Partial Versus Radical Nephrectomy in Patients With Adverse Clinical or Pathologic Characteristics

Claudio Jeldres, Jean-Jacques Patard, Umberto Capitanio, Paul Perrotte, Nazareno Suardi, Maxime Crepel, Vincenzo Ficarra, Luca Cindolo, Alexandre de La Taille, Jacques Tostain, Christian Pfister, Baptiste Albouy, Marc Colombel, Arnaud Méjean, Hervé Lang, Didier Jacqmin, Jean-Christophe Bernhard, Jean-Marie Ferrière, Karim Bensalah, and Pierre I. Karakiewicz

OBJECTIVES
To assess cancer-specific survival of partial nephrectomy (PN) patients with ≥7-cm lesions or unfavorable pathology (stage T3a or Fuhrman grades III-IV).

MATERIAL AND METHODS
At 13 participation centers, 4072 partial or radical nephrectomies (RN) were performed for RCC between 1984 and 2001. Of all procedures, 925 (22.7%) were for tumors ≥7 cm, 973 (23.9%) had Fuhrman grades III or IV, and 861 (21.1%) had stage pT3a. None had nodal or distant metastases. Matched (age, gender, tumor size, T stage, histologic subtype, and Fuhrman grade [FG]) survival analyses addressed the effect of nephrectomy type (partial vs radical) on cancer-specific mortality.

RESULTS
Partial nephrectomy for tumors ≥7 cm was associated with higher mortality than RN (HR = 5.3; P = .025). No significant cancer-specific survival differences were recorded after PN for FG III-IV (HR = 0.7, P = .5) or for pT3a lesions (HR = 2.5, P = .9).

CONCLUSIONS
Partial nephrectomy may undermine cancer control in patients with tumors ≥7 cm. Conversely, after PN, the same cancer control rates as after RN may be expected in patients with Fuhrman grades III-IV or with pT3a histology.

Nephrectomy is the cornerstone of treatment for renal cancer in patients with localized renal cell carcinoma (RCC).1-7 Radical nephrectomy (RN) or partial nephrectomy (PN) may be considered as treatment modalities for most patients with localized RCC.4,8,9

The indications for PN have broadened over the past decade.3,10-18 The use of PN in patients with increasingly larger tumors led to incidental diagnoses of perinephric fat invasion.19 This finding may be worrisome to many urologists who are confronted with such a pathology report. Some may wonder whether a radical nephrectomy would have resulted in better cancer control. Unfortunately, there are no clear data addressing cancer control outcomes in patients with pathologic T3a stage tumors, who were treated with PN.3,14,20,21

Similarly, many renal tumors treated with PN may demonstrate the presence of high Fuhrman grade (FG), defined as grade III or IV.22 Again, it is unclear whether the presence of high FG may undermine cancer control after PN. For example, high FG might be associated with a higher rate of multifocality, which might be an argument against PN.22

Finally, less strict PN indications have resulted in an increasing proportion of PN candidates with large primary tumors. This attitude has been promoted by reports of cancer control equivalence between PN and RN for stage T1a and T1b RCC. In some instances, those encouraging results have been extrapolated to T2 lesions.23 Like T1a and T1b patients, such individuals may be considered for PN, owing to either imperative (solitary kidney or impaired renal function) or relative (renal function protection despite normal contralateral kidney) indications.
Unfortunately, the 3 potentially adverse characteristics (tumors >7 cm, FG III–IV, or pT3a lesions) have not yet received an adequate amount of attention to validate cancer control outcomes of PN relative to RN. In consequence, we decided to assess the effect of these 3 variables on cancer-specific mortality after either PN or RN.

**MATERIAL AND METHODS**

**Study Population**
Of 4116 RN and PN cases, 935 patients had tumors >7 cm, 982 patients had high FG (grade III or IV), and 884 patients had pT3a lesions at nephrectomy, with no clinical or preoperative evidence of nodal metastases. Of those, 18, 1, 15, and 10 patients, were respectively excluded owing to missing age, gender, tumor size, and follow-up time. This resulted in 925 assessable patients for analyses addressing the effect of PN for lesions >7 cm. None had evidence of lymph node metastases at hilar lymphadenectomy. The analyses targeting the effect of FG III or IV relied on 973 patients. Finally, we used 861 patients in analyses focusing on patients with pT3a stage.

