Association of Prevalence of Benign Pathologic Findings After Partial Nephrectomy With Preoperative Imaging Patterns in the United States From 2007 to 2014

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IMPORTANCE Although the intent of nephron-sparing surgery is to eradicate malignant tumors found on preoperative imaging, benign masses often cannot be differentiated from malignant tumors. However, in the past there have been discrepancies in the reported percentages of benign masses removed by partial nephrectomy (PNx).

OBJECTIVE To investigate the annual trend of prevalence of benign pathologic findings after PNx and to investigate what potential factors are associated with this prevalence.

DESIGN, SETTING, AND PARTICIPANTS A total of 18,060 patients who underwent PNx between 2007 and 2014 were selected from Truven Health MarketScan Research Databases. We selected those patients who underwent PNx as an inpatient from 2007 and set the surgery date as the index date. Overall, a total of 21,445 patients with International Classification of Diseases, Ninth Revision, Clinical Modification code of 55.4 were identified from 2007 to 2015.

MAIN OUTCOMES AND MEASURES The annual trend of benign pathologic findings was described as an actual number and as a proportion. Univariate and multiple analyses were performed to investigate factors predictive of a benign final pathologic diagnosis, including type of preoperative imaging modality or performance of a renal mass biopsy.

RESULTS Among the 18,060 patients, mean (SD) age was 57 (12) years, and there were 10,637 (58.9%) men and 7,423 (41.1%) women. The overall prevalence of benign pathologic findings was 30.9% and the annual trends demonstrated a prevalence of over 30% for nearly every year of the study period. On univariate analysis, the performance of magnetic resonance imaging (MRI) and renal mass biopsy was associated with benign pathologic findings (P = .02 and P < .001, respectively). On multivariable analysis, female sex (odds ratio [OR], 0.62; 95% CI, 0.58-0.66; P < .001), older age (>65 years) (OR, 0.99; 95% CI, 0.99-0.99; P < .001), and computed tomography (CT) only preoperative imaging (OR, 1.16; 95% CI, 1.05-1.28; P = .004) were associated with benign pathologic findings after PNx.

CONCLUSIONS AND RELEVANCE We found that the overall prevalence of benign pathologic findings after PNx was higher than the literature suggests, with consistent year-over-year rates exceeding 30%. Female sex, older age (>65 years), and CT only preoperative imaging were predictive of a benign tumor. Further elucidation concerning covariates associated with a benign diagnosis should be the focus of future investigations to identify a cohort of patients who could potentially avoid unnecessary surgical intervention.
S
mall, localized, incidentally discovered lesions repre-
sent the tumors that account for the largest increase in
the incidence rate of renal cell carcinoma (RCC) and al-
most half of the new cases of RCC are localized tumors.1 It is
thought that increasing use of imaging modalities is responsible
for the increased incidence of these incidentalomas.3 Con-
sidering the increasingly well-understood disadvantages of
radical nephrectomy in localized RCC, partial nephrectomy
(PNx) is being used more often and the indications for its use
are expanding. American and European guidelines recom-
mand nephron-sparing surgery as the standard of care for pa-

The receipt of PNx is rising, while that of radical nephrec-
tomy is declining3–5 and the increasing use of PNx has yielded
a variable frequency of benign pathologic findings, ranging
from 8.1% to 27.5%.6,7 To date, only a few studies have at-
tempts to investigate the prevalence of benign pathologic
findings after PNx and possible risk factors associated with pre-
dicting benign pathologic findings after PNx.8,9 Moreover, no
nationally representative study has investigated the overall
prevalence of benign pathologic findings after PNx and its as-

The aim of this study was to investigate the prevalence of
benign pathologic findings after PNx and its association with
preoperative imaging patterns using a nationally representa-
tive database.

Methods

Data Source

Data were derived from the nationally representative Truven
Health Analytics MarketScan Commercial Claims and En-
counters and Medicare Supplemental Databases (Truven Health
truenhealth.com/marketscanportal/). The data conformed
to the Health Insurance Portability and Accountability Act of
1996 confidentiality requirements. Truven Health Market-
Scan Research Databases includes a database containing in-
dividual-level inpatient and outpatient insurance billing claims,
which enables longitudinal tracking of patients regardless of
different sites of care and multiple treatment years, as well
as information regarding inpatient and outpatient treatment,
demographic data, diagnoses, procedures, and costs. The use
of this database without informed consent of the patients was
approved by institutional review board of Stanford Univer-
sity because all data were deidentified.

