Five-Year Survival After Surgical Treatment for Kidney Cancer

A Population-Based Competing Risk Analysis

John M. Hollingsworth, MD1
David C. Miller, MD, MPH2
Stephanie Daignault, MS1
Brent K. Hollenbeck, MD, MS1

1 Department of Urology, University of Michigan, Ann Arbor, Michigan.
2 Department of Urology, University of California at Los Angeles, Los Angeles, California.

BACKGROUND. Kidney cancer's rising incidence is largely attributable to the increased detection of small renal masses. Although surgery rates have paralleled this incidence trend, mortality continues to rise, calling into question the necessity of surgery for all patients with renal masses. Using a population-based cohort, a competing risk analysis was performed to estimate patient survival after surgery for kidney cancer, as a function of patient age and tumor size at diagnosis.

METHODS. With data from the Surveillance, Epidemiology, and End Results Program (1983–2002), a cohort was assembled of 26,618 patients with surgically treated, local-regional kidney cancer. Patients were sorted into 20 age-tumor size categories and the numbers of patients that were alive, dead from kidney cancer, and dead from other causes were tabulated. Poisson regression models were fitted to obtain estimates of cancer-specific and competing-cause mortality.

RESULTS. Age-specific kidney cancer mortality was stable across all size strata but varied inversely with tumor size. Patients with the smallest tumors enjoyed the lowest cancer-specific mortality (5% for masses ≤ 4 cm). Competing-cause mortality rose with increasing patient age. The estimated 5-year competing-cause mortality for elderly subjects (≥ 70 years) was 28.2% (95% confidence interval [CI]: 25.9%–30.8%), irrespective of tumor size.

CONCLUSIONS. Despite surgical therapy, competing-cause mortality for patients with renal masses rises with increasing patient age. After 5 years, one-third of elderly patients (≥ 70 years) will die from other causes, suggesting the need for prospective studies to evaluate the role of active surveillance as an initial therapeutic approach for some small renal masses. Cancer 2007;109:1763–8.

© 2007 American Cancer Society.

KEYWORDS: mortality, kidney neoplasms, surgery, SEER program.

The rising incidence of kidney cancer demonstrated over the past 2 decades1,2 is largely attributable to an increase in the number of small renal masses.3 Reflecting the current treatment paradigm,4 the rising incidence has been paralleled by greater use of nephrectomy.5 Despite these trends, kidney cancer mortality rates have continued their monotonous rise.5 This apparent disconnect—between increasing treatment and increasing mortality—raises questions regarding the necessity of surgery for all patients with small kidney tumors.

There is growing evidence to suggest that the anticipated survival benefit derived from the surgery for suspicious renal masses is nonuniform. To begin, kidney cancer is now recognized as a heterogeneous disease, whose histopathologic subtypes have variable natural

and adenocarcinoma not otherwise specified (NOS),
behavior codes 2 and 3 [for adenocarcinoma in situ
8317, 8318, 8319, 8320, 8960, 8963, and 8966; and
8032, 8041, 8140, 8240, 8260, 8270, 8290, 8310, 8312,
were extracted. With the exception of patient age trea-
low-up, surgery type, and vital status at last contact,
year of diagnosis, race, marital status, length of fol-
yielding a final study sample of 26,618 patients.
patients (4.8%) with missing data for tumor size,
identified 27,968 patients with surgically treated,
appended with these codes. Using this approach, we
surgery codes 10, 20, 30, 40, 50, 60, 70, and 90 (1983 to
mor excision (22, 23, 24, 25, 26, and 27), and nephrec-
for local tumor destruction (12, 13, and 14), local tu-
1997). For the years 1998 to 2002, SEER added codes
of surgical therapy based on SEER's site-specific sur-
gical therapy (ie, radical or partial nephrectomy and
were enrolled in the analysis. Of these, 1337 (2.8%)
were then plotted for each age-tumor size stratum. All
were still alive 5 years after diagnosis. These estimates
3 outcomes of interest (alive, dead from kidney can-
and dead from other causes) for each of our 20
age-tumor size combinations.

We then used separate Poisson regression models
to obtain estimates of the mortality rates from kidney
cancer and other competing medical conditions.
Finally, we applied the fitted rates of kidney cancer
death and other-cause death to the proportion of
patients still alive at the beginning of each successive
1-year follow-up interval. This provided us with esti-
mates of the proportion of patients who died from
kidney cancer and other competing causes, or who
were still alive 5 years after diagnosis. These estimates
were then plotted for each age-tumor size stratum. All
statistical tests were 2-tailed and performed at a sig-
nificance level of .05 using the SAS system (v. 9.1, SAS
Institute, Cary, NC). Institutional Review Board ap-
approval was waived for this study.