**Clinical and Pathologic Evaluation**
Tumor necrosis marker stages were retrospectively assigned according to the 2002 American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) classification. Tumor size definition was based on pathologic specimens and was defined as the greatest tumor diameter, in centimeters. We stratified histologic subtypes according to the 2002 AJCC/UICC classifications and included only tumors of clear cell, chromophobe, and papillary histology.24 Patients were staged preoperatively with computed tomography (CT) of the abdomen and pelvis, chest CT, or chest x-ray, serum electrolytes, and liver function tests. The absence of distant metastases was confirmed based on radiographic findings. No preoperative biopsies were performed.

We obtained the cause of death from medical charts and death certificates. RCC-specific survival (RCC-SM) included deaths that were directly attributable to RCC. We undertook all data collection and analyses with the approval and institutional oversight of the Institutional Review Boards for the Protection of Human Subjects.

**Statistical Analysis**
We analyzed 3 separate endpoints: the effect of tumor size >7 cm, high FG (III–IV), and pT3a stage on cancer-specific mortality after PN relative to RN. For each endpoint matched, we performed analyses.

We used the Kaplan–Meier method to assess the effect of PN vs RN for all 3 endpoints. We performed matched analyses using all covariates. Exact matching was done for age, gender, tumor size, FG, and histologic subtype. We performed caliper matching for tumor size (±0.5 cm) and age (±2.5 years). Up to 4 RN cases were matched with each PN case to maximize the statistical significance of the results.25 The rationale for matching consists of better control for selection biases, especially in...
the context of comparisons of a small group relative to a substantially larger cohort.\textsuperscript{25} Because of small patient numbers and loss of patients in the matched analyses, we also performed all 3 analyses in multivariate unmatched analyses. For all, we performed two-sided tests; statistical significance was set at $P < .05$.

**RESULTS**

Results are presented for each of the 3 separate subcohorts: patients with tumor size $> 7$ cm, ($n = 925$), patients with FG III-IV ($n = 973$), and patients with pT3a lesions ($n = 861$).

**Matched Analysis of Association Between Nephrectomy Type and RCC-SS in Patients With Tumors $> 7$ cm**

Table 1 shows the descriptive characteristics of patients with tumors $> 7$ cm. Of all 925 patients treated, 29 (3.1\%) underwent PN. Stratification of the population with tumor size $> 7$ cm according to PN vs RN resulted in statistically significant differences in pathologic T stage distributions (PN 48.0\% pT3 vs 6.9\% for RN, $P < .001$) and age (PN median age 57 vs 63 years for RN, $P = .02$). These differences dissipated after matching. The median follow-up of the entire cohort ranged from 0.1 to 24.9 years (mean, 4.6 years).

Of 29 PN cases, 17 were matched with 45 of 896 RN cases. Twelve petanewtons cases were left unmatched and were excluded from the matched analyses. Between 1 and 4 (mean 2.6) RN cases could be matched to each of the 17 PN cases. After matching, Kaplan-Meier plots were generated (Fig. 1A) and addressed cancer-specific survival after surgery. The life table analyses demonstrated 2- and 5-year disease-specific survival rates of 86.2 vs 95.0\% and 67.0 vs 87.2\%, after PN vs RN, respectively. PN was associated with a 5.3-fold higher rate of cancer-specific mortality compared with RN ($P = .025$).

*Figure 1.* Cause-specific survival stratified according to treatment type (PN vs RN) in patients with tumor $> 7$ cm (A), patients with high Fuhrman grade (III/IV) (B), and patients with pathologic pT3a lesions (C).
In the multivariate unmatched analyses that focused on 29 PN and 896 RN patients, PN was associated with a higher rate of cancer-specific mortality compared with RN (HR 1.4, \( P = 0.04 \)).

