and management of RCC is slowly changing concomitant with an awareness of onconeurology as a key part of the training and practice of a kidney physician. Given the complexity and intellectual challenge of RCC biology, the shared RCC and CKD risk factors and the adverse renal events that are associated with the treatment of RCC, the need for input of nephrologists into the teams that manage this disease is all the more pressing.

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Acknowledgements

R.H.W.'s work is supported by NIH grant 1R01DK107416-01A1 and by a grant from Dialysis Clinics Incorporated.

Competing interests

The authors declare no competing interests.