Published in final edited form as:

Urol Oncol. 2016 October ; 34(10): 433.e9–433.e17. doi:10.1016/j.urolonc.2016.05.021.

Toward greater adoption of minimally-invasive and nephron-sparing surgical techniques for renal cell cancer in the U.S.

Matthew P. Banegas^{1,*},

Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA

Linda C. Harlan²,

Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD, USA

Bhupinder Mann³, and

Division of Cancer Treatment and Diagnosis, National Cancer Institute, Bethesda, MD, USA

K. Robin Yabroff²

Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD, USA

Abstract

Purpose—To examine national, population-based utilization trends of nephron-sparing and minimally invasive techniques for the surgical management of adult renal cell cancer patients in the United States (US).

Methods—Linked data from the National Cancer Institute's Patterns of Care studies and the Area Health Resource File were used to evaluate trends of nephron-sparing and minimally invasive techniques in a sample of 1,110 patients newly diagnosed with American Joint Committee on Cancer (AJCC) stages I-II RCC, in 2004 and 2009, who underwent surgery. Descriptive statistics were used to assess patterns of surgery between 2004 and 2009. Multivariable logistic regression analyses were used to evaluate the associations between demographic, clinical, hospital and area-level healthcare characteristics with surgery utilization, stratified by the subset of patients who were potentially eligible for partial nephrectomy (PN) versus radical nephrectomy (RN) and laparoscopic (LRN) versus open radical nephrectomy (ORN), respectively.

*Corresponding Author (Present Address): Matthew P. Banegas, PhD, MPH, Kaiser Permanente Center for Health Research, 3800 N Interstate Ave, Portland, OR 97227, Phone: 503-335-6765, Fax: 503-335-6311, Matthew.P.Banegas@kpchr.org.

¹Kaiser Permanente, The Center for Health Research, 3800 N Interstate Ave, Portland, OR 97227

²Healthcare Assessment Research Branch, Healthcare Delivery Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, 9609 Medical Center Drive, Bethesda, MD 20892

³Clinical Investigations Branch, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, 9609 Medical Center Drive, MSC9739, Bethesda, MD 20892

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest statement. None declared.

This article is a US Government work and, as such, is in the public domain in the United States of America. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

Results—Between 2004 and 2009, PN use among stage I patients with tumors ≤ 4 cm increased from 29% to 41%, respectively ($p=0.22$). Among patients with stage I tumors ≤ 4 cm, use of PN significantly increased from 43% in 2004 to 55% in 2009 ($p=0.05$). Among patients with stage I tumors $>4-7$ cm, LPN increased from 8% to 15%, while LRN increased from 38% to 69%, between 2004 and 2009 ($p=0.07$). Significant increases in LRN use were observed for both stage I (from 43% in 2004 to 58% in 2009; $p=0.05$) and stage II patients (from 16% in 2004 to 47% in 2009; $p=0.01$). Patients diagnosed at an older age, with larger tumors, non-clear cell RCC and who did not receive treatment in a hospital with residency training were significantly less likely to receive PN versus RN; whereas, those diagnosed in 2009 with stage I disease were significantly more likely to receive LRN versus ORN.

Conclusions—This study highlights a significant shift toward increased use of nephron-sparing and minimally-invasive surgical techniques to treat RCC patients in the U.S. Our findings are among the first population-based reports in which the majority of eligible RCC patients received PN over RN. In light of the longstanding evidence on the improved patient outcomes, future investigation is warranted to identify the barriers to increased adoption of these nephron-sparing and minimally-invasive approaches.

Keywords

renal cell cancer; patterns of care; partial nephrectomy; radical nephrectomy; open radical nephrectomy; laparoscopic radical nephrectomy; nephron-sparing surgery

1. INTRODUCTION

Renal cell cancer (RCC) represents approximately 4% of all new cancer cases in the United States (US), with 61,560 estimated new cases in 2015¹. Over the past few decades, incidence rates of RCC in the US have been rising, with a general shift toward diagnosis of stage I (localized), smaller sized tumors (≤ 4 cm)² that are detected as a result of widespread abdominal imaging ($>50\%$ detected incidentally)³. Alongside the increase in early stage RCC, nephron-sparing and minimally-invasive surgical techniques such as partial nephrectomy (PN) and laparoscopic radical nephrectomy (LRN), respectively, have evolved as viable options to open radical nephrectomy (ORN) for management of these patients. Moreover, a growing body of evidence points to demonstrated benefits of PN and LRN compared to ORN, including improved postoperative morbidity while achieving equal oncological outcomes. Since approximately 2009, guidelines from the American Urologic Association (AUA), National Comprehensive Cancer Network (NCCN) and European Association of Urology (EAU) recommend PN as the preferred standard of care for T1 tumors (≤ 7 cm). RN is an alternative standard of care for T1 tumors not amenable to PN or not technically feasible as determined by the urologic surgeon and thermal ablation or active surveillance are other options.⁴⁻⁶ The EAU lists LRN as the recommended standard of care for patients with T2 tumors and smaller renal masses not suitable for nephron-sparing surgery, with ORN as an optional standard of care, while the NCCN and AUA cite similar oncological outcomes between the laparoscopic and open approaches.⁴⁻⁶

