



Increasing Volume of Non-Neoplastic Parenchyma in Partial Nephrectomy Specimens Is Associated With Chronic Kidney Disease Upstaging

Srinath Kotamarti, Michael B. Rothberg, Matthew R. Danzig, Jared Levinson, Shumaila Saad, Ruslan Korets, James M. McKiernan, Ketan K. Badani

Abstract

We examined the effect of the non-neoplastic parenchymal volume (NNPV) in partial nephrectomy (PN) specimens on postoperative renal function. Ellipsoid and Modification of Diet in Renal Disease formulas were used to calculate the specimen volumes and estimated glomerular filtration rate. On multivariate analysis, increased NNPV during PN was associated with postoperative chronic kidney disease upstaging, emphasizing the need for healthy parenchymal preservation during PN.

Introduction: We examined the effect of non-neoplastic parenchymal volumes (NNPVs) in partial nephrectomy (PN) surgical specimens on long-term postoperative renal function. PN for renal cortical neoplasms has demonstrated superior long-term renal function outcomes compared with radical nephrectomy. Minimizing the distance between the surgical margin and tumor will reduce the NNPV removed. The role of NNPV on postoperative outcomes has been preliminarily investigated, with varying results. Thus, we sought to determine the association between the NNPV removed and postoperative chronic kidney disease (CKD) staging. **Materials and Methods:** Our institutional database was queried for patients who had undergone PN from 1990 to 2012. The demographic and pathologic data were collected. The ellipsoid formula was used to calculate the surgical specimen and tumor volumes, which were then subtracted from each other to determine the NNPV. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula. Binary logistic regression analysis was used to determine the predictors of postoperative CKD upstaging according to the eGFR. **Results:** A total of 584 patients meeting the inclusion criteria had undergone PN. On binary logistic regression analysis, controlling for age, tumor volume, surgical modality, and preoperative CKD stage, an increasing NNPV in the surgical specimen was independently associated with postoperative CKD upstaging (odds ratio, 1.004; $P = .007$). **Conclusion:** An increasing NNPV removed during PN correlated with CKD upstaging using the eGFR; therefore, additional emphasis should be placed on healthy parenchymal preservation, with long-term follow-up to ensure adequate oncologic outcomes.

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Introduction

The use of partial nephrectomy (PN) for renal cortical neoplasms has steadily increased, owing to emerging evidence

suggesting a reduced risk of postoperative chronic kidney disease (CKD) compared with radical nephrectomy (RN).^{1,2} The indications for PN have also evolved to encompass larger, more complex, renal tumors measuring ≤ 7.0 cm in diameter.³⁻⁵ PN for renal tumors has not only demonstrated equivalent oncologic outcomes, but has also achieved superior postoperative renal functional outcomes compared with RN.^{2,5-8} Moreover, the development and widespread adoption of minimally invasive techniques for PN have afforded patients decreased analgesic requirements and a shorter convalescence compared with traditional open approaches.^{8,9}

Department of Urology, Columbia University Medical Center, New York, NY

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Address for correspondence: Srinath Kotamarti, BS, Department of Urology, Columbia University College of Physicians and Surgeons, 161 Fort Washington Avenue, Herbert Irving Pavilion, 11th Floor, New York, NY 10032
E-mail contact: srikotamarti@gmail.com

Increasing Volume of NNPV Associated With CKD

With surgical excision of any localized renal tumor, the oncologic outcomes and renal function outcomes must be balanced to optimize the overall patient results. Minimizing the distance between the surgical margin and tumor preserves the surrounding healthy kidney parenchyma, theoretically improving renal function outcomes. However, the risk of attaining a positive margin also becomes more likely, potentially compromising the long-term oncologic outcomes.^{10,11} However, over time, the prognostic significance of a positive margin after PN has become conflicted, with evidence suggesting that positive surgical margins (PSMs) might not increase a patient's risk of local cancer recurrence or progression to metastatic disease.¹²⁻¹⁴

Although the concept of the non-neoplastic parenchymal volume (NNPV) removed during PN has been preliminarily investigated, studies of the specific role of the NNPV removed on postoperative renal function have produced mixed results. A study by Golan et al¹⁵ showed that the NNPV removed had no effect on the postoperative estimated glomerular filtration rate (eGFR). However, a report by Mir et al¹⁶ associated the percentage of parenchymal volume preserved with improvement in the postoperative eGFR. Given the limited sample sizes and varied results produced from these studies, a larger study is warranted to elucidate the effect of the NNPV removed during PN on renal function outcomes. Therefore, we sought to determine the association between the NNPV in the surgical specimen and the risk of worsening postoperative CKD stage after PN at our institution.