Study Population

All adults aged 18 years or older with a primary procedure code
(using the International Classification of Diseases, Ninth Revi-


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surgery date was regarded as preoperative imaging for PNx. Additional outcomes included cost analysis regarding surgery, cost by person, and average total cost within 90 days after surgery by person. Cost estimation was as follows: total gross payment to a clinician for a specific service; i.e., the amount eligible for payment after applying pricing guidelines such as fee schedules and discounts, and before applying deductibles, copayments, and coordination of benefits. Another additional analysis included prevalence of benign pathologic diagnosis and malignant disease after PNx according to age (>65 years).

Statistical Analyses
A χ² test was conducted to investigate the overall and annual prevalence rate of benign pathologic diagnosis after PNx, and also to compare the difference of performance of imaging patterns during univariate analysis. Post hoc subgroup analysis was performed according to age groups. Multiple logistic regression analyses were undertaken to investigate the significant factors predicting benign pathologic findings. During multiple logistic regression analyses the variable performance of each imaging pattern was not included owing to multicollinearity. All analyses were performed with SAS statistical software (version 9.3; SAS Institute, Inc).

### Results

#### Study Population
A total of 21 445 patients with ICD-9-CM code of 55.4 were identified from 2007 to 2015 using the Truven database system. Patients with no records of preoperative imaging within 1 year from index date (n = 1602) and those patients with nonrelevant diagnostic codes (exclusion criteria and patients with no diagnostic code) (n = 567) were excluded. A total of 18 060 patients were selected for final inclusion (eFigure in the Supplement). Among the 18 060 participants, 10 637 (58.9%) were men and 7423 (41.1%) were women. Basic characteristics of the study cohort are described in Table 1. Mean (SD) age of the total cohort was 56.6 (11.6) years. Female sex was prominent in the
benign pathologic findings group compared with the malignant tumor group (2731 [48.9%] vs 4692 [37.6%], respectively). Male sex was prominent in the cancer findings group compared with those in the benign findings group (7780 [62.4%] vs 2857 [51.1%], respectively). Preferred provider organization (PPO) insurance was the most prevalent type (10 568 [58.5%]).

Prevalence of Benign Pathologic Findings After PNx

The crude number of benign pathologic diagnoses was 5588 among the 18 060 patients, and the overall prevalence was 30.9%. The annual prevalence of benign pathologic findings after PNx was lowest in 2007 as 19.9% and was highest in 2010 as 33.52%. The Figure shows the annual prevalence of benign and malignant pathologic diagnoses after PNx. With the exception of 2007, the annual rate of benign pathologic findings exceeded 30%. In additional analyses according to age, overall prevalence of benign pathologic diagnoses among patients younger than 65 and 65 years or older was 29.6% and 35.9%, respectively (Table 2). In both age groups, the prevalence rate showed an increasing pattern until 2012, with a slightly decreased pattern thereafter. Average annual percentage change (AAPC) was estimated to be 4.0% by methodology of NIH and approximately 4.0% to 6.85% by log-adjusted modelling.

Prediction of Benign or Malignant Pathologic Findings After PNx

Table 3 summarizes the univariate analysis of imaging patterns including imaging performance and imaging combination types. Performance of MRI and biopsy was significantly associated with higher rates of malignant pathologic diagnoses ($P = .02$ and $P < .001$, respectively). Table 4 shows the findings of multiple logistic regression analyses to predict final pathologic results (benign or malignant) after PNx. Significant factors predicting benign pathologic diagnosis were sex (odds ratio [OR], 0.62; 95% CI, 0.58-0.66), older age (OR, 0.99; 95% CI, 0.99-0.99), and residence in the North Central region compared with the West region (OR, 0.88; 95% CI, 0.79-0.98). Significant factors predicting malignant pathologic findings were all imaging combinations compared with CT imaging only (OR, 1.16; 95% CI, 1.05-1.28).

Cost Analysis

The cost analysis included surgery cost and total cost within 90 days after surgery by person and are summarized in Table 1. Median cost of PNx surgery of the benign pathologic diagnosis group by person was US $413 (interquartile range [IQR], $73-$18 458). The median total cost within 90 days after PNx of the benign pathologic diagnosis group by person was US $99 23 (IQR, $15 61-$22 478) (eTable in the Supplement). Total cost burden for all PNx of the benign pathologic diagnoses group was US $90 766 792 for all observation years (2007-2014).