Notwithstanding the benefits and guideline recommendations of PN and LRN for localized RCC, nationwide trends suggest ORN has remained the predominant surgical approach in

the US. Using data from the Surveillance, Epidemiology and End Results (SEER) program between 1999-2006, Dulabon et al., found that 55% of RCC patients with tumors ≥ 4 cm received ORN rather than LRN.⁷ Similarly, based on data from hospital discharges in the National Inpatient Sample, among RCC patients aged 18 and older who received partial or radical nephrectomy (by open or radical technique) between 2002 and 2008, ORN was the most commonly used approach, from 77% in 2002 to 62% in 2008⁸. In this population-based study, we used linked multi-level data with information on health insurance, comorbidity and area-level health care characteristics, to examine more contemporary trends in use of nephron-sparing and minimally invasive techniques for the surgical management of adult RCC patients in US community practice between 2004 and 2009, as well as the association of individual- and area-level characteristics with surgical management.

2. METHODS

2.1. Data Sources

Data for the current study were obtained from the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) program, which collects information on all cancer diagnoses in defined US geographic regions, currently covering approximately 28% of the US population⁹. In SEER, patient information is primarily obtained from hospital records, including tumor characteristics, first course of treatment and select demographic characteristics. To collect therapy information that is not well collected by routine SEER activities, NCI annually conducts Patterns of Care (POC) studies on select cancer sites, obtaining information from each treating physician about their patient's cancer treatment.¹⁰ SEER registries obtain approval as required from their institutional review boards prior to study initiation.

Following centralized training, abstractors from the 14 participating SEER registries (the metropolitan areas of San Francisco/Oakland, Detroit, Seattle, Atlanta, San Jose/Monterey, Los Angeles County, and the states of Connecticut, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah, and the remainder of California) re-abstract the hospital records of sampled patients to verify tumor characteristics and demographic information. To obtain comprehensive treatment information on the care received by these patients, the treating physician is asked to verify therapy provided. The physician is also asked whether any other providers might have treated the patient and supply that provider's contact information. Identification and contact of additional treating physicians is common in POC studies. To ensure quality control of measures in the SEER POC studies, 5% of the abstracted patient records are re-abstracted.

The Area Health Resource File (AHRF), maintained by the US Health Resources and Services Administration (HRSA), collects information on health system resources and socioeconomic indicators that influence healthcare, according to geographical units. We obtained county-level information on: surgeons (including general surgeons and surgeon specialties), Medicaid inpatient discharges and Medicare inpatient discharges, and the 2008 US population. All information used from the AHRF was based on 2008 estimates, which was the most recent year of data available to link with the SEER data included in our

analysis of 2004 and 2009¹¹. AHRF data was linked to SEER data using the state and county FIP codes of each patient.

2.2 Study Sample

This study included SEER patients diagnosed with renal cell cancer (International Classification of Diseases, Oncology, 3rd revision [ICD-O-3] Site code: C64.9, Behavior: 3 (invasive) and Histology: All codes except lymphoma/hematopoietic M-9590-9989) in 2004 and 2009. Patients previously diagnosed with cancer (other than non-melanoma skin cancer), a simultaneous cancer diagnosis (within 60 days), diagnosed at autopsy or on the death certificate only, or who were under age 20 years were ineligible for the study. Eligible patients were stratified by registry, sex, race/ethnicity and in 2009 stage stratification was included as well, and randomly sampled within strata. Women, non-Hispanic blacks, Asian/Pacific Islanders, Hispanics, American Indians and Alaskan natives were oversampled to obtain more stable estimates. Sampling fractions were used to calculate weighted percentages that reflect the SEER populations from which the data were obtained. For the current analysis, we focused on patients with AJCC stage I-II tumors who underwent surgery by partial nephrectomy (including partial or subtotal nephrectomy) or radical nephrectomy (including complete/total/simple nephrectomy and radical nephrectomy) within 12 months after diagnosis (n=1,110).

2.3. Measures

To examine factors associated with receipt of nephron-sparing and minimally invasive surgical techniques among adult RCC patients, we included multilevel variables that incorporated both patient-level characteristics and area-level healthcare characteristics. Characteristics were selected based on prior evidence showing an association with surgical management of RCC, or which we hypothesized to have an association, and were available in the data sources. Patient-level characteristics included: *demographic* - age at diagnosis, sex, race/ethnicity, marital status, insurance status, and Census tract median household income; *clinical* - American Joint Commission on Cancer (AJCC) 6th edition tumor stage, tumor size, cell type, histological grade, and Charlson Comorbidity score; and *hospital* - hospital bed size and residency training program status. Area-level healthcare characteristics included total number of surgeons, Medicaid inpatient discharges and Medicare inpatient discharges per 10,000 population.

We defined two primary outcomes based on receipt of cancer-directed surgery within 12 months after diagnosis, including (1) *partial nephrectomy* versus *radical nephrectomy*: evaluated among patients who were diagnosed with AJCC stage I tumors that measured ≤ 7 cm in greatest dimension only (e.g., T1a and T1b,) and (2) *open radical nephrectomy* versus *laparoscopic radical nephrectomy*: evaluated in patients who were diagnosed with AJCC stage I-II tumors, who received radical nephrectomy and had complete data on type of surgery only (n=849). Our secondary outcome was based on the receipt of minimally invasive partial or radical nephrectomy within 12 months of diagnosis among patients diagnosed with AJCC stage I tumors that measured ≤ 7 cm and was measured as: *open partial nephrectomy* (OPN) versus *laparoscopic partial nephrectomy* (LPN) versus *open radical nephrectomy* (ORN) versus *laparoscopic radical nephrectomy* (LRN).

