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News and topics

Small renal mass management in the elderly and the calibration of risk

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Abstract

Due to the increased utilization of cross-sectional imaging and prolonged life expectancy, the incidence of incidentally diagnosed renal tumors continues to rise. While partial nephrectomy is currently recommended as the gold standard treatment of cT1a small renal mass whenever technically feasible, the perceived benefits of partial nephrectomy may not be applicable to all patient groups. Selecting between treatment options in elderly and the infirm can present a significant challenge. Informed and thoughtful small renal mass management decisions require consideration and balance of patient, tumor, and procedural risks to maintain oncological efficacy while minimizing treatment associated morbidity. Herein we review the comparative effectiveness of partial versus radical nephrectomy in the elderly and the role of standardized tools to quantify risk.

Keywords: Partial nephrectomy; Radical nephrectomy; Kidney cancer

Increased use of abdominal imaging has led to a significant downward stage migration and increased incidental detection of localized small renal mass (SRM) [1]. A concurrent increase in the median age at renal cell carcinoma (RCC) diagnosis has also been observed, with the greatest increase in incidence among patients aged 70 to 90 years [2]. With increased utilization of cross-sectional imaging and prolonged life expectancy, the incidence of incidentally diagnosed renal tumors in the elderly will continue to rise [3]. Current practice guidelines recommend partial nephrectomy for treatment of cT1a SRMs whenever technically feasible [4]. Nephron preservation may prevent the sequelae of chronic kidney disease, with reports of improved overall survival (OS) [5,6] and decreased cardiovascular (CV) events [7] following partial nephrectomy (PN) compared with radical (RN) nephrectomy. However, results from a randomized trial of PN vs. RN failed to demonstrate an OS benefit [8] or a significant difference in the rates of advanced kidney disease or kidney failure [9] between PN and RN. These data have raised concerns that the potential protective benefit of PN may not be applicable to all patient groups, such as elderly or infirm patients in whom the increased perioperative risks of PN are nontrivial and for whom long-term benefits of PN are uncertain [10].

Informed and thoughtful SRM management decisions require consideration and balance of patient, tumor, and procedural risks to maintain oncologic efficacy while minimizing treatment-associated morbidity. Surgical management of stage I SRMs can provide excellent oncologic outcomes with reported 5-year cancer-specific survival rates in excess of 95% [4]. However, such exemplary tumor control may be in part owing to the indolent biology of SRMs. In fact, excellent intermediate-term oncologic outcomes are reported for patients who are managed expectantly [11,12]. In a large pooled analysis of 880 patients undergoing active surveillance for SRM, only 2% of lesions progressed to metastases [12]. These data underscore the largely nonaggressive nature of small localized renal tumors in carefully preselected cohorts. As such, when the urologic surgeon finds her/himself faced with a decision between treatment options, the question regarding whether the mass requires any intervention at all must first be answered. Indeed, competing risks from comorbidity may outweigh the benefit of any treatment, especially in elderly and infirm patients [12,13].

Percutaneous ablation, especially, carries great promise for frail and comorbid cohorts who are deemed imperfect

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candidates for neither surgery nor active surveillance, offering an opportunity to avoid general anesthesia and intraperitoneal dissection [14,15]. Nevertheless, extended oncologic efficacy remains to be established [4,11]. Albeit recent data suggest that oncologic outcomes may be comparable to surgical intervention even for patients with larger masses [16], such comparative effectiveness assessments are limited by marked selection biases and lack of robust follow-up [17]. Furthermore, percutaneous ablation is not without complications. Indeed, the reported overall complication rates range from 0% to 42% (mean = 17%) with major and minor complications occurring in 10.2% and 6.8%, respectively [18]. Moreover, intensive surveillance imaging is generally required following ablative therapy [18].

