A meta-analysis for comparison of partial nephrectomy vs. radical nephrectomy in patients with pT3a renal cell carcinoma

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Background: Kidney cancer is the most common malignant tumor of the kidney in adults. However, in terms of the treatment for pT3a renal cell carcinoma (RCC), whether partial nephrectomy (PN) can be selected is still controversial. This study was conducted to compare the efficacy of PN and radical nephrectomy (RN) in treatment for patients with pT3a RCC.

Methods: The relative English databases including PubMed and EMBASE were searched for studies comparing PN and RN for pT3a RCC between 2010 and 2020. Stata 13.0 software was used to compare the cancer-specific survival (CSS), overall survival (OS), cancer-specific mortality (CSM), relapse-free survival (RFS), complications and positive surgical margin.

Results: Nine articles were included with a total of 3,391 patients, of whom 2,113 received RN and 1,278 received PN. The results showed that there is no statistical difference in CSS, OS, CSM, RFS, complications and positive surgical margin between RN and PN. No heterogeneity was shown in study.

Conclusions: There were no differences in the CSS, OS, CSM, RFS, complications and positive surgical margin of the patients in RN and PN group. For pT3a RCC, RN did not provide a better survival benefit compared to PN. Considering PN can suppress the progression of tumor and reduce the risk of postoperative chronic renal insufficiency, we found PN is a good choice for pT3a RCC. However, further large-sample, studies are still needed in future.

Keywords: Radical nephrectomy (RN); partial nephrectomy (PN); survival; pT3a renal cell carcinoma (pT3a RCC); meta-analysis

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Introduction

Kidney cancer is the most common malignant tumor of the kidney in adults, accounting for 2% to 3% of adult malignant tumors (1). At present, the incidence of kidney cancer is increasing at a rate of about 2% per year, which is the lethal tumor among urinary tract tumors. The Union for International Cancer Control (UICC) tumor-node-metastasis (TNM) classification system classifies tumors...
with perirenal fat invasion (PFI), renal sinus fat invasion
(SFI), or renal vein invasion (RVI) as stage pT3a (2). This
advanced disease state is typically aggressive with 5-year
disease-free survival rates ranging from 30% to 85% (3,4),
including a median time to recurrence ranging from 11
to 22 months (5-8). Surgery is the first choice for the
treatment of kidney cancer, and also the only way to cure.
RN is considered the “gold standard” for the treatment of
localized renal cancer. With the continuous development
of medical technology, the tumor control effect of PN is the
same as that of RN (9-13), and it can preserve renal function
and improve the quality of life of patients after surgery. It
has become the new standard for the treatment of stage T1a
renal cancer (14). However, for pT3a renal cell carcinoma
(RCC), whether PN can be selected is still controversial.

The aim of this study was to compare the survival
outcomes in patients with RN or PN. This study aims to
provide evidence for pT3a RCC in the clinic through meta-
analysis. We present the following article in accordance
with the PRISMA reporting checklist (available at http://
dx.doi.org/10.21037/tau-20-1262).

Methods

Document retrieval

Databases including PubMed and EMBASE were searched
for studies from 2010 to 2020. The keywords used were as
follow: partial nephrectomy, radical nephrectomy, survival
and pT3a RCC. Professional search style was used to search
for related references manually.

Study selection

Exclusion criteria: (I) duplicates; (II) absence of specific
data; (III) case, case reports, reviews; (IV) patients with a
history of other tumors.

Literature screening

Literature was independently screened by two reviewers
based on the inclusion criteria, first screening the title and
abstract. Then the full text of the documents was read to
include the studies that may meet the inclusion criteria. After
cross-checking the results, data were extracted from cohort
studies. A unified table was used to record the information
of each study, including the first author, publication year,
research design, general case information, tumor size,
surgery approach and data of cancer-specific survival (CSS),
overall survival (OS) and cancer-specific mortality (CSM).

Literature quality evaluation

Modified Newcastle-Ottawa Scale (NOS) was used to
evaluate the quality of the included documents. The
scale consists of three large blocks, including: selection
of research populations, comparability between groups
and exposure evaluation or result evaluation. NOS uses a
semi-quantitative star system to evaluate the quality of the
literature, with a perfect score of nine stars. Two researchers
evaluated each study independently.

Statistical analysis

This research used statistical software Stata13.0 to merge
data. The data of CSS, OS, CSM, relapse-free survival (RFS),
complications and positive surgical margin were extracted
for analysis. Between-study statistical heterogeneity was
assessed using $I^2$ and the Cochrane Q test. If the studies are
homogeneous ($P>0.10$, $I^2<50\%$), it is considered that there
is no heterogeneity in the included literature, and the fixed-
effect model is used (15). Counting data was analyzed by rate
ratio (RR). The significance level was set to $\alpha=0.05$, and 95%
confidence interval (95% CI) was taken. The funnel plot was
drawn and the symmetry of the funnel was tested by linear
regression to detect the publication bias (16).

