Open Partial Nephrectomy for the Treatment of Renal Cell Carcinoma

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Open partial nephrectomy, or nephron-sparing surgery (NSS), is now considered the standard of care for the treatment of small renal tumors. The oncologic efficacy and safety of NSS for the treatment of stage-T1a renal tumors has been repeatedly demonstrated to be equivalent to radical nephrectomy. NSS initially was reserved for patients with solitary kidneys, impaired renal function, hereditary tumor syndromes, bilateral renal tumors, and those with significant comorbidities predisposing to future renal failure. The indications have expanded recently to allow elective partial nephrectomy in the setting of a normal contralateral kidney. Furthermore, recent data demonstrate that partial nephrectomy for larger tumors (T1b), which have been historically treated with radical nephrectomy, is a viable option when surgical margins can safely be achieved. In the era of minimally invasive techniques, laparoscopic NSS is technically feasible, yet long-term studies are still needed to assess oncologic efficacy. New NSS ablative technologies, such as cryoablation and radiofrequency ablation, are on the horizon. In this article, we discuss the role of open NSS and surgical technique in the contemporary management of renal tumors.

Indications for Nephron-sparing Surgery
The contemporary indications for partial nephrectomy or nephron-sparing surgery (NSS) can be categorized as absolute, relative, or elective. Partial nephrectomy was reserved initially for patients with a solitary kidney, impaired renal function, hereditary tumor syndromes (eg, von Hippel-Lindau [VHL] disease, hereditary papillary renal carcinoma [HPRC]), bilateral renal tumors, and comorbidities predisposing patients to future renal insufficiency. For this select group of patients, NSS was not considered the gold standard, but offered as an alternative to avoid the morbidity of dialysis or renal transplantation. However, the desire to spare renal parenchyma does not supersede the primary goal of effectively removing the malignancy.

In current practice, elective indications perhaps are the most controversial. A small renal mass, usually smaller than 4 cm, located peripherally, and easily amenable to resection, is the generally suggested indication based on existing data [7–9,10••]. Although elective NSS generally is performed in patients with tumors ≤ 4 cm, there are emerging data that NSS can be performed on patients with larger tumors that are anatomically amenable, provided an adequate surgical margin can be safely obtained [10••,11•,12]. The rationale for expanding the indications for elective NSS for larger tumors include an increase in the life expectancy of the general population, along with an increase in incidental diagnosis at an earlier age and have led to increased concerns regarding the long-term risk of renal insufficiency or metachronous tumor recurrence in patients who undergo radical nephrectomy [2].

Introduction
The incidence of renal cell carcinoma (RCC) has increased in recent years [1,2]. With improvement in imaging studies, patient presentation transitioned from the classic triad of flank mass, pain, and hematuria to small incidental masses found on CT scans or MRI [2]. The initial management of localized renal tumors as described by Robson et al. [3] in 1969 was radical nephrectomy, which included removal of the kidney, excision of Gerota’s fascia and ipsilateral adrenal gland, and an extensive lymph node dissection. With improved imaging and long-term data, the technique evolved to minimize unnecessary ipsilateral adrenalectomy and lymph node dissection [4••,5•]. The next stage of surgical management aimed to minimize the sacrifice of viable parenchyma [6•].
Outcomes
The oncologic efficacy of NSS has been demonstrated in major series by its equivalence to radical nephrectomy, with 5-year disease-free survival ranging from 86% to 100% for tumors smaller than 7 cm [7–9,10••,12–17]. The long-term survival and recurrence rate for stage-T1a tumors treated with NSS is equivalent to treatment with radical nephrectomy. In this patient population, the removal of normal parenchyma provides no survival benefit and may be detrimental to the patient. Patients with an absolute indication for NSS have lower cancer-specific survival rates compared with those with an elective indication secondary to increased age, tumor size, stage, and overall decreased health [8,18]. However, the outcomes are relatively consistent with the size- and stage-stratified, disease-free survival reported in historic radical nephrectomy series [5•].

In patients with hereditary renal tumor syndromes, the risk of local recurrence is extremely high owing to the multifocal nature of the malignancy. As a result, disease-free survival following partial nephrectomy is reduced relative to that for patients with sporadic RCC. Ultimately, many patients undergo multiple nephron-sparing procedures. Walther et al. [19] retrospectively evaluated the National Cancer Institute experience on 52 patients with VHL disease and RCC. None of the patients with tumors smaller than 3 cm had metastatic disease; therefore, the authors recommended observing tumors until they are 3 cm in size in this population of patients, minimizing the need for more frequent surgery.

Several investigators have reported on the outcome of partial nephrectomy in patients with locally advanced and metastatic RCC. In such cases, in addition to the conventional rationale for partial nephrectomy, preservation of renal mass may be desirable to allow adequate renal function to receive systemic therapy. Angermeyer et al. [20] reported on a series of nine patients with RCC and inferior vena cava involvement in solitary kidneys who underwent NSS. Four of the nine patients died of metastatic disease, two of whom had local recurrences in the renal remnant. Similarly, Sengupta et al. [21] described the NSS approach for 13 patients with RCC in a solitary kidney with extension into the renal vein or inferior vena cava (T3b). At a median follow-up of 24 months (range, 0–204), eight patients had died, four from RCC (all having had NSS) at a median interval of 9.5 months (range, 7–16). Of the five patients alive at a median follow-up of 25 months, four had no identifiable disease, whereas one had systemic recurrence. Krishnamurthi et al. [22] reported on 15 patients with a solitary kidney and metastatic RCC who underwent NSS. Nine patients had previously undergone contralateral radical nephrectomy and resection of metastatic disease and presented with recurrence in the remaining kidney. Of these patients, 67% were disease-free after partial nephrectomy at a mean follow-up of 31 months.

The oncologic success of early NSS series encouraged the application of NSS to a new patient population. Elective partial nephrectomy in the setting of a normal contralateral kidney was explored for small renal tumors. Sparing parenchyma with an elective partial nephrectomy may avoid future non-elective NSS for a new primary tumor. The major argument against elective NSS is the risk of local recurrence in the spared kidney due to incomplete excision or the risk of multifocal disease. Multifocal tumor development can occur in 3% to 25% of patients [23–25]. Despite these concerns, the role of NSS in the treatment of RCC continued to be investigated. Large series have demonstrated that open NSS provides excellent oncologic control (Table 1). Contemporary series have definitively demonstrated 5-year cancer-specific survival rates of 95% or higher, which is comparable with the survival of patients undergoing radical nephrectomy for similar sized lesions [8,14,16,17]. Initial data demonstrated that renal tumors larger than 4 cm treated with partial nephrectomy displayed poorer cancer-specific survival than those smaller than 4 cm [7,9,14]. Thus, 4 cm was established as a cutoff for stage T1b classification and as the threshold for performing NSS. Recent data, including some from a large, multi-institutional series [10••] demonstrated that although T1b tumors may have worse overall outcome, the choice of surgery does not influence prognosis [11•,12]. These data suggest that the indications for partial nephrectomy can be safely expanded up to 7 cm.

The UCLA database of patients undergoing NSS or radical nephrectomy is a well-matured cohort that has been extensively reported in the literature and is

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Patients, n</th>
<th>Recurrence-free, %</th>
<th>Cancer-specific mortality, %</th>
<th>Mean follow-up, y</th>
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