RESULTS

The characteristics of the study cohort (n = 26,618)
are described in Table 1. The typical study subject
was a married, white male over age 60. Nearly all
(92%) underwent a radical nephrectomy for manage-
ment of their local-regional disease. Five years of fol-
low-up data were available for 46%, and 37% died
from kidney cancer or other causes over the study
interval.

Table 2 presents the distribution of death from
kidney cancer or competing causes stratified by tu-
mor size and age at diagnosis. Among patients with
small (<4 cm) surgically treated lesions, only 5% died
from kidney cancer within 5 years. In contrast, even
with surgery 27% of patients with the largest (>7 cm)
lesions died from their disease.

Figure 1 depicts the smooth, model-derived,
5-year cumulative mortality estimates. Age-specific
mortality from kidney cancer showed relative stability

MATERIALS AND METHODS

We used data from 9 Surveillance, Epidemiology, and
End Results (SEER) registries (San Francisco-Oakland,
Connecticut, Metropolitan Detroit, Hawaii, Iowa, New
Mexico, Seattle-Puget Sound, Utah, Metropolitan
Atlanta, San Jose-Monterey, Los Angeles, Alaska) to
identify incident cases of kidney cancer based on
International Classification of Disease for Oncology,
Second Edition site code C64.9; histology codes
8032, 8041, 8140, 8240, 8260, 8270, 8290, 8310, 8312,
8317, 8318, 8319, 8320, 8960, 8963, and 8966; and
behavior codes 2 and 3 [for adenocarcinoma in situ
and adenocarcinoma not otherwise specified (NOS),

Our study cohort was limited to those patients
with local-regional disease (according to SEER's 'best'
staging system) who were treated with definitive sur-
gical therapy (ie, radical or partial nephrectomy and
locally ablative therapies). We ascertained the receipt
of surgical therapy based on SEER's site-specific sur-
gery codes 10, 20, 30, 40, 50, 60, 70, and 90 (1983 to
1997). For the years 1998 to 2002, SEER added codes
for local tumor destruction (12, 13, and 14), local tu-
mor excision (22, 23, 24, 25, 26, and 27), and nephrec-
tomy with ureterectomy (80). The preceding list was
appended with these codes. Using this approach, we
ascertained the receipt of surgical therapy based on
SEER's site-specific surgical therapy codes 10, 20, 30,
40, 50, 60, 70, and 90 (1983 to 1997). For the years
1998 to 2002, SEER added codes for local tumor destruc-
tion (12, 13, and 14), local tumor excision (22, 23,
24, 25, 26, and 27), and nephrectomy with ureterectomy
(80). The preceding list was appended with these
codes. Using this approach, we ascertained the receipt
of surgical therapy based on SEER's site-specific sur-
gery codes 10, 20, 30, 40, 50, 60, 70, and 90 (1983 to
1997). For the years 1998 to 2002, SEER added codes
for local tumor destruction (12, 13, and 14), local tu-
mor excision (22, 23, 24, 25, 26, and 27), and nephrec-
tomy with ureterectomy (80). The preceding list was
appended with these codes. Using this approach, we
ascertained the receipt of surgical therapy based on
SEER's site-specific surgical therapy codes 10, 20, 30,

within each of our 4 size strata, eg, for tumors 2–4 cm in size: those <50 years had a 5-year mortality rate of 2.8% (95% confidence interval [CI]: 2.4%–3.2%); those 50–59 years had a 5-year mortality rate of 4.6% (95% CI: 4.1%–5.3%); those 60–69 years had a 5-year mortality rate of 5.5% (95% CI: 4.8%–6.2%); those 70–79 years had a 5-year mortality rate of 6.3% (95% CI: 5.5%–7.1%); and those ≥80 years had a 5-year mortality rate of 7.5% (95% CI: 6.4%–8.8%). However, cancer-specific mortality varied inversely with tumor size, such that patients with the smallest cancers had the lowest predicted cancer-specific mortality (5.3%, 95% CI: 4.6%–6.1%, for those with tumors ≤4 cm vs 18.1%, 95% CI: 16.4%–20.0%, for those with tumors >4 cm). In contrast, competing-cause mortality rose with increasing patient age. For instance, the predicted, 5-year competing risk mortality for those aged 70 years and older was 28.2% (95% CI: 25.9%–30.8%), irrespective of tumor size.