Results

Features of included literature

According to the inclusion and exclusion criteria, a total of
nine articles were included in this study (17-25) (Figure 1).
The characteristics of the studies are showed in Table 1.
A total of 3,391 patients were included, including
1,278 patients in the PN group, 2,113 patients in the RN
group. Among the nine studies, two of them compared
the tumor-specific survival rates between RN and PN group
(19,22), five studies compared OS rates (18-22), two studies
compared CSM (17,20), three studies compared RFS
(18,23,24), three studies compared complications (20,22,25)
and five studies compared positive surgical margin
(18,20,22-24). The baseline characteristics of included
studies were shown in Table 2.

Qualitative analysis

The quality of the articles included was satisfactory. The
research quality evaluation is shown in Table 3.

**Meta-analysis**

**CSS**
No heterogeneity was found among the studies comparing the tumor-specific survival rates ($I^2=0\%$, $P=0.38$), and the fixed-effects model was used for combined analysis. No statistically significant difference was found in tumor-specific survival rate between PN and RN groups (RR: 1.02, 95% CI: 0.97–1.07) (Figure 2).

**OS**
Six studies involved OS. The $I^2=55\%$ ($P=0.05$) indicated that there was no heterogeneity and the fixed-effects model was utilized. The combined RR of these studies were RR: 1.04, 95% CI: (0.96, 1.11) (Figure 3) and there is no statistical difference.

**CSM**
Two studies involved CSM. There is no heterogeneity among the studies ($I^2=0\%$, $P=0.72$), and the fixed-effects model is used for combined analysis. No statistically significant difference was found in CSM rate between RN and PN groups (RR: 1.00, 95% CI: 0.72–1.41) (Figure 4).

**RFS**
Three studies involved RFS. No statistically significant difference was found in RFS rate between RN and PN groups (RR: 0.93, 95% CI: 0.75–1.16) (Figure 5).

**Complications**
Three studies reported complications, including secondary bleeding and wound infection. No statistically significant difference was found in complications between RN and PN groups (RR: 0.78, 95% CI: 0.50–1.23) (Figure 6).

**Positive surgical margin**
Five studies reported positive surgical margin. No statistically significant difference was found in positive surgical margin between RN and PN groups (RR: 1.05, 95% CI: 0.78–1.41) (Figure 7).

**Publication bias**
Funnel plots were used for the test of publication bias, and
Table 1 Basic situation of nine documents

<table>
<thead>
<tr>
<th>Studies</th>
<th>Year</th>
<th>Size</th>
<th>Study type</th>
<th>Intervention</th>
<th>Outcome quality score; age; EENAL score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hansen (17)</td>
<td>2012</td>
<td>954</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>CSM 7; 64; NA</td>
</tr>
<tr>
<td>Hamilton (18)</td>
<td>2020</td>
<td>360</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>RFS, OS 8; 60.7; RN: 7.8, PN: 7.7</td>
</tr>
<tr>
<td>Weight (19)</td>
<td>2011</td>
<td>203</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>CSS, OS 8; 64; NA</td>
</tr>
<tr>
<td>Patel (20)</td>
<td>2020</td>
<td>929</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>CSM, OS 7; 63; RN: 8.81, PN: 9.9</td>
</tr>
<tr>
<td>Ziegelmueller (21)</td>
<td>2019</td>
<td>55</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>OS 8; 67.9; RN: 7.3, PN: 7.3</td>
</tr>
<tr>
<td>Andrade (22)</td>
<td>2017</td>
<td>140</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>CSS, OS 8; 62.4; RN: 8, PN: 8</td>
</tr>
<tr>
<td>Patel (23)</td>
<td>2017</td>
<td>501</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>RFS 7; 63.2; NA</td>
</tr>
<tr>
<td>Jeong (24)</td>
<td>2016</td>
<td>91</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>RFS 8; 58.6; RN: 7.5, PN: 7.6</td>
</tr>
<tr>
<td>Mühlbauer (25)</td>
<td>2020</td>
<td>158</td>
<td>Retrospective</td>
<td>RN, PN</td>
<td>OS 9; 67.0; RN: 10, PN: 8</td>
</tr>
</tbody>
</table>

RN, radical nephrectomy; PN, partial nephrectomy; CSM, cancer-specific mortality; RFS, relapse-free survival; OS, overall survival; CSS, cancer-specific survival.

Table 2 Features of included studies

<table>
<thead>
<tr>
<th>Study detail, year</th>
<th>No. of patients, type</th>
<th>Male/female</th>
<th>Median age (years)</th>
<th>tumor size</th>
<th>Median follow-up duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hansen, 2012</td>
<td>RN: 477, PN: 477</td>
<td>RN: 363/114, PN: 363/114</td>
<td>RN: 64, PN: 64</td>
<td>RN: 3.9, PN: 3.9</td>
<td>NA</td>
</tr>
<tr>
<td>Hamilton, 2020</td>
<td>RN: 240, PN: 120</td>
<td>RN: 169/71, PN: 84/36</td>
<td>RN: 60.9, PN: 60.5</td>
<td>RN: 4.9, PN: 4.6</td>
<td>RN: 50.8, PN: 53.2</td>
</tr>
<tr>
<td>Ziegelmueller, 2019</td>
<td>RN: 17, PN: 38</td>
<td>RN: 12/5, PN: 28/10</td>
<td>RN: 67.6, PN: 70.3</td>
<td>RN: 4, PN: 3.9</td>
<td>80</td>
</tr>
</tbody>
</table>

RN, radical nephrectomy; PN, partial nephrectomy.