**Matched Analyses of Association Between Nephrectomy Type and RCC-SS in Patients With High FG (III/IV)**

Table 2 shows the descriptive characteristics of patients with high FG at nephrectomy. Stratification of the population between PN and RN resulted in important differences in pathologic T stage (PN 80.4% pT1 vs 23.2% for RN, \( P < 0.001 \), mean tumor size (PN 3.6 vs 7.8 cm for RN), and histology (PN papillary 20.9 vs 6.7% for RN, \( P = 0.04 \)). The median follow-up of the entire cohort ranged from 0.1 to 24.9 years (mean, 3.9 years).

Of 158 PN cases, 72 were matched with 142 of 815 RN cases. Of all PN, 86 cases were left unmatched and were excluded from the matched analyses. Between 1 and 4 (mean 2.0) RN cases could be matched to each of the 72 PN cases. After matching, we generated Kaplan-Meier plots (Fig. 1B) and addressed cancer-specific survival after nephrectomy. The life table analyses demonstrated 2- and 5-year disease-specific survival rates of 97.7 vs 93.0% and 84.2 vs 71.0%, after PN vs RN, respectively (HR 0.7; \( P = 0.5 \)).

In the multivariate unmatched analyses that focused on 158 PN and 815 RN patients, PN was not associated with a higher rate of cancer-specific mortality compared with RN (HR 1.06; \( P = 0.85 \)).

**Matched Analysis of Association Between Nephrectomy Type and RCC-SS in Patients With pT3A Lesions**

Table 3 shows the descriptive characteristics of patients with pT3a lesions. The median follow-up of the entire cohort ranged from 0.1 to 20.7 years (mean, 4.2 years). Of all 861 patients, 72 (8.4%) underwent PN. Stratification of the population between PN and RN resulted in important differences in tumor size (mean PN 3.8 vs 8.3 cm in RN, \( P < 0.001 \)) and FG (PN 54.2% Fuhrman grade II vs 31.7% for RN, \( P = 0.006 \)). These differences dissipated after matching. The median follow-up of the entire cohort ranged from 0.1 to 20.7 years (mean, 4.2 years).

Of 78 partial nephrectomy cases, 30 could be matched with 63 of 789 RN cases. Of all PN, 42 cases were left unmatched and were excluded from matched analyses. Between 1 and 4 (mean 2.1) RN cases could be matched to each of the 30 PN cases.

After matching, we generated Kaplan-Meier plots (Fig. 1C) and addressed cancer-specific survival after surgery. The life table analyses demonstrated 2- and 5-year disease-specific survival rates of 88.7 vs 94.3% and 81.9 vs 90.1%, after PN vs RN, respectively. PN was associated with a 2.5-fold higher rate of cancer-specific mortality compared with RN (\( P = 0.9 \)).

In the multivariate unmatched analyses that focused on 72 PN and 789 RN patients, PN was not associated with a higher rate of cancer-specific mortality compared with RN (HR 0.62; \( P = 0.11 \)).
The hypothesis of this study rested on the assumption that cancer-specific survival after PN is equivalent to that of RN despite large tumor size, high Fuhrman grade (III or IV) at surgery, or the presence of pathologic stage T3a. Our results demonstrated that PN cancer control rates indeed appear to be equivalent to RN, when either high-grade Fuhrman or pT3a stage is diagnosed at surgery.

Conversely, the analyses of patients with tumor size > 7 cm revealed that cancer-specific survival is statistically inferior when PN is performed instead of RN (HR = 5.3, P = .025). When population differences were controlled for by matching for tumor size, pathologic T stage, Fuhrman grade, histologic subtype, patient age, and gender, PN conferred a 5.3-fold higher rate of cancer-specific mortality relative to RN (P = .025).

Taken together, our data indicate that the presence of unfavorable pathologic features at PN does not undermine the cancer-specific survival as long as these patients do not have a tumor size > 7 cm.

