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Kidney Cancer

# Functional Comparison of Renal Tumor Enucleation Versus Standard Partial Nephrectomy

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## **Abstract**

**Background:** Tumor enucleation (TE) optimizes parenchymal preservation and could yield better function than standard partial nephrectomy (SPN), although data on this are conflicting.

Objective: To compare functional outcomes for TE and SPN strategies.

Design, setting, and participants: Patients managed with partial nephrectomy (PN) with necessary data for analysis of preservation of ipsilateral parenchymal mass (IPM) and global glomerular filtration rate (GFR) from two centers were included. All studies were required <2 mo before and 3–12 mo after surgery. Patients with a solitary kidney or multifocal tumors were excluded.

Intervention: Partial nephrectomy.

Outcome measurements and statistical analysis: Vascularized IPM was estimated from contrast-enhanced CT scans preoperatively and postoperatively. Serum creatinine-based estimates of global GFR were also obtained in the same timeframes. Univariable and multivariable linear regression evaluated factors associated with new-baseline global GFR. Results/limitations: Analysis included 71 TE and 373 SPN cases. The median preoperative global GFR was comparable for TE and SPN (75 vs 78 ml/min/1.73 m<sup>2</sup>; p = 0.6). The median tumor size was 3.0 cm for TE and 3.3 cm for SPN (p = 0.03). The median RENAL score was 7 in both cohorts. For TE, warm ischemia and zero ischemia were used in 51% and 49% of cases, respectively. For SPN, warm ischemia and cold ischemia were used in 72% and 28% of patients, respectively. Capsular closure was performed in 46% of TE and 100% of SPN cases (p < 0.001). Positive margins were found in 8.5% of TE and 4.8% of SPN patients (p = 0.2). The median vascularized IPM preserved was 95% (interquartile range [IQR] 91– 100%) for TE and 84% (IQR 76–92%) for SPN (p < 0.001). The median global GFR preserved was 101% (IQR 93–111%) and 89% (IQR 81–96%) for TE and SPN, respectively (p < 0.001). On multivariable analysis, resection strategy, preoperative GFR, and vascularized IPM preserved were all significantly associated (p < 0.001) with new-baseline global GFR. Limitations include the retrospective design and the lack of resection outcome data.

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**Conclusions:** Our analysis suggests that TE has potential for maximum IPM preservation compared to SPN and may provide optimized functional recovery. Further investigation will be required to evaluate the clinical significance of these findings.

**Patient summary:** Tumor enucleation for kidney cancer involves dissection along the tumor capsule and optimally preserves normal kidney tissue, which may lead to better functional recovery. The importance of this approach in various clinical settings will require further investigation.

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#### 1. Introduction

Recent studies suggest that the new-baseline glomerular filtration rate (GFR) after partial nephrectomy (PN) is an important predictor of long-term survival for patients with localized kidney cancer, particularly for those with preexisting chronic kidney disease (CKD) [1,2]. Nephron mass preservation appears to be the most important modifiable factor related to new-baseline GFR, presuming that extended warm ischemia has been avoided [3–7]. Traditionally, standard partial nephrectomy (SPN) involves intentional removal of a rim of normal healthy parenchyma along with the tumor [8–10]. Hence, SPN will always be associated with some degree of functional decline, in part because of this excised parenchyma but also related to the devascularization that can occur during the reconstructive phase of the procedure [6,11,12].

Tumor enucleation (TE) is an alternative nephron-sparing technique in which the renal mass is dissected away from the normal parenchyma via an avascular plane along the fibrous tumor pseudocapsule [13-21]. TE thus minimizes the amount of normal renal parenchyma excised with the tumor [13-21]. Recent studies have confirmed that TE can optimize preservation of vascularized parenchymal mass when compared to SPN [14]. However, most previous studies have failed to demonstrate a statistically significant functional advantage for TE [13-21]. Other purported advantages of TE include shorter operative time and lower estimated blood loss, and some have argued that capsular closure may not be routinely required after TE, in contrast to SPN [14-18]. Furthermore, TE may facilitate zero-ischemia approaches to PN [13,14]. Most recent studies have reported lower rates of positive surgical margins and better local control with TE compared to SPN [13,19-22]. However, many of these studies were retrospective and further data are needed.

In this study we analyzed substantial cohorts of patients managed with intent for TE and SPN, with a primary focus on functional outcomes. Our study includes a number of TE cases that were performed without capsular closure and with zero ischemia, which may allow for a more robust exploration of the ultimate functional implications of TE relative to SPN.

# 2. Patients and methods

## 2.1. Patient population

With institutional review board approval, 444 patients (2008–2015) managed with PN from two centers were analyzed. All patients were

required to have necessary analyses to determine ipsilateral parenchymal mass and global GFR before and after surgery. Contrast-enhanced computed tomography (CT) scans and serum creatinine–based estimates of GFR were required <2 mo before and 3–12 months after surgery, after new-baseline GFR was established. Patients with a solitary kidney or multifocal tumors were excluded. All patients in our databases meeting these criteria were included in the analysis with no exceptions. All TE and 58 SPN (16%) procedures were performed at Loyola University Medical Center by a single surgeon (G.N.G.), while all other SPN procedures were performed at Cleveland Clinic by high-volume surgeons.

PN was performed as intent for TE or SPN according to surgeon and center preferences taking into account tumor characteristics and surgical complexity. Surgical techniques for TE and SPN have been described previously [8-15]. The choice of warm versus cold versus zero ischemia, and open versus minimally invasive surgery (MIS), and decisions about capsular closure were also according to surgeon preference. A major focus for SPN was minimal but negative margins [8-15]. Intraoperative ultrasound was routinely used to help define tumor location for TE and the margins of resection for SPN. Capsular closure, when chosen, was routinely performed with interrupted sutures tied over Surgicel Fibrillar (Ethicon, Somerville, NJ, USA) for open cases, and horizontal mattress sutures were tightly approximated with sliding clips for MIS procedures. The hilum was dissected in preparation for possible clamping in all cases. For warm/cold ischemia cases, the renal artery was clamped uniformly while the vein was occluded selectively. All TE cases were selected preoperatively and there were no conversions for resection strategy or intent for TE or SPN. Demographic and pathologic parameters were obtained via retrospective review.

# 2.2. Measurement of vascularized parenchymal mass

Vascularized parenchymal mass in the ipsilateral kidney was measured as previously described [3]. In brief, volume measurement was conducted from axial CT scans in the venous phase via freehand scripting to define the area of interest from both preoperative and postoperative studies. The parenchymal mass preserved was defined as (postoperative ipsilateral parenchymal mass).

# 2.3. Functional assessment

Serum creatinine levels before and after surgery were measured at the same clinical reference laboratory for each patient, and global GFR was estimated using the Modification of Diet in Renal Disease-2 equation [23]. Global GFR preserved was defined as new-baseline global GFR normalized by preoperative global GFR. Global GFR was graded according to National Kidney Foundation guidelines [24].

## 2.4. Statistics

Continuous variables were expressed as median and interquartile range (IQR) and compared using a Mann-Whitney U test. Categorical variables were presented as number (percentage) and compared using a Pearson  $\chi^2$  or Fisher exact test. Potential predictive factors for new-baseline GFR

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