### DISCUSSION

The relative benefit of definitive surgical therapy for small renal masses (≤4 cm) is partially mitigated by competing causes of mortality in older patients. For example, nearly one-third of patients aged 70 years and older will die from unrelated comorbid disease within 5 years of curative surgery for their kidney cancer. Prior work has demonstrated a rise in the incidence of these small, presumably curable, renal masses that has been paralleled by increases in surgical ther-

### TABLE 1

**Characteristics of Patients With Treated Local-Regional Kidney Cancer (1983–2002)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 26,618 No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEER site</td>
<td></td>
</tr>
<tr>
<td>San Francisco</td>
<td>3394 (13)</td>
</tr>
<tr>
<td>Connecticut</td>
<td>4136 (15)</td>
</tr>
<tr>
<td>Metro Detroit</td>
<td>5439 (20)</td>
</tr>
<tr>
<td>Hawaii</td>
<td>964 (4)</td>
</tr>
<tr>
<td>Iowa</td>
<td>3816 (14)</td>
</tr>
<tr>
<td>New Mexico</td>
<td>1575 (6)</td>
</tr>
<tr>
<td>Seattle</td>
<td>4031 (15)</td>
</tr>
<tr>
<td>Utah</td>
<td>1224 (5)</td>
</tr>
<tr>
<td>Atlanta</td>
<td>2039 (8)</td>
</tr>
<tr>
<td>Age at diagnosis ± standard deviation, y</td>
<td>60.8 ± 15.4</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>21,390 (81)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1291 (5)</td>
</tr>
<tr>
<td>Black</td>
<td>2518 (9)</td>
</tr>
<tr>
<td>Other</td>
<td>1337 (5)</td>
</tr>
<tr>
<td>Women</td>
<td>10,031 (38)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>2964 (11)</td>
</tr>
<tr>
<td>Married</td>
<td>17,270 (65)</td>
</tr>
<tr>
<td>Separated/divorced</td>
<td>1951 (7)</td>
</tr>
<tr>
<td>Widowed</td>
<td>3181 (12)</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
</tr>
<tr>
<td>Until death</td>
<td>9966 (37)</td>
</tr>
<tr>
<td>Alive at 1 y</td>
<td>22,708 (85)</td>
</tr>
<tr>
<td>Alive at 3 y</td>
<td>16,631 (62)</td>
</tr>
<tr>
<td>Alive at 5 y</td>
<td>12,295 (46)</td>
</tr>
<tr>
<td>Treatment within 6 mo</td>
<td></td>
</tr>
<tr>
<td>Total nephrectomy</td>
<td>24,502 (92)</td>
</tr>
<tr>
<td>Partial nephrectomy</td>
<td>2013 (7.5)</td>
</tr>
<tr>
<td>Other surgery*</td>
<td>92 (0.5)</td>
</tr>
<tr>
<td>Vital status at last contact</td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>16,652 (63)</td>
</tr>
<tr>
<td>Deceased due to renal cell</td>
<td>4006 (15)</td>
</tr>
<tr>
<td>Deceased due to other causes</td>
<td>5960 (22)</td>
</tr>
</tbody>
</table>

* Examples include cryosurgery and laser ablation.

### TABLE 2

**Five-Year Outcomes for Those Patients With Treated Local-Regional Kidney Cancer According to Tumor Size**

<table>
<thead>
<tr>
<th>Age at diagnosis</th>
<th>Total no. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td></td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>Sample size</td>
</tr>
<tr>
<td></td>
<td>(n = 1291)</td>
</tr>
<tr>
<td>No. of patients deceased due to RCC</td>
<td>14 18 24 20 3 79 (6)</td>
</tr>
<tr>
<td>Other causes</td>
<td>27 27 81 101 17 253 (20)</td>
</tr>
<tr>
<td>No. of patients alive</td>
<td>278 229 242 179 31 959 (74)</td>
</tr>
<tr>
<td>2–4 cm</td>
<td></td>
</tr>
<tr>
<td>Sample size (n = 8278)</td>
<td>No. of patients deceased due to RCC</td>
</tr>
<tr>
<td>Other causes</td>
<td>113 243 626 749 279 2010 (25)</td>
</tr>
<tr>
<td>No. of patients alive</td>
<td>1286 1365 1615 1294 262 5822 (70)</td>
</tr>
<tr>
<td>&gt;4–7 cm</td>
<td></td>
</tr>
<tr>
<td>Sample size (n = 9105)</td>
<td>No. of patients deceased due to RCC</td>
</tr>
<tr>
<td>Other causes</td>
<td>97 282 659 867 313 2218 (24)</td>
</tr>
<tr>
<td>No. of patients alive</td>
<td>1312 1449 1542 1041 254 5598 (62)</td>
</tr>
<tr>
<td>&gt;7 cm</td>
<td></td>
</tr>
<tr>
<td>Sample size (n = 7944)</td>
<td>No. of patients deceased due to RCC</td>
</tr>
<tr>
<td>Other causes</td>
<td>107 211 438 522 201 1479 (19)</td>
</tr>
<tr>
<td>No. of patients alive</td>
<td>1412 1065 994 650 152 4273 (54)</td>
</tr>
<tr>
<td>All tumors</td>
<td></td>
</tr>
<tr>
<td>Sample size (n = 26,618)</td>
<td>No. of patients deceased due to RCC</td>
</tr>
<tr>
<td>Other causes</td>
<td>344 763 1804 2239 810 5960 (22)</td>
</tr>
<tr>
<td>No. of patients alive</td>
<td>4288 4108 4383 3164 699 16,652 (63)</td>
</tr>
</tbody>
</table>

RCC indicates renal cell carcinoma.
apy. However, despite these 2 epidemiological trends, kidney cancer mortality has continued its gradual climb, suggesting that the current treatment algorithm be revisited.