Discussion

To our knowledge, this is the first nationally representative study to report the most recent prevalence of benign pathologic diagnosis after PNx and its association with preoperative imaging patterns. The prevalence of benign pathologic findings after PNx routinely exceeded 30% and performance of MRI or biopsy before surgery could provide a better prediction of true malignant abnormalities. As the proportion of PNx compared with radical nephrectomy continues to increase, most of the research has focused on expansion of indications of PNx, even with clinical stage 3 lesions, with sinus fat invasion and on complications including ischemia time and blood loss, and CKD. To date, only a few reports have focused on the benign pathologic findings after PNx and the prevalence of benign pathologic diagnoses has varied widely from 8% to 30%. Among the studies reporting the prevalence of benign pathologic findings, 6 studies reported a high rate (>25%), similar to our findings.

Considering the crucial problem of the socioeconomic burden of PNx and its related complications among patients with benign pathologic findings, it is clear that urologists have to focus on attempting to reduce nonmalignant final pathologic findings. Among the solutions, ascertaining the accuracy of preoperative radiologic imaging modalities is important; however, no study has thus far included the preoperative imaging modalities as a potential factor.

The role of pre-PNx imaging modalities is well established with good accuracy in predicting RCC. However, to date, no studies have addressed the trends of preoperative imaging or in its efficacy in predicting for malignant histologic findings. We found that the combination of MRI and biopsy were associated with a higher rate of malignant pathologic diagnoses, which implies that a multimodality approach may be more accurate. Furthermore, multiple logistic regression analysis showed that imaging combinations were superior to the performance of CT alone to accurately predict malignant pathologic findings.

Although CT is still the standard modality to predict a renal mass and still displays a high accuracy rate, for the past decade, other studies have demonstrated that MRI and renal
mass biopsy can be highly predictive. However, current imaging modalities are still limited in differentiating benign from malignant lesions, especially in the case of distinguishing oncocytoa or lipid-poor angiomyolipoma from RCC.

### Table 2. Prevalence of Benign and Malignant Pathologic Findings After Partial Nephrectomy by Age

<table>
<thead>
<tr>
<th>Year</th>
<th>Benign Pathologic Findings</th>
<th>Malignant Pathologic Findings</th>
<th>Benign Pathologic Findings</th>
<th>Malignant Pathologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤64 y</td>
<td></td>
<td></td>
<td>≥65 y</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>174 (19.61)</td>
<td>713 (80.38)</td>
<td>36 (17.39)</td>
<td>171 (82.60)</td>
</tr>
<tr>
<td>2008</td>
<td>408 (28.87)</td>
<td>1005 (71.12)</td>
<td>133 (35.84)</td>
<td>238 (64.15)</td>
</tr>
<tr>
<td>2009</td>
<td>522 (30.40)</td>
<td>1195 (69.59)</td>
<td>170 (43.14)</td>
<td>224 (56.85)</td>
</tr>
<tr>
<td>2010</td>
<td>572 (32.81)</td>
<td>1171 (67.18)</td>
<td>173 (36.11)</td>
<td>306 (63.88)</td>
</tr>
<tr>
<td>2011</td>
<td>647 (29.86)</td>
<td>1518 (70.11)</td>
<td>217 (35.51)</td>
<td>394 (64.48)</td>
</tr>
<tr>
<td>2012</td>
<td>748 (30.87)</td>
<td>1675 (69.12)</td>
<td>258 (38.27)</td>
<td>416 (61.72)</td>
</tr>
<tr>
<td>2013</td>
<td>551 (29.65)</td>
<td>1307 (70.34)</td>
<td>192 (32.37)</td>
<td>401 (67.62)</td>
</tr>
<tr>
<td>2014</td>
<td>555 (28.86)</td>
<td>1368 (71.13)</td>
<td>232 (38.53)</td>
<td>370 (61.46)</td>
</tr>
<tr>
<td>Total</td>
<td>4177 (29.6)</td>
<td>9952 (70.4)</td>
<td>1411 (35.9)</td>
<td>2520 (64.1)</td>
</tr>
</tbody>
</table>

* Percentage reflected the annual benign or malignant prevalence of findings among total patients according to years.