2.4. Statistical Analyses

Patient, clinical, hospital and area-level healthcare characteristics are presented as total counts and weighted percentages, and were compared by year of diagnosis, using Pearson's chi-square test. We evaluated the proportion of patients who received (1) PN versus RN, among patients diagnosed with AJCC stage I tumors that measured ≤ 7 cm (n=835); (2) OPN versus LPN versus ORN versus LRN, among patients diagnosed with AJCC stage I tumors that measured ≤ 7 cm (n=816); and (3) ORN versus LRN, among patients diagnosed with AJCC stage I-II tumors, who received radical nephrectomy and had complete data on type of surgery only (n=849), stratified by year of diagnosis, tumor stage and size, using Pearson's chi-square test. Separate logistic regression models were used to evaluate the association of each primary outcome with patient-level and area-level characteristics. Only those characteristics with a statistical association at $p \leq 0.10$ in bivariate analyses were retained in the final multivariate regression models. This is a standard approach for creating parsimonious models [Hosmer, 2013 #3029]. To account for the effect of clustering of patients within counties (and the corresponding county-level healthcare characteristics) on utilization of surgery, we created multilevel models with random effects to examine factors associated with the primary outcomes. Characteristics of the individual patient represented the level 1 fixed effects of our model, and the county of residence (based on state/county FIPS codes) represented level 2. Age at diagnosis, year of diagnosis and SEER registry were included in all multivariate models. Only those variables used in the final multivariable models are presented in the results. All tests of significance were 2-sided, at an alpha level of 0.05. Stata/SE 11.0 (StataCorp LP, College Station, TX) statistical software was used to incorporate sample weights in all analyses.

3. RESULTS

Patient, clinical, hospital and area-level healthcare characteristics are presented in Table 1. The majority of patients were age <65 years at diagnosis, male, White non-Hispanic, married and privately insured. In regard to characteristics of the renal cell tumors, $>75\%$ were clear cell type, $>85\%$ were stage I at diagnosis and $\sim 50\%$ were 4cm or less in size. More than half of patients lived in areas where the supply of surgeons was <6.57 per 10,000 population.

Overall, the proportion of patients with stage I tumors ≤ 7 cm who received PN versus RN rose from 29% in 2004 to 41% in 2009 (Figure 1), though this increase was not statistically significant ($p=0.22$). When stratified by tumor size, there was a significant increase in the proportion of patients with tumors ≤ 4 cm who received PN between 2004 (43%) and 2009 (55%) ($p=0.04$), and a non-significant increase among patients with tumors >4 -7cm from 9% in 2004 to 18% in 2009 ($p=0.53$).

As shown in Figure 2, between 2004 and 2009, there was a considerable shift in the surgical approaches most commonly used to treat patients with stage I tumors ≤ 7 cm, varying by tumor size. Among patients with stage I tumors ≤ 4 cm, use of OPN increased from 27% in 2004 to 33% in 2009 and LPN increased from 15% in 2004 to 22% in 2009, while ORN decreased from 33% to 31% and LRN decreased from 25% to 15% over the same time period; although, these changes were not statistically significant ($p=0.21$). Among patients

with stage I tumors >4-7cm, OPN use increased from 2% in 2004 to 3% in 2009, LPN use increased from 8% in 2004 to 15% in 2009, while LRN use increased from 38% in 2004 to 69% in 2009 and ORN use decreased from 53% in 2004 to 13% in 2009 ($p=0.07$).

Among patients with stage I-II tumors who underwent RN, the proportion who received surgery by LRN significantly increased from 38% in 2004 to 56% in 2009 ($p<0.01$) (Figure 3). Use of LRN among stage I patients increased from 43% in 2004 to 58% in 2009 ($p=0.04$), whereas among stage II patients the proportion receiving LRN increased from 16% in 2004 to 47% in 2009 ($p<0.01$).

Results of the multivariable regression analysis of PN versus RN are shown in Table 2. Among stage I patients, those aged ≥ 65 at diagnosis, who had a tumor >4-7cm, had non-clear cell RCC and who received treatment at a hospital without residency training status were significantly less likely to receive PN versus RN compared to those aged <65 at diagnosis (OR=0.38, 95% CI: 0.17- 0.83, $p=0.02$), who had a tumor ≤ 4 cm (OR=0.10, 95% CI: 0.04-0.29, $p<0.01$), had clear-cell RCC (OR=0.32, 95% CI: 0.13-0.81, $p=0.02$) and received care at a hospital with residency training status (OR=0.28, 95% CI: 0.13-0.61, $p<0.01$), adjusting for other characteristics. Stage I patients with a Charlson Comorbidity score ≥ 1 were approximately 2.5 times more likely to receive PN over RN, compared to those with a Charlson Comorbidity score of zero ($p=0.04$), in the fully adjusted model.

