Management of the Incidental Kidney Mass in the Nephrology Clinic

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Introduction
The most common urologic malignancy seen in the nephrology clinic is clear cell renal cell carcinoma (RCC), which is generally asymptomatic and often found incidentally during imaging. Greater than 25% of patients with RCC have concomitant CKD at diagnosis, presumably because of overlapping risk factors (1). CKD and unrecognized concurrent nonmalignant kidney disease are parts of the equation that greatly benefit from the nephrologist’s expertise and management decisions. In addition, the new medical therapies, albeit providing invaluable benefit to the patient, are associated with kidney-related adverse effects, which are best managed in close collaboration between the urologist and/or oncologist and the nephrologist. Here, we provide management recommendations useful both before and during surgical and oncologic referral of patients with kidney cancer.

Discussion
Preoperative CKD Risk Factors
RCC commonly presents as an incidental finding of a localized kidney mass in a patient who has shared CKD/RCC risk factors, including advanced age, smoking history, and comorbidities of diabetes mellitus, hypertension, and obesity (1). The prevalence rates of diabetes and hypertension in patients with RCC are 20% and 50%, respectively. The presence of preexisting CKD at surgery doubles the risk of eGFR decline from this intervention, whereas the presence of diabetes alone increases the probability of developing postoperative CKD significantly compared with the overall cohort with small kidney masses. Even albuminuria at baseline predisposed patients to eGFR decline after surgical resection of a kidney mass (1).

Preoperative CKD Evaluation and Management
In patients with RCC undergoing surgery, we recommend preoperative evaluation, including serum creatinine measurement for eGFR and urinalysis for proteinuria assessment. The nephrologist may need to order these tests, because many surgeons do not regularly do this, although it is now recommended by the American Urological Association (AUA) and the American Society of Clinical Oncology (ASCO) according to the 2017 “Renal mass and localized renal cancer: AUA guideline” (2) as well as the 2017 “Management of small renal masses: American Society of Clinical Oncology clinical practice guideline” (3). Nephrology referral is recommended for patients with known CKD, including individuals with proteinuria, diabetes, or poor BP control. Differential function using nuclear scintigraphy may help predict postoperative GFR; however, it tends to underestimate GFR, and surgical factors may have a larger effect on GFR (4). Additionally, nephrology follow-up will be essential for preservation of what will be the “remaining” GFR, optimization of BP, glycemic control and antiproteinuric treatment, and continuing medication review.

Contacting the pathologist before surgery will ensure that the noncancerous kidney tissue for other unsuspected kidney diseases is evaluated (5), which would allow for diagnosis as well as optimal long-term prognostication, management, and follow-up of CKD.

Nephron-Sparing Approaches and CKD
Minimizing nephron loss for T1a kidney masses or Bosniak 3/4 complex cysts or with solitary kidney, in particular, should be prioritized with either partial nephrectomy or thermal ablation to lower the risk of CKD onset or its progression according to current AUA/ASCO guidelines. Oncologic outcomes for nephron-sparing procedures are similar to radical nephrectomy; CKD risk reduction (61%) was better for partial compared with radical nephrectomy, and overall survival and oncologic survival for partial nephrectomy were 19% and 29%, respectively, lower than with radical nephrectomy in meta-analyses (1). Although such favorable survival was not clearly seen in the sole randomized, controlled trial, the European Organization for Research and Treatment of Cancer Study (6), kidney protection was apparent, with fewer patients reaching eGFR<60 ml/min per 1.73 m² after partial versus radical nephrectomy (7). For these reasons, we suggest that it is the nephrologist’s role to advocate for the partial nephrectomy approach in patients with small kidney masses where oncologic survival is high, particularly for those with at least some CKD risk.

