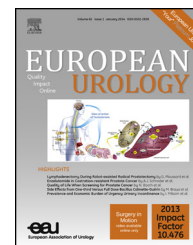


available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com](http://www.europeanurology.com)



## Kidney Cancer

# Management of Localized Kidney Cancer: Calculating Cancer-specific Mortality and Competing Risks of Death for Surgery and Nonsurgical Management

Maxine Sun<sup>a,b,1,\*</sup>, Andreas Becker<sup>a,c,1</sup>, Zhe Tian<sup>a</sup>, Florian Roghmann<sup>a,d</sup>, Firas Abdollah<sup>a,e</sup>, Alexandre Larouche<sup>a</sup>, Pierre I. Karakiewicz<sup>a,f</sup>, Quoc-Dien Trinh<sup>a,f</sup>

<sup>a</sup> Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada; <sup>b</sup> Department of Public Health, Faculty of Medicine, University of Montreal, Montreal, Canada; <sup>c</sup> Martini-Clinic, Prostate Cancer Center Hamburg-Eppendorf, Hamburg, Germany; <sup>d</sup> Department of Urology, Universitätsklinik Marienhospital, Herne, Germany; <sup>e</sup> Department of Urology, Vita-Salute San Raffaele University, Milan, Italy; <sup>f</sup> Department of Urology, University of Montreal Health Center, Montreal, Canada

### Article info

#### Article history:

Accepted March 15, 2013  
Published online ahead of  
print on March 27, 2013

#### Keywords:

Localized kidney cancer  
Nephrectomy  
Nonsurgical management  
SEER

### Abstract

**Background:** For elderly individuals with localized renal cell carcinoma (RCC), surgical intervention remains the primary treatment option but may not benefit patients with limited life expectancy.

**Objective:** To calculate the trade-offs between surgical excision and nonsurgical management (NSM) with respect to competing causes of mortality.

**Design, setting, and participants:** Relying on a cohort of Medicare beneficiaries, all patients with nonmetastatic node-negative T1 RCC between 1988 and 2005 were abstracted.

**Intervention:** All patients were treated with partial nephrectomy (PN), radical nephrectomy (RN), or NSM.

**Outcome measurements and statistical analysis:** Cancer-specific mortality (CSM) and other-cause mortality (OCM) rates were modeled through competing-risks regression methodologies. Instrumental variable analysis was used to account for the potential biases associated with measured and unmeasured confounders.

**Results and limitations:** A total of 10 595 patients were identified. In instrumental variable analysis, patients treated with PN (hazard ratio [HR]: 0.45; 95% confidence interval [CI], 0.24–0.83;  $p = 0.01$ ) or RN (HR: 0.58; 95% CI, 0.35–0.96;  $p = 0.03$ ) had a significantly lower risk of CSM than those treated with NSM. In subanalyses restricted to patients  $\geq 75$  yr, the instrumental variable analysis failed to detect any statistically significant difference between PN (HR: 0.48;  $p = 0.1$ ) or RN (HR: 0.57;  $p = 0.1$ ) relative to NSM with respect to CSM. Similar trends were observed in T1a RCC only.

**Conclusions:** PN or RN is associated with a reduction of CSM among older patients diagnosed with localized RCC, compared with NSM. The same benefit failed to reach statistical significance among patients  $\geq 75$  yr. The harms of surgery need to be weighed against the marginal survival benefit for some patients.

Crown Copyright © 2013 Published by Elsevier B.V. on behalf of European Association of Urology. All rights reserved.

<sup>1</sup> Equal contribution.

\* Corresponding author. Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, 264 Blvd. Rene-Levesque East, #228, Montreal (QC), Canada H2X 1P1.

Tel. +1 514 890 8000, ext: 35335; Fax: +1 514 227 5103.

E-mail address: [mcw.sun@umontreal.ca](mailto:mcw.sun@umontreal.ca) (M. Sun).

## 1. Introduction

Current management of patients with localized renal cell carcinoma (RCC)  $\leq 7$  cm consists of surgical excision, preferably partial nephrectomy (PN) over radical nephrectomy (RN) whenever technically feasible [1–3]. Alternatively, initial observation has gained considerable precedence in recent years; the utilization rate was nearly 20% in 2008 relative to nephrectomy for patients with T1a RCC [1–4].

The growing acceptance of observation began when several reports demonstrated a lack of declining mortality rates for localized RCC over time, despite earlier detection resulting from widespread imaging use [5], thereby challenging the longstanding role of expedient surgical excision after RCC diagnosis. Previous studies showed that suspicious tumors grow slowly over time (0.3 cm/yr), frequently follow a protracted course (40%), and are unlikely to metastasize ( $<1\%$ ) [6–9]. Further arguments in favor of initial observation include the substantial proportion of older patients with clinically node-negative T1a disease and other-cause mortality (OCM) [10,11]. Recent data further confirm the importance of active surveillance; the data indicated a lack of survival benefit between PN or RN relative to active surveillance among elderly patients with clinically localized RCC [12].

Under the light of a changing treatment paradigm for small renal masses, many physicians may feel sufficiently reassured by existing data to recommend observation for individuals with limited life expectancy and/or decreased functional status, while other physicians may feel apprehensive about the potential risk of an aggressive disease phenotype, thus favoring surgery to avoid uncertainties with respect to disease-specific mortality. We sought to calculate the trade-offs of surgical intervention (PN or RN) compared with nonsurgical management (NSM) with respect to survival in a large sample of patients with T1 RCC to optimize treatment-related decision making.

## 2. Methods

### 2.1. Data source

Data originated from the US Surveillance Epidemiology and End Results (SEER)–Medicare linked database. Medicare provides federally funded health insurance for approximately 97% of persons  $\geq 65$  yr in the United States [13]. Linkage to the SEER database is complete for approximately 94% of patients [14].

### 2.2. Study population

Between 1988 and 2005, individuals aged  $\geq 66$  yr with a primary diagnosis of nonmetastatic RCC, who had both Medicare Part A and Part B claims available, and who were not enrolled in a health maintenance organization throughout the duration of the study period were abstracted. Only individuals with node-negative T1 RCC tumors  $\leq 7$  cm of clear cell, papillary, chromophobe, RCC unspecified, or other (collecting duct, granular, medullary, cystic) histologic subtypes were included. Other exclusions consisted of patients diagnosed only at autopsy or on death certificate, patients whose original or current reason for Medicare entitlement was listed as a disability or Medicare status

code, and patients with unknown tumor size. The result was 10 595 assessable individuals for our study.

### 2.3. Variable definition

Patients treated within 6 mo of RCC diagnosis with PN or RN were identified [15,16]. NSM was defined as the absence of active treatment codes (ie, PN, RN, ablative techniques), which resulted in 3271 assessable individuals. Of those patients, 114 (3.5%) underwent a nephrectomy  $>6$  mo after diagnosis. Of those patients, 29 died of any cause, which is 0.08% of the NSM group. Given their small numbers, such individuals remained in the analyses despite having a delayed nephrectomy. For each patient, age at diagnosis, sex, race, and marital status were assigned using the SEER data. Socioeconomic status was computed using a previously described methodology [17]. Baseline conditions were measured through a modified version of the Charlson comorbidity index based on claims 1 yr before RCC diagnosis [18] and grouped as 0, 1, and  $\geq 2$ . Tumor size and Fuhrman grade were also considered.

### 2.4. End points

Patients who died of RCC-specific death were classified as *cancer-specific mortality (CSM)*. Patients who died of other causes were classified as *other-cause mortality (OCM)*. Data on cause-specific mortality and follow-up were available throughout the end of 2007. The duration of survival was measured as the interval between RCC diagnosis and the Medicare data of mortality or last follow-up.

### 2.5. Statistical analyses

Two-sided  $\chi^2$  tests and Mann-Whitney tests were used to evaluate associations between treatment type (nephrectomy compared with NSM) and covariates. To reduce residual confounding due to unmeasured patient and/or other pertinent characteristics, we relied on instrumental variable analysis [19].

The instrument variable used was the local area treatment intensity of surgery (RN and PN). The instrument variable was created by grouping patients from the SEER-Medicare database according to hospital referral regions, as developed by the Dartmouth Atlas of Health Care [20]. This variable was calculated as the proportion of patients who received surgery in each health service area (HSA). Prior to the instrument's use, we assessed its validity by confirming that the intensity of nephrectomy use according to HSA was highly correlated with receipt of surgery ( $\chi^2$  test  $p < 0.001$ , multivariable F statistic  $>10$ ) but was not associated with survival in multivariable models (CSM hazard ratio [HR]: 0.98,  $p = 0.8$ ; OCM HR: 0.98,  $p = 0.4$ ).

In primary analyses, comparative effectiveness of nephrectomy compared with NSM was tested through competing risks regression models for prediction of CSM after adjusting for OCM, and vice versa [21], in the entire cohort and then among patients with exclusively T1a RCC. Finally, subanalyses were conducted by restricting the cohort to patients  $\geq 75$  yr [22], patients without any secondary malignancies, patients diagnosed in the year 2000 and onward, and patients with T1a RCC who were  $\geq 75$  yr. All statistical testing was two-sided, with a level of significance set at 5%. Analyses were performed using the R software environment for statistical computing and graphics (v.2.15.2).

## 3. Results

### 3.1. Baseline characteristics

Of 10 595 T1 RCC individuals, 3271 (30.9%), 1051 (9.9%), and 6273 (59.2%) were treated with NSM, PN, and RN,

Download English Version:

<https://daneshyari.com/en/article/3925049>

Download Persian Version:

<https://daneshyari.com/article/3925049>

[Daneshyari.com](https://daneshyari.com)