In multivariable regression analysis of LRN versus ORN (Table 3), patients diagnosed in 2009 were approximately 2.6 times more likely to receive LRN compared to those diagnosed in 2004 ($p=0.02$) and patients with stage II RCC were significantly less likely to receive LRN over ORN compared to those stage I RCC (OR=0.28, 95% CI: 0.12-0.64, $p<0.01$), adjusting for other characteristics.

4. DISCUSSION

In this population-based study of adult RCC patients in the United States, we highlight a significant shift toward increased use of minimally-invasive and nephron-sparing surgical techniques between 2004 and 2009. Despite long-standing evidence indicating equivalent oncological outcomes¹²⁻¹⁵, demonstrated postoperative benefits¹⁶⁻¹⁹, and professional society guideline recommendation^{5,6,20}, this is among the first population-based reports in which the majority of eligible RCC patients received PN over RN. These findings extend prior studies on RCC to provide a clear example of the slow adoption of evidence-based cancer care and further question the use of historical surgical approaches for RCC, and novel alternatives with limited evidence of clinical benefit. Importantly, understanding factors associated with the “de-adoption” of medical treatment is the basis of one of NCI's Provocative Questions (PQ – 12), since efforts to improve the quality of cancer care should focus on ensuring access to the latest evidence-based care²¹.

We found that the use of PN among patients with stage I tumors ≤ 4 cm (e.g. T1a) increased from 43% in 2004 to 55% in 2009, which supports prior research^{7,22-24} showing an increased adoption of PN over time. Among these studies, an analysis using SEER data on renal cancer patients with tumors ≤ 4 cm showed an increase in PN from nearly 20% in 1999

to 45% in 2006⁷, whereas results from a study using the National Cancer Database showed that PN use among patients with stage I renal tumors increased from 18% in 2000 to 41% in 2008²². Our study suggests use of PN in the surgical management of patients with stage I tumors ≤ 4 cm in US community practice has finally crossed the 50% threshold; while this is a sign of progress, future research is needed to identify the factors at all levels (e.g., system-, provider-, and patient-level) driving slow adoption of this evidence-based approach.

In assessing the type of PN technique used between 2004 and 2009, our study found increased LPN use over time. Though OPN remained the more common PN technique among patients with stage I tumors ≤ 4 cm (27% in 2004 and 33% in 2009), LPN use in this group increased from 15% to 22% between 2004 and 2009. Moreover, LPN was the predominant PN technique among patients with stage I tumors >4 -7cm (8% in 2004 and 15% in 2009). These findings add to those from prior studies^{25,26}, including an analysis using SEER-Medicare data that showed increasing use of LPN among RCC patients with tumors ≤ 7 cm, between 1995 and 2007. Some studies suggest such growth in LPN use over time may be due, in part, to the increased use of robot-assisted LPN (RALPN) for localized tumors^{27,28}. A study by Patel et al.²⁷ of patients who underwent RN, PN, or renal ablation in the state of Maryland from 2000 to 2011, found that the increase in PN use over the study period (of 18%) was largely driven by RALPN, accounting for nearly 66% of the rise in PN. However, with no evidence comparing oncological outcomes from RALPN to those from conventional LPN or OPN, and studies suggesting similar oncologic outcomes between LPN and OPN^{29,30}, the overall increase in PN use and adoption of specific PN techniques may be driven by surgical expertise and resource capability^{6,28} rather than practice guideline recommendations for RCC care.

There is a body of literature to suggest that the slow adoption of PN over time may, in part, be the result of a simultaneous rise in LRN use for localized tumors (e.g., T1a and T1b)^{25,31,32}. Our findings support prior research indicating increases in LRN may be outpacing those of PN for localized tumors over the same time period. Specifically, among patients with tumors >4 -7cm, we found that LRN use increased from 38% in 2004 to 69% in 2009, while PN use increased from 9% in 2004 to 18% in 2009; although, these findings were not statistically significant at the $\alpha=0.05$ level. However, guidelines indicate that, according to oncological and quality-of-life outcomes, localized RCC tumors (T1a and T1b) are best managed by PN rather than RN, and that RN should not be employed when PN is technically feasible^{6,33}. Accordingly, studies have pointed to potential overuse of LRN in the management of localized RCC tumors^{5,34,35}.

LRN has become a well-established surgical treatment strategy for patients with stage T2 RCC tumors and stage T1 RCC tumors not suitable for nephron-sparing surgery^{20,36-38}, while there is no evidence from randomized controlled trials assessing oncological outcomes of LRN versus ORN, results from observational studies have shown equivalent oncologic outcomes, but improved perioperative and postoperative outcomes (e.g., less blood loss and post-operative pain and shorter convalescence) for LRN^{36,39-44}. Few studies have assessed population-based trends in use of LRN versus ORN in the United States, although a SEER-Medicare analysis of 10,917 patients with early-stage kidney cancer showed a significant annual increase in use of LRN from 1.4% in 1995 to 44.9% in 2005⁴⁵. Harper et al.⁴⁶

evaluated LRN use among all RCC patients undergoing radical nephrectomy in Washington state between 1998-2007, reporting a statewide increase in laparoscopic nephrectomy use from 2.3% in 1998 to 29.3% in 2007. Our findings extend this prior research and reflect more recent data on population-based patterns of radical nephrectomy in US community practices, showing significant increases in use of LRN for patients with stage I and stage II RCC (e.g., T1 and T2), from 43% to 58% ($p = 0.05$) and from 16% to 47% ($p = 0.01$), respectively, between 2004 and 2009.