Nonsurgical nephron-sparing procedures, such as thermal ablation, have overall and oncologic survival rates similar to that of partial nephrectomy among
those with small kidney masses. Oncologic progression with ablative therapies may be greater with more advanced-stage tumors, but ablative therapies are associated with lower procedure-related morbidity, hospitalization, and eGFR decline (8). The major advantage of ablative therapies is the lower operative risk and greater GFR preservation, particularly for those who are poor surgical candidates with high cardiovascular disease burden or poor kidney function. Percutaneous core biopsy of kidney masses, required before ablative therapies, has been found to be safe with minimal risk of tumor seeding, and it has a high concordance rate with surgical diagnosis. We recommend kidney biopsy in patients in whom the tumor is suspected to be noncancerous by diagnostic imaging criteria or there is any diagnostic uncertainty, particularly in frail patients, or patients who are initially reluctant to undergo surgical intervention (1,2).

Alternatively, active surveillance with scheduled monitoring and planned intervention when necessary had equivalent oncologic outcomes to nephron-sparing procedures for a select group (9). The AUA and the ASCO guidelines support active surveillance as a viable treatment option, particularly for those with masses <2 cm or high surgical risk (2,3). We recommend that nephrologists counsel this high-risk population about such treatment options, particularly those individuals at risk for new-onset CKD or CKD progression, in collaboration with surgical colleagues.

Advocacy by the nephrologist for preoperative assessment of CKD risk and encouragement of nephron-sparing

Figure 1. The recommended workup and management of a kidney mass is a multidisciplinary approach including the nephrologist and urologist. AIN, acute interstitial nephritis; CPI, immune checkpoint inhibitor; CT, computed tomography; DM, diabetes mellitus; HTN, hypertension; RCC, renal cell carcinoma; Rx, therapy; TKI, tyrosine kinase inhibitor.
procedures should occur early in the course of patient management, well before the possible onset of postoperative CKD, to provide the best chances for preservation of kidney function. Although the risk of CKD progression as well as mortality among those with surgically induced CKD seems to be less likely than that related to medically induced CKD, ongoing postoperative management of CKD due to surgical parenchymal loss by the nephrologist should be similar to that of those patients with medical CKD (10).

Advanced RCC and Kidney Complications
Therapy for patients with advanced clear cell RCC has evolved considerably in the past decade. Before 2005, the widely used systemic agents were IFN-α and IL-2, which yielded, at best, modest efficacy, albeit with substantial toxicity. After 2005, angiogenesis inhibitors and mammalian target of rapamycin pathway inhibitors displaced standard cytokine therapy, but these agents are associated with hypertension or proteinuria (treated medically with antihypertensive or antiproteinuric agents) and a high degree of resistance after a few years. More recently, the use of immune checkpoint inhibitors in combination therapy has become a promising choice, with impressive responses, although accompanied by occasional serious autoimmune-type adverse effects, such as acute interstitial nephritis, which are generally treatable with drug discontinuation and steroids. As many of the adverse effects of these advanced RCC therapeutics are nephrologic in nature (e.g., hypertension, AKI, and acute interstitial nephritis), the nephrologist needs to be aware of them for effective comanagement in concert with the oncologist and/or the urologist (1).

Conclusions
Asymptomatic kidney masses are commonly seen in the daily practice of nephrology, but the management of this issue is a topic under-represented in the nephrology curriculum and at professional meetings among both trainees and seasoned nephrologists. As we have discussed in this article, there are several key take-home points that we believe the nephrologist will find useful, the most important being the need for the nephrologist to play an active role in the multidisciplinary team diagnosing and managing patients with kidney cancer (Figure 1). Active nephrologist participation in RCC management will help minimize the substantial kidney morbidity associated with the cancer itself and the highly prevalent and concurrent incidence as well as progression of CKD in this patient population.

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Disclosures
None.

References
10. Lane BR, Campbell SC, Demirjian S, Fergany AF; Surgically induced chronic kidney disease may be associated with a lower risk of progression and mortality than medical chronic kidney disease. J Urol 189: 1649–1655, 2013

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