Table 3 Quality assessment of included studies (the modified NOS)

<table>
<thead>
<tr>
<th>Selection of patients</th>
<th>Comparability of groups</th>
<th>Evaluation of the treatment outcome</th>
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</table>

NOS, Newcastle-Ottawa Scale.
Figure 2 Forest plot of CSS rates between PN and RN. CSS, cancer-specific survival; RN, radical nephrectomy; PN, partial nephrectomy.

Figure 3 Forest plot of OS rates between PN and RN. OS, overall survival; RN, radical nephrectomy; PN, partial nephrectomy.

Figure 4 Forest plot of CSM rates between PN and RN. CSM, cancer-specific mortality; RN, radical nephrectomy; PN, partial nephrectomy.

Figure 5 Forest plot of RFS rates between PN and RN. RFS, relapse-free survival; RN, radical nephrectomy; PN, partial nephrectomy.

Figure 6 Forest plot of complication between PN and RN. RN, radical nephrectomy; PN, partial nephrectomy.
the results were shown from Figures 8-13.

**Discussion**

PN for the management of T1a tumors has evolved during the last two decades, which may become the standard care for T1b tumors as well, demonstrating oncological safety and renal function preservation (26). PN is already an established and widely adopted approach for the surgical treatment of renal masses (27), and contemporary studies have demonstrated its feasibility in more complex cases with the growing experience with this technique (28-30). Nonetheless, PN is still a challenging technique for the treatment pT3a tumors and its utility in this setting warrants further debates. In this study, we compared the survival outcomes of patients with pT3a tumors who underwent PN with those treated by RN.

The safety of PN for T3a tumors has already been addressed in some studies, most of them suggesting
equivalent oncological outcomes when comparing PN with RN. However, these studies included all types of surgical modalities, incorporated cases with aggressive tumors characteristics other than pathological T3a, or used prior T3a classification. In a recent multi-institutional study, Oh and colleagues (31) demonstrated that PN had lower recurrence rate comparable with RN in the subset pathological T3a and supported the notion that, for selected cases, PN is a safe treatment even in the face of adverse pathological findings.

Similarly, Weight et al. (19) noted no difference in OS for RN versus PN in pT3a patients. In recent years, it has been reported that PN not only can control the tumor progression, but also reduces the risk of postoperative chronic renal insufficiency and improves the long-term quality of life. However, the renal blood vessels are rich and the tissue is relatively brittle. The vascular end of the surgical wound of the kidney may form a pseudoaneurysm, arteriovenous fistula, etc., resulting in renal hematoma or hematuria after surgery. At present, there are relatively few reports on local recurrence after PN, but PN does not clearly indicate whether resection of the affected kidney is more likely to cause tumor recurrence and metastasis. From the perspective of underestimated risk of tumor margin positive, risk of serious complications and tumor control, we must pay attention to the high risk of PN. Bertolo (32) assessed the role of three-dimensional (3D) reconstruction in aiding preoperative planning for highly complex renal tumors amenable to robotic partial nephrectomy (RPN). After viewing the respective 3D reconstructions, in 148 cases the responders changed their idea: indication to RPN raised in 404 cases (74.5%) (P<0.001). The use of this technology might translate into a larger adoption of nephron-sparing approach, and more advanced technologies are needed in the future. Hansen (17) made a regression analysis of patients with tumor size >7.0 cm and found tumor size had no statistical significance to the survival outcomes [hazard ratio (HR): 0.67, 95% CI: 0.30–2.17]. Therefore, the outcomes of pT3a tumors could apply to cT3a tumors.

Our study had some limitations. First, the analysis of heterogeneity sources required more subgroup data. Second, the diagnostic criteria were inconsistent in the studies. Finally, this only nine studies were included in this analysis, more studies are still needed in future.

There were no differences in the CSS, OS, CSM, RFS, complications and positive surgical margin of the patients between RN and PN group. In pT3a RCC, RN did not provide a better survival benefit compared to PN. Considering PN has a good tumor control effect and can reduce the risk of postoperative chronic renal insufficiency, we suggest a universal application of PN for pT3a RCC.

**Conclusions**

There were no differences in the CSS, OS, CSM, RFS, complications and positive surgical margin of the patients between RN and PN group. In pT3a RCC, RN did not provide a better survival benefit compared to PN. Considering PN has a good tumor control effect and can reduce the risk of postoperative chronic renal insufficiency, we found PN is a good choice for pT3a RCC. PN for pT3 is a challenge for surgeons and requires experience. In the future, further large-sample, studies are needed.

**Acknowledgments**

We have invited Ms. Yu-Qing Wu to polish our language.

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Footnote

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Peer Review File: Available at http://dx.doi.org/10.21037/tau-20-1262

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tau-20-1262). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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