Materials and Methods

Our institutional review board-approved urologic oncology database was queried to identify all patients who had undergone PN from 1990 to 2012. The patient demographic and perioperative data were collected from the initial hospital admission records. The pathologic data, including tumor and specimen dimensions without perinephric fat, and margin status were obtained. The margin distance was defined as the shortest distance between the tumor and surgical margin. The ellipsoid formula ($\pi/6 \times \text{length} \times \text{width} \times \text{height}$) was used to calculate the surgical specimen and tumor volumes, which were then subtracted from each other to determine the NNPV removed in each PN specimen, as previously described.¹⁷

The renal function outcomes are represented by changes in the eGFR, determined from the pre- and postoperative creatinine values and converted using the Modification of Diet in Renal Disease formula. The preoperative creatinine measurement used for analysis was that value nearest to the date of surgery. The change in eGFR was calculated by subtracting the latest postoperative eGFR available from the preoperative eGFR. Determined from the associated CKD stage, whether upstaging had occurred postoperatively (from a lower CKD stage to a higher CKD stage) was also noted.

Patients underwent a standard follow-up protocol with laboratory tests for renal function and abdominal imaging with either computed tomography or magnetic resonance imaging to detect recurrent disease. The follow-up period was defined as the interval between the date of surgery and the date of the most recent abdominal imaging study or creatinine value available.

Binary logistic regression analysis was performed to determine the association between the demographic and clinicopathologic

variables and the likelihood of postoperative CKD upstaging using the eGFR. The analysis was performed with univariate and multivariate approaches, and $P < .05$ was set as the level of significance. Statistical analyses were performed using the SPSS, version 21.0 (IBM, Armonk, NY).

Results

A total of 662 patients underwent PN during the study period. Of these patients, 75 were excluded because of inadequate renal function follow-up data, and 3 were excluded because of preoperative end-stage renal disease. Thus, 584 patients were available for analysis. The patient demographic, laboratory, operative, and pathologic data are listed in Table 1. The mean follow-up period for these patients was 22.9 months (range, 0-17.7 years). The median operative time was 178 minutes (range, 55-472 minutes), and the median estimated blood loss was 200 mL (range, 10-2500 mL). Of the 584 procedures, 397 were open, 154 were laparoscopic, and 42 were robotic assisted. The median ischemia time for all cases was 23 minutes (range, 10-60 minutes). Intraoperative complications were infrequent, occurring in only 9 patients (1.5%). The complications included blood transfusions (range, 1-3 units packed red blood cells), ureteral transection during renal mobilization, and persistent bleeding. The mean $\pm$ SD preoperative eGFR was 73.22 ± 21.6 mL/min/1.73 m², and the mean postoperative eGFR was 66.04 ± 23.4 mL/min/1.73 m². Using the preoperative eGFR, 115 patients (19.7%) had CKD stage 1, 331 (56.7%) stage 2, 88 (15.1%) stage 3a, 41 (7.0%) stage 3b, and 9 (1.5%) had stage 4.

Overall, 451 renal masses (77.2%) were malignant, with most having a pathologic stage of pT1a (51.3%). The median tumor size was 2.5 cm (range, 0.4-15 cm). Of the 133 renal masses with benign pathologic features, 67 (50.4%) were oncocytomas and 44 (33.1%) were angiomyolipomas. Overall, 29 PSMs (4.9%) were identified. Of the specimens with negative surgical margins, the average distance between the tumor and margin was 2.51 ± 2.89 mm. Lymphovascular invasion was found in 95 specimens (16.0%). The average tumor volume and NNPV was 14.63 ± 34.42 cm³ and 33.54 ± 84.28 cm³, respectively.

The results from the binary logistic regression analysis for postoperative CKD upstaging using the eGFR are listed in Table 2. An increasing NNPV removed in the surgical specimen was independently associated with postoperative CKD upstaging using the eGFR (odds ratio [OR], 1.004; $P = .007$) when the multivariate model was adjusted for tumor volume, surgical era, surgical modality, intraoperative complications, malignancy on pathologic examination, presence of multifocal disease, and initial preoperative CKD stage using the eGFR. Older age at surgery was another significant predictor of CKD upstaging postoperatively (OR, 1.032; $P < .001$). No significance was associated with the intraoperative ischemia time as a predictor of renal function change on a separate univariate analysis ($P = .826$; data not shown).

Discussion

As previous studies have demonstrated, PN is a viable treatment option for renal cortical neoplasms ≤ 7.0 cm in diameter and can provide equivalent oncologic outcomes and superior renal function outcomes compared with RN in select patients.²⁻⁸ Patients with more advanced tumors who might require RN will have a greater

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