Tumor size and stage were the risk factors found to have the strongest association with PN and LRN use, respectively, supporting those results from prior studies^{7,20,22-24,36-38}. Our findings coincide with prior research indicating older patients were less likely to receive PN than RN compared to younger patients, even in multivariate analyses^{5,7,47}. In our study, patients with a higher comorbid burden (Charlson Comorbidity score ≥ 1) were 2.5 times more likely to receive PN than RN, which is likely due to concerns of achieving renal function preservation, lower risk of chronic kidney disease, and lower risk of cardiovascular events with PN compared to RN^{16-18,24,48,49}. While PN has been shown to have decreased overall mortality compared to RN in observational studies^{18,49} results from a large randomized controlled trial (EORTC 30904) showed no significant difference in overall survival between RN and nephron-sparing surgery⁵⁰. In fully adjusted models, the association with presence of a hospital residency training program remained significant for use of PN over RN, but was attenuated for use of LRN over ORN. Similar results have been reported elsewhere, and could be related to access to the technologies related to nephron-sparing and minimally invasive approaches, as well as surgical training^{22,26,47,51}. We found an association between higher LRN use in patients who reside in areas with a higher number of surgeons in bivariate analysis; although, this association was attenuated after adjusting for effects of other characteristics. While similar studies have reported associations between surgical trends in RCC and other health care system or provider variables (e.g., hospital, geographic region, resources within a hospital referral regions, surgery volume, physician specialty)^{8,28}, our study is among the first to assess the impact of number of surgeons on LRN use.

The strength of our study is the use of a linked SEER POC/AHRF population-based dataset, which enabled us to include multilevel, detailed information on treatment, insurance status, clinical characteristics (e.g. comorbid conditions) and area-level healthcare characteristics (e.g., surgeon density and number of Medicare/Medicaid discharges) to assess patterns in surgical approaches to RCC in US community practices in a contemporary time period. The unique data that we used are excellent resources for investigating the association of multiple patient, hospital and area-level factors with patterns of care. However, our findings must be considered with respect to certain limitations. We did not have information on providers and, thus, were not able to assess provider training and practice style, which has been shown to be associated with treatment for RCC^{26,47}. Information on patient preferences was not available in our study data. Lastly, small sample sizes precluded us from conducting multivariable regression analysis of all surgical approaches (e.g. OPN, LPN, ORN, LRN), as well as differences in survival between surgical approaches.

5. CONCLUSIONS

The present study points to an increased adoption of partial nephrectomy and laparoscopic radical nephrectomy for treatment of RCC patients in US community practices. While encouraging, the adoption of these nephron-sparing and minimally-invasive approaches warrants further investigation to identify the barriers to use; particularly, in light of the longstanding evidence of improved patient outcomes and guideline recommendation of these procedures. Additionally, with research showing rapid adoption of newer techniques in the surgical management of RCC, including robot-assisted surgery, it will be imperative to assess the factors underlying the dissemination of these approaches, despite evidence of clinical advantage, and the value to patients. Future research efforts should incorporate multilevel information on patients, providers and health care resources to improve our understanding of the patterns in surgical management of RCC.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the work of the SEER Cancer Registries. This research would not be possible without their efforts.

Funding Sources: Supported by National Cancer Institute contracts: HHSN261201000024C; HHSN261201000025C; HHSN261201000032C; HHSN261201000027C; HHSN261201000026C; HHSN2612010000140C; HHSN261201000037C; HHSN261201000033C; HHSN261201000034C; HHSN261201000035C; HHSN261201000029C; HHSN261201000031C; HHSN261201000028C; HHSN261201000030C

REFERENCES

1. Howlader, N.; Noone, AM.; Krapcho, M., et al. SEER Cancer Statistics Review, 1975-2012. 2015. http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to SEER website, April 2015
2. Chow WH, Devesa SS. Contemporary epidemiology of renal cell cancer. *Cancer J*. 2008; 14(5): 288–301. [PubMed: 18836333]
3. Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2014; 25(Suppl 3):iii49–56. [PubMed: 25210086]
4. Ljungberg B, Cowan NC, Hanbury DC, et al. EAU guidelines on renal cell carcinoma: the 2010 update. *Eur Urol*. 2010; 58(3):398–406. [PubMed: 20633979]
5. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. *J Urol*. 2009; 182(4):1271–1279. [PubMed: 19683266]
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Kidney Cancer, v.2.2016. 2015. <http://www.nccn.org/index.asp>
7. Dulabon LM, Lowrance WT, Russo P, Huang WC. Trends in renal tumor surgery delivery within the United States. *Cancer*. 2010; 116(10):2316–2321. [PubMed: 20225227]
8. Patel SG, Penson DF, Pabla B, et al. National trends in the use of partial nephrectomy: a rising tide that has not lifted all boats. *J Urol*. 2012; 187(3):816–821. [PubMed: 22248514]
9. National Cancer Institute: Surveillance E, and End Results (SEER) program. Number of Persons by Race and Hispanic Ethnicity for SEER Participants. 2010 Census Data. <http://seer.cancer.gov/registries/data.html>
10. National Cancer Institute. Patterns of Care/Quality of Care Studies. <http://healthcaredelivery.cancer.gov/poc/>
11. Area Health Resource File (AHRF) 2012-2013. US Department of Health and Human Services, Health Resources and Services Administration, Bureau of Health Professions; <http://ahrf.hrsa.gov/index.htm>