The balance between death owing to cancer and death because of competing risks has made patient comorbidities increasingly important in the selection of candidates for surveillance [10,19]. In a retrospective review of 7,177 patients diagnosed with localized T1a RCC in the Surveillance, Epidemiology, and End Results (SEER) database, Patel et al. [19] assessed modification of cancer-specific survival by CV risk for patients treated with PN, RN, or "deferred therapy", a surrogate definition for active surveillance. Patients at high CV risk had similar cancer-specific survival (CSS) to patients at low CV risk, but CV risk modified comparative CSS between treatment strategies [19]. Patients with low CV risk had better cancer survival with surgery than with delayed therapy (2- to 4-fold CSS benefit), whereas those with high CV risk had similar cancer survival regardless of treatment strategy [19]. Although retrospective with significant inherent biases, these data highlight the likely importance of CV comorbidity in patient selection. Consideration of pre-existing renal dysfunction is likewise important, as patients undergoing partial or radical nephrectomy for renal cancer experience perioperative nephron loss, which may result in de novo chronic kidney disease or advancement of pre-existing disease [20].

Albeit built on post–renal surgery data, competing risks predictive models have been reported [10,13]. The latest published nomogram harnesses clinicopathologic variables from a large administrative data set to quantify and compare risks of kidney cancer and non–kidney cancer death and has been operationalized for point-of-care use at www.cancernomograms.com. Employing the model, an 83-year-old African American man with a Charlson comorbidity index of 3 and a 4.5-cm renal mass is calculated to have ~6% chance of dying owing to kidney cancer at 5 years after the diagnosis, whereas his chance of dying owing to other causes in the next 5 years is more than 55%. Meanwhile, a 70-year-old white woman with no comorbidities who presents with a 9-cm renal mass can be expected to have a ~9% chance of dying owing to kidney cancer and ~5% chance of dying owing to other causes over the next 5 years. Regardless of surgery type, tumor stage, or tumor grade, age is detrimentally associated with worse other-cause mortality, and septuagenarians and octogenarians represent the predominant groups at higher risk of succumbing to other-cause mortality [21]. For patients ≥75 years, surgery with RN or PN may add no additional cancer-specific survival benefit compared with nonsurgical management [22].

With the advent of nephron-sparing surgery (NSS), the treatment for localized RCC has shifted from radical extirpation to NSS with the goal of preserving long-term renal function while maintaining oncologic efficacy [23]. Abundant retrospective observational data suggest superior outcomes for patients undergoing PN, but the superiority of PN in preselected cohorts is likely owing to significant selection bias [23,24]. The paradoxical 29% cancer-specific survival advantage of PN compared with RN reflects the selection bias inherent to all retrospective data [24]. The biases inherent to patient selection for surgery are profound and difficult to capture in administrative cohorts. As evidence, Shuch et al. [25] recently demonstrated that patients undergoing NSS exhibited higher OS over time than control patients without cancer, indicating that patients chosen for PN appear to possess a baseline higher likelihood of long-term survival [25]. The survival benefit with nephron preservation also appears to become less pronounced in patients of advancing age, with no demonstrable survival advantage at 5 or 10 years from surgery in Medicare beneficiaries of any age [26].

The ongoing debate between PN and RN for management of SRM has been thoroughly outlined [23], but the effect of an aging population on RCC management has been incompletely addressed. Between 1982 and 2003, the population older than 65 years doubled and the population older than 85 years quadrupled [27]. Unfortunately, the conclusions of methodologically sound clinical investigations in younger patients do not necessarily apply to the geriatric age group, and complication rates, mortality, length of hospital stay, and intensive care unit admissions increase with patient age, which can offset oncologic treatment goals [28]. As such, careful patient selection for surgical intervention is important, as frail elderly patients are clearly at higher risk of overall and severe complications compared with their fit younger counterparts [29]. Following radical or partial nephrectomy, the overall burden of 90-day complications in the elderly (≥75 y) and infirm is >22% when rigorously measured, and risk status as opposed to surgery type appears to be a major driver of complication rates [3]. Indeed, elderly and comorbid patients with RCC are nearly twice as likely to experience a complication regardless of treatment type [3]. Thus, treatment decisions for potentially vulnerable elderly patients should take into account data obtained from the evaluation of geriatric syndromes, such as frailty, functional and cognitive limitations, malnutrition, comorbidities, and polypharmacy, as well as social support [27].

Models for predicting postoperative morbidity and mortality in the elderly have been developed [30], and