This long-standing treatment paradigm for patients with a suspicious renal mass generally involves expedient surgical excision shortly after diagnosis. The reasons for this are 2-fold. First, systemic medical therapy and radiation regimens for kidney cancer have been shown to be generally ineffective. Accordingly, surgery represents the best opportunity for curative intervention. Second, patients with larger, more advanced cancers face a dismal prognosis; therefore, surgery early in the disease is believed to improve their chance of survival.

With respect to this treatment paradigm, an important underlying assumption, one not supported by several case series, is that all small renal masses have the universal capacity to grow and metastasize. This assumption, however, has several possible flaws. First, kidney cancer is not a single entity; rather, it is a family of neoplasms with observed variants that have distinct cytogenetic defects and histopathologic features. For example, nonclear-cell sporadic types (eg, chromophobe renal cell carcinoma) often have an indolent course and a much lower metastatic potential compared with the clear-cell variety. In addition to the heterogeneous behavior of the various histologies, kidney cancers may exhibit variable growth according to their size. Indeed, small, suspicious tumors tend to grow at a relatively slow pace (0.28 cm/year). The indolent nature of these lesions is further bolstered by autopsy data, revealing that many incidentally found, small renal masses have less malignant potential than clinically detected tumors. Given these data, it is possible that a proportion of newly diagnosed renal masses may not merit immediate surgical removal.

Nonetheless, in the absence of robust data regarding the natural history of these small renal masses, it is impossible to truly understand their nature. Indeed, all large renal masses, which these data and that of many case series suggest are clearly lethal even after treatment, were small at one time or another. However, the current study suggests that the relative

FIGURE 1. Five-year survival after surgical treatment for kidney cancer. Cumulative mortality for kidney cancer and all causes up to 5 years after diagnosis, after definitive surgical therapy. White indicates survival; gray indicates nonkidney cancer mortality; black indicates kidney cancer mortality.
benefits of surgical treatment are lowest among older patients (eg, age ≥70 years) with renal masses ≤4 cm in size. Thus, in this population, especially where there is significant concurrent comorbidity, a period of active surveillance may be warranted.

For the most part, contemporary surveillance protocols for small renal masses have been limited to patients with substantial medical comorbidity, generally thought to be too infirm to tolerate extirpative procedures. However, as safety of active surveillance increases through improvements in imaging and biopsy techniques, its role will likely continue to broaden. Until this time, these data provide insight into current clinical practice. Despite the fact that partial nephrectomy offers equivalent local tumor control to its radical counterpart,27,28 national trends illustrate that the uptake of nephron-sparing surgery for small (≤4 cm) renal masses has been slow.29 These utilization trends are troubling when considered in the context of recent findings that show radical nephrectomy to be a significant risk factor for the development of chronic kidney disease.30 The potential consequences of kidney disease, coupled with increasing competing-cause mortality with age, encourage a rethinking of the treatment algorithm for small renal masses.

Our findings must be considered in the context of several limitations. SEER does not collect data on comorbid status, which worsens with age and affects patient survival. However, we would argue that case-mix adjustment in the setting of our competing risk analysis would have been inappropriate, as our intent was to estimate a patient’s probability of cancer-specific vs competing-cause mortality—a probability intimately related to a patient’s comorbidities. In addition, we determined the underlying cause of a patient’s death using SEER’s cause-of-death item. The validity of this construct, which is based on death certificate reporting, has been called into question in several settings, specifically as it relates to issues of race and socioeconomic.31–33 However, this approach of measuring cause-of-death has compared favorably with that obtained from autopsy among patients with cancer diagnoses when tested empirically.34 Thus, although we cannot exclude residual bias related to coding, these data support the use of this construct in the current context.

Conclusions
In summary, our study demonstrates that a significant proportion of kidney cancer patients will die within 5 years of diagnosis despite definitive surgical therapy, given the relation between competing-cause mortality and increasing age. While we are not encouraging an abrupt departure from the current treatment paradigm, our data do prompt reflection on contemporary practice patterns for kidney cancer. Further, our data suggest the need for prospective studies to evaluate the role of active surveillance as an initial therapeutic approach for some small renal masses.

REFERENCES