### Table 3. Univariate Analysis of Imaging Patterns to Predict Benign Tumor or Malignant Abnormality After Partial Nephrectomy

<table>
<thead>
<tr>
<th>Imaging Pattern</th>
<th>Benign Pathologic Findings</th>
<th>Malignant Pathologic Findings</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any CT</td>
<td>5109 (91.4)</td>
<td>11 386 (91.3)</td>
<td>.76</td>
</tr>
<tr>
<td>Any MRI</td>
<td>1774 (31.8)</td>
<td>4176 (33.5)</td>
<td>.02</td>
</tr>
<tr>
<td>Any USG</td>
<td>2950 (52.8)</td>
<td>6413 (51.4)</td>
<td>.09</td>
</tr>
<tr>
<td>Any biopsy</td>
<td>345 (6.2)</td>
<td>1022 (8.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT + MRI</td>
<td>596 (10.7)</td>
<td>1421 (11.4)</td>
<td>.002</td>
</tr>
<tr>
<td>CT+MRI+USG</td>
<td>701 (12.5)</td>
<td>1629 (13.1)</td>
<td></td>
</tr>
<tr>
<td>CT only</td>
<td>1760 (31.5)</td>
<td>3579 (28.7)</td>
<td></td>
</tr>
<tr>
<td>CT only</td>
<td>1742 (31.2)</td>
<td>3838 (30.8)</td>
<td></td>
</tr>
<tr>
<td>All other combinations</td>
<td>789 (14.1)</td>
<td>2055 (16.1)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5588</td>
<td>12 472</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4. Multiple Logistic Analysis to Predict Benign Pathologic Findings After Partial Nephrectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female vs male</td>
<td>0.62 (0.58-0.66)</td>
<td>&lt;.001</td>
<td>0.62 (0.58-0.66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age</td>
<td>0.989 (0.986-0.991)</td>
<td>&lt;.001</td>
<td>0.989 (0.986-0.991)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Imaging pattern</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any CT</td>
<td>NA</td>
<td>1.01 (0.90-1.14)</td>
<td>.87</td>
<td>1.01 (0.90-1.14)</td>
</tr>
<tr>
<td>Any MRI</td>
<td>NA</td>
<td>1.07 (0.99-1.15)</td>
<td>.08</td>
<td>1.07 (0.99-1.15)</td>
</tr>
<tr>
<td>Any USG</td>
<td>NA</td>
<td>0.94 (0.89-1.01)</td>
<td>.07</td>
<td>0.94 (0.89-1.01)</td>
</tr>
<tr>
<td>Any biopsy</td>
<td>NA</td>
<td>1.38 (1.21-1.57)</td>
<td>&lt;.001</td>
<td>1.38 (1.21-1.57)</td>
</tr>
<tr>
<td>Imaging pattern</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All other combinations vs CT only</td>
<td>1.16 (1.05-1.28)</td>
<td>.004</td>
<td>1.16 (1.05-1.28)</td>
<td>.004</td>
</tr>
<tr>
<td>CT + MRI vs CT only</td>
<td>1.07 (0.96-1.20)</td>
<td>.25</td>
<td>1.07 (0.96-1.20)</td>
<td>.25</td>
</tr>
<tr>
<td>CT + USG vs CT only</td>
<td>1.03 (0.93-1.15)</td>
<td>.54</td>
<td>1.03 (0.93-1.15)</td>
<td>.54</td>
</tr>
<tr>
<td>CT + USG vs CT only</td>
<td>0.93 (0.86-1.01)</td>
<td>.08</td>
<td>0.93 (0.86-1.01)</td>
<td>.08</td>
</tr>
<tr>
<td>Geographic region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North Central vs West</td>
<td>0.88 (0.79-0.98)</td>
<td>.02</td>
<td>0.88 (0.79-0.97)</td>
<td>.01</td>
</tr>
<tr>
<td>Northeast vs West</td>
<td>1.05 (0.94-1.17)</td>
<td>.37</td>
<td>1.05 (0.94-1.17)</td>
<td>.37</td>
</tr>
<tr>
<td>South vs West</td>
<td>1.03 (0.93-1.14)</td>
<td>.57</td>
<td>1.03 (0.93-1.14)</td>
<td>.56</td>
</tr>
<tr>
<td>Unknown vs West</td>
<td>1.02 (0.83-1.25)</td>
<td>.85</td>
<td>1.02 (0.83-1.25)</td>
<td>.85</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; USG, ultrasonography.

* Multiple logistic regression analysis was done without adjustment of imaging pattern.

b Multiple logistic regression analysis was done without adjustment of imaging combination pattern.
However, the present results are still notable because of the superiority of all other complex combinations including MRI only, MRI and USG, any other combinations with biopsy when compared with performance of CT alone.

To date, there is no consensus on the utility of pre-PNx imaging other than for CT. Most reports on the accuracy of MRI to predict RCC in small renal masses are based on retrospective studies. The retrospective interpretation of MRI is different from the real-time interpretation in clinical practice. The ultimate interpretation technologies of CT or MRI that could be helpful to predict RCC in small renal masses is a time-intensive undertaking that is not feasible in clinical practice. Kim et al. reported a poor diagnostic accuracy of CT and MRI to predict RCC in small renal mass, with a sensitivity of 79.7% and 88.1%, respectively, and specificity of 44.4% and 33.3%, respectively, using subjective radiologic interpretation in real clinical practice.

There are several studies worth mentioning that investigate other nonradiologic factors that might affect the histologic prediction. Although most recently Bauman et al. reported no relationship with sex and age, several studies have focused on sex and age, in which female sex and younger age predominantly predicted benign pathologic findings. Female predominance in benign pathologic diagnoses could be explained by association between AML and women. Our study also showed female predominance in benign pathologic findings after PNx. However, with regard to age, the older age group showed higher predominance in benign pathologic findings after PNx.

Reducing the benign pathologic findings after PNx is an important issue considering the inherent surgical risk and surgery-related costs. Given our findings, it may be helpful for urologists to focus more on the extended role of MRI and the performance of biopsy to reduce benign pathologic findings after PNx. Recently, more high-quality evidence of the performance of biopsy in patients with suspicious small renal malignant tumors has been published, which provide further information about the possible final diagnosis in situations with equivocal clinical and radiographic findings.

Limitations

Although this study is the first nationally representative cohort study about the prevalence of benign pathologic findings after PNx, several limitations exist. First, as this is an administrative data set, there is no information about tumor size and pathologic stage. Although this study used diagnosis codes for identification of the cohort and outcomes, there is a possibility of misclassification bias. We could not surmise a reason why there were patients in the database who were excluded because they had no records of pre-PNx imaging. Second, we could not classify the types of surgical approaches including open, laparoscopic, or robotic surgery. Increasing availability of robotic surgery could be an important factor for benign pathologic diagnoses after PNx as well as increased imaging modalities. Moreover, there is a marked difference of the prevalence between 2007 and other years, which could be explained by fast dissemination of robotic assisted PNx. Third, the cost data we used were total payments, which is directly associated with consumers’ total expense. However, it is possible that this may not be reflective of the total charge cost, which is related to a variety of charges including the direct and indirect cost of the hospital stay. Although there was a marked difference in the total payment costs between the benign and malignant diagnoses groups, this difference could not be fully explained. It is possible that fixed cost may account for the difference, which is associated with surgical equipment costs and increased operation times. Moreover, there are 2 types of fee paying: fee-for-service and encounter. In addition, immunohistochemical staining cost, oncotyping, additional radiologic imaging before or during the operation after admission could be possible factors for the difference.

Conclusions

Prevalence of benign pathologic findings after PNx is not low, and exceeds 30% on an ongoing annual basis. Each imaging modality including MRI and biopsy, and combinations of modalities affect the prediction of benign pathologic findings. Urologists have to focus more on high prevalence of benign pathologic findings after PNx and consider other imaging modalities including MRI and biopsy. Avoiding unnecessary surgery is more than an issue of cost-effectiveness in patients’ view. Clinicians have to focus more to make every effort to reduce the likeleyhood of benign pathologic findings after PNx.

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Drafting of the manuscript: Kim, Khandwala

Critical revision of the manuscript for important intellectual content: Li, Khandwala, K. Chung, Park, B. Chung

Statistical analysis: Li

Obtained funding: Kim

Administrative, technical, or material support: K. Chung

Supervision: Park, B. Chung

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Original Investigation Research