Our results cannot be corroborated or refuted with similar studies. Such studies are nonexistent or have not yet been reported. Therefore, other surgical series need to address these questions. Specifically, large multi-institutional studies with sample sizes larger than in our study will be required to either refute or corroborate our findings regarding the effect of tumor size (>7 cm) on PN cancer control rates. Only 29 of 925 patients (3.1%) with tumor size > 7 cm were treated with PN at 1 of 13 participating centers. Therefore, very large samples will be required to address this specific point.

Sample size, owing to the rarity of the unfavorable pathologic characteristics at PN, represents a cornerstone limitation in the current study, despite its multi-institutional nature (n = 4116). This limitation should be anticipated in future studies. Larger cohorts would be needed to either confirm or refute our results.

Despite its limitations, our study provides important insight into the association between treatment type and RCC-SS. It suggests that no treatment modifications (for example, early adjuvant therapy) are needed if pT3a stage lesions are encountered at PN or if the tumor at PN shows Fuhrman grade III-IV. Conversely, our report demonstrates that PN may have limits when tumor size exceeds 7 cm.

**CONCLUSIONS**

Partial nephrectomy does not appear to lower cancer-specific survival in patients with high-grade Fuhrman or pT3a histology. Conversely, partial nephrectomy may be related to inferior cancer-specific survival in patients with tumors > 7 cm.

**References**


**Table 3.** Descriptive characteristics of patients with pathologic pT3a lesions, stratified according to type of surgery

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall Cohort</th>
<th>Unmatched Cohort (n = 861)</th>
<th>Matched Cohort (n = 93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>861</td>
<td>72</td>
<td>789</td>
</tr>
<tr>
<td>Age Mean (median)</td>
<td>63.4 (65.0)</td>
<td>64.2 (66.0)</td>
<td>63.3 (65.0)</td>
</tr>
<tr>
<td>Range</td>
<td>10-94</td>
<td>30-89</td>
<td>10-94</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 574 (66.7%)</td>
<td>51 (70.8%)</td>
<td>523 (66.3%)</td>
</tr>
<tr>
<td>Tumor size (cm) Mean (median)</td>
<td>7.9 (7.5)</td>
<td>3.8 (3.5)</td>
<td>8.3 (8.0)</td>
</tr>
<tr>
<td>Range</td>
<td>1.0-23.0</td>
<td>1.0-9.5</td>
<td>1.0-23.0</td>
</tr>
<tr>
<td>Fuhrman grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>59 (6.9%)</td>
<td>7 (9.7%)</td>
<td>52 (6.6%)</td>
</tr>
<tr>
<td>II</td>
<td>289 (33.5%)</td>
<td>39 (54.2%)</td>
<td>250 (31.7%)</td>
</tr>
<tr>
<td>III</td>
<td>428 (49.7%)</td>
<td>25 (34.7%)</td>
<td>403 (51.1%)</td>
</tr>
<tr>
<td>IV</td>
<td>85 (9.9%)</td>
<td>1 (1.4%)</td>
<td>84 (10.6%)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear cell</td>
<td>768 (89.2%)</td>
<td>49 (68.1%)</td>
<td>719 (91.1%)</td>
</tr>
<tr>
<td>Papillary</td>
<td>58 (6.7%)</td>
<td>16 (22.2%)</td>
<td>42 (5.3%)</td>
</tr>
<tr>
<td>Chromophobe</td>
<td>35 (4.1%)</td>
<td>7 (9.7%)</td>
<td>28 (3.6%)</td>
</tr>
<tr>
<td>RCC-specific mortality</td>
<td>233 (27.1%)</td>
<td>14 (19.4%)</td>
<td>219 (27.8%)</td>
</tr>
<tr>
<td>Overall study follow-up time (y) Mean (median)</td>
<td>4.2 (3.0)</td>
<td>3.1 (2.5)</td>
<td>4.4 (3.2)</td>
</tr>
<tr>
<td>Range</td>
<td>0.1-20.7</td>
<td>0.1-13.3</td>
<td>0.1-20.7</td>
</tr>
<tr>
<td>Median actuarial cause-specific survival (y)</td>
<td>14.7</td>
<td>7.7</td>
<td>14.7</td>
</tr>
</tbody>
</table>