12. Becker F, Siemer S, Humke U, Hack M, Ziegler M, Stockle M. Elective nephron sparing surgery should become standard treatment for small unilateral renal cell carcinoma: Long-term survival data of 216 patients. *Eur Urol.* 2006; 49(2):308–313. [PubMed: 16359779]
13. Lee BR, Chow GK, Ratner LE, Kavoussi LR. Laparoscopic live donor nephrectomy: outcomes equivalent to open surgery. *J Endourol.* 2000; 14(10):811–819. discussion 819-820. [PubMed: 11206614]
14. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. *Mayo Clin Proc.* 2000; 75(12):1236–1242. [PubMed: 11126830]
15. Dash A, Vickers AJ, Schachter LR, Bach AM, Snyder ME, Russo P. Comparison of outcomes in elective partial vs radical nephrectomy for clear cell renal cell carcinoma of 4-7 cm. *BJU Int.* 2006; 97(5):939–945. [PubMed: 16643474]
16. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *The lancet oncology.* 2006; 7(9):735–740. [PubMed: 16945768]
17. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *The New England journal of medicine.* 2004; 351(13):1296–1305. [PubMed: 15385656]
18. Thompson RH, Boorjian SA, Lohse CM, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. *J Urol.* 2008; 179(2):468–471. discussion 472-463. [PubMed: 18076931]
19. Kim SP, Murad MH, Thompson RH, et al. Comparative Effectiveness for Survival and Renal Function of Partial and Radical Nephrectomy for Localized Renal Tumors: A Systematic Review and Meta-Analysis. *J Urol.* 2012
20. Ljungberg B, Bensalah K, Bex A, et al. EAU GUIDELINES ON RENAL CELL CARCINOMA. 2014 <http://www.uroweb.org/guidelines/online-guidelines/>.
21. Institute, NC. Provocative Questions - Identifying Perplexing Problems to Drive Progress Against Cancer. 2015. <http://provocativequestions.nci.nih.gov/>
22. Small AC, Tsao CK, Moshier EL, et al. Trends and variations in utilization of nephron-sparing procedures for stage I kidney cancer in the United States. *World J Urol.* 2013; 31(5):1211–1217. [PubMed: 22622394]
23. Yabroff KR, Harlan L, Stevens J, Martin A. Patterns of care in adults with renal cell carcinoma: findings in a population based sample. *J Urol.* 2009; 181(6):2462–2468. discussion 2469. [PubMed: 19371892]
24. Thompson RH, Siddiqui S, Lohse CM, Leibovich BC, Russo P, Blute ML. Partial versus radical nephrectomy for 4 to 7 cm renal cortical tumors. *J Urol.* 2009; 182(6):2601–2606. [PubMed: 19836797]
25. Smaldone MC, Kutikov A, Egleston B, et al. Assessing performance trends in laparoscopic nephrectomy and nephron-sparing surgery for localized renal tumors. *Urology.* 2012; 80(2):286–291. [PubMed: 22704174]
26. Poon SA, Silberstein JL, Chen LY, Ehdaie B, Kim PH, Russo P. Trends in partial and radical nephrectomy: an analysis of case logs from certifying urologists. *J Urol.* 2013; 190(2):464–469. [PubMed: 23454156]
27. Patel HD, Mullins JK, Pierorazio PM, et al. Trends in renal surgery: robotic technology is associated with increased use of partial nephrectomy. *J Urol.* 2013; 189(4):1229–1235. [PubMed: 23085300]
28. Chandra A, Snider JT, Wu Y, Jena A, Goldman DP. Robot-assisted surgery for kidney cancer increased access to a procedure that can reduce mortality and renal failure. *Health Aff (Millwood).* 2015; 34(2):220–228. [PubMed: 25646101]
29. Gill IS, Kavoussi LR, Lane BR, et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. *J Urol.* 2007; 178(1):41–46. [PubMed: 17574056]
30. Gong EM, Orvieto MA, Zorn KC, Lucioni A, Steinberg GD, Shalhav AL. Comparison of laparoscopic and open partial nephrectomy in clinical T1a renal tumors. *J Endourol.* 2008; 22(5):953–957. [PubMed: 18363510]

31. Abouassaly R, Alibhai SM, Tomlinson G, Timilshina N, Finelli A. Unintended consequences of laparoscopic surgery on partial nephrectomy for kidney cancer. *J Urol*. 2010; 183(2):467–472. [PubMed: 20006875]
32. Miller DC, Saigal CS, Banerjee M, Hanley J, Litwin MS. Urologic Diseases in America P. Diffusion of surgical innovation among patients with kidney cancer. *Cancer*. 2008; 112(8):1708–1717. [PubMed: 18330868]
33. Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. *Eur Urol*. 2015; 67(5):913–924. [PubMed: 25616710]
34. Hollenbeck BK, Taub DA, Miller DC, Dunn RL, Wei JT. National utilization trends of partial nephrectomy for renal cell carcinoma: a case of underutilization? *Urology*. 2006; 67(2):254–259. [PubMed: 16442601]
35. Scherr DS, Ng C, Munver R, Sosa RE, Vaughan ED Jr, Del Pizzo J. Practice patterns among urologic surgeons treating localized renal cell carcinoma in the laparoscopic age: technology versus oncology. *Urology*. 2003; 62(6):1007–1011. [PubMed: 14665345]
36. Dunn MD, Portis AJ, Shalhav AL, et al. Laparoscopic versus open radical nephrectomy: a 9-year experience. *J Urol*. 2000; 164(4):1153–1159. [PubMed: 10992356]
37. Eskicorapci SY, Teber D, Schulze M, Ates M, Stock C, Rassweiler JJ. Laparoscopic radical nephrectomy: the new gold standard surgical treatment for localized renal cell carcinoma. *ScientificWorldJournal*. 2007; 7:825–836. [PubMed: 17619767]
38. Hemal AK, Kolla SB. Comparison of laparoscopic and open radical cystoprostatectomy for localized bladder cancer with 3-year oncological followup: a single surgeon experience. *J Urol*. 2007; 178(6):2340–2343. [PubMed: 17936813]
39. Burgess NA, Koo BC, Calvert RC, Hindmarsh A, Donaldson PJ, Rhodes M. Randomized trial of laparoscopic v open nephrectomy. *J Endourol*. 2007; 21(6):610–613. [PubMed: 17638555]
40. Colombo JR Jr, Haber GP, Aron M, et al. Oncological outcomes of laparoscopic radical nephrectomy for renal cancer. *Clinics (Sao Paulo)*. 2007; 62(3):251–256. [PubMed: 17589664]
41. Hemal AK, Kumar A, Kumar R, Wadhwa P, Seth A, Gupta NP. Laparoscopic versus open radical nephrectomy for large renal tumors: a long-term prospective comparison. *J Urol*. 2007; 177(3):862–866. [PubMed: 17296361]
42. Andersen MH, Mathisen L, Oyen O, et al. Postoperative pain and convalescence in living kidney donors-laparoscopic versus open donor nephrectomy: a randomized study. *Am J Transplant*. 2006; 6(6):1438–1443. [PubMed: 16686768]
43. Gill IS, Schweizer D, Hobart MG, Sung GT, Klein EA, Novick AC. Retroperitoneal laparoscopic radical nephrectomy: the Cleveland clinic experience. *J Urol*. 2000; 163(6):1665–1670. [PubMed: 10799156]
44. Harano M, Eto M, Omoto K, et al. Long-term outcome of hand-assisted laparoscopic radical nephrectomy for localized stage T1/T2 renal-cell carcinoma. *J Endourol*. 2005; 19(7):803–807. [PubMed: 16190832]
45. Filson CP, Banerjee M, Wolf JS Jr, Ye Z, Wei JT, Miller DC. Surgeon characteristics and long-term trends in the adoption of laparoscopic radical nephrectomy. *J Urol*. 2011; 185(6):2072–2077. [PubMed: 21496845]
46. Harper JD, Spencer ES, Porter MP, Gore JL. Adoption of laparoscopic radical nephrectomy in the state of Washington. *Urology*. 2012; 79(2):326–331. [PubMed: 22310748]
47. Bianchi M, Becker A, Abdollah F, et al. Rates of open versus laparoscopic and partial versus radical nephrectomy for T1a renal cell carcinoma: a population-based evaluation. *IntJ Urol*. 2013; 20(11):1064–1071. [PubMed: 23418921]
48. Kim SP, Thompson RH, Boorjian SA, et al. Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis. *J Urol*. 2012; 188(1):51–57. [PubMed: 22591957]
49. Weight CJ, Larson BT, Gao T, et al. Elective partial nephrectomy in patients with clinical T1b renal tumors is associated with improved overall survival. *Urology*. 2010; 76(3):631–637. [PubMed: 20451967]
50. Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical

nephrectomy for low-stage renal cell carcinoma. *Eur Urol*. 2011; 59(4):543–552. [PubMed: 21186077]

51. Schiffmann J, Bianchi M, Sun M, Becker A. Trends in surgical management of T1 renal cell carcinoma. *Curr Urol Rep*. 2014; 15(2):383. [PubMed: 24414526]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

- Linked data from SEER Patterns of Care and Area Health Resource File were used
- Over 50% of T1a RCC patients received partial nephrectomy by 2009
- LRN may be outpacing PN for T1b RCC patients
- Use of LRN significantly increased for stage I and II RCC patients

Figure 1. Percentage of participants receiving partial versus radical nephrectomy, by tumor size and year of diagnosis

Notes: Estimates are based on patients diagnosed with AJCC stage I tumors 7cm or less, who received surgery of the primary tumor site within 12 months following diagnosis, who underwent partial nephrectomy (including partial or subtotal nephrectomy) or radical nephrectomy (including complete/total/simple nephrectomy and radical nephrectomy). Percentages are presented among all patients with AJCC stage I tumors 7cm or less, among those with stage I tumors 4cm or less only, and those with stage I tumors >4-7cm only, separately. Data for 2004 are weighted to SEER 2006, whereas data for 2009 are weighted to SEER 2011. *p 0.05.

Figure 2. Percentage of participants receiving open partial, laparoscopic partial, open radical and laparoscopic radical nephrectomy, by tumor size and year of diagnosis

Notes: Estimates are based on patients diagnosed with AJCC stage I tumors 7cm or less, who received surgery of the primary tumor site within 12 months following diagnosis, who underwent partial nephrectomy (including partial or subtotal nephrectomy) or radical nephrectomy (including complete/total/simple nephrectomy and radical nephrectomy). Individuals with missing information on type of nephrectomy (laparoscopic or open) were excluded. Percentages are presented among all patients with AJCC stage I tumors 7cm or less, among those with stage I tumors 4cm or less only, and those with stage I tumors >4-7cm only, separately. Data for 2004 are weighted to SEER 2006, whereas data for 2009 are weighted to SEER 2011.

Figure 3. Percentage of participants receiving laparoscopic versus open radical nephrectomy, by tumor stage at diagnosis and year of diagnosis

Notes: Estimates are based on the number of patients diagnosed with tumor stages I-II, who received surgery of the primary tumor site within 12 months following diagnosis, who received radical nephrectomy via laparoscopic or open surgical techniques. Percentages are presented among all patients with tumor stages I-II, among those with stage I tumors and those with stage II tumors, separately. *p 0.05. **p 0.01

Table 1**Characteristics of Patient Population**

	Total Patients 2004 (n = 787)	Total Patients 2009 (n = 323)	p-value
	n (weighted %)	n (weighted %)	
<i>Sociodemographic Characteristics</i>			
Age at Diagnosis ^a , years			
<65	505 (64.7)	220 (60.7)	0.40
65	282 (35.3)	103 (39.3)	
Sex ^a			
Female	397 (44.5)	152 (36.0)	<0.01
Male	390 (55.5)	171 (64.1)	
Race/Ethnicity ^a			
Asian, NH	113 (4.1)	68 (5.3)	<0.01
Black, NH	212 (10.7)	79 (10.9)	
Hispanic	141 (11.5)	76 (14.3)	
White, NH	311 (73.3)	78 (68.8)	
Other	10 (0.4)	22 (0.7)	
Health Insurance Coverage ^b			
Private	524 (74.1)	216 (76.3)	0.16
Public	209 (20.1)	85 (21.5)	
Uninsured/Unknown	54 (5.9)	22 (2.2)	
Marital Status ^a			
Married/Living with partner	478 (63.1)	184 (53.2)	0.22
Other	309 (36.9)	139 (46.8)	
Median Household Income ^b (tertile)			
<\$44,896	304 (29.7)	120 (33.3)	0.24
\$44,896-\$61,826	227 (29.3)	99 (38.0)	
\$61,827	256 (41.0)	104 (28.7)	
<i>Clinical Characteristics</i>			
Charlson Comorbidity Score ^b			
0	518 (65.1)	205 (63.5)	0.80
1	269 (34.9)	118 (36.5)	
Cell type ^a			
Clear cell/renal cell NOS	589 (77.0)	238 (77.7)	0.88
Non-clear cell	198 (23.0)	85 (20.8)	
Tumor Stage ^a			
I	662 (86.2)	174 (87.5)	0.55
II	125 (13.8)	149 (12.6)	
Tumor Size ^a (cm)			
4	393 (50.1)	111 (53.2)	0.77
>4-7	268 (36.1)	63 (34.2)	
>7	125 (13.8)	149 (12.6)	

	Total Patients 2004 (n = 787)	Total Patients 2009 (n = 323)	p-value
	<i>n</i> (weighted %)	<i>n</i> (weighted %)	
<i>Health Care Provider/Facility Characteristics</i>			
Hospital-level			
# Hospital Beds ^b			
<300/OPD/Unknown	307 (44.9)	126 (42.5)	0.66
300-499	311 (36.0)	115 (32.5)	
500	169 (19.1)	82 (25.0)	
Hospital Residency Training ^b			
Yes	473 (56.4)	187 (60.3)	0.58
No/Unknown	314 (43.7)	136 (39.7)	
Area-level ^{c†}			
Total Surgeons per 10,000 population			
<6.57	452 (56.6)	176 (54.3)	0.76
6.57	335 (43.4)	147 (45.7)	
Medicaid Inpatient Discharges per 10,000 population			
<192.24	336 (53.1)	152 (48.3)	0.55
192.24	451 (46.9)	171 (51.7)	
Medicare Inpatient Discharges per 10,000 population			
<398.8	342 (46.6)	155 (50.9)	0.48
398.8	445 (53.4)	168 (49.2)	

Notes. Data for 2004 are weighted to SEER 2006, whereas data for 2009 are weighted to SEER 2011;

^aData from standard SEER

^bData from SEER Patterns of Care

^cAll area-level data were obtained from the Area Health Resource File variables and are county level rates per 10,000 population based on 2008 US population estimates. Counts and percentages are based on patients with non-missing information on each characteristic and may not add to 100% due to rounding.

Table 2

Multivariate regression analyses of factors associated with receipt of Partial Nephrectomy vs. Radical Nephrectomy

Characteristic	Partial vs. Radical Nephrectomy ^a (n=835)			
	Bivariate OR [95% CI]	p-value	Multivariate OR [95% CI]	p-value
Age at Diagnosis, years				
<65	Ref.	0.16	Ref.	0.02
≥65	0.57 [0.26, 1.25]		0.38 [0.17, 0.83]	
Year of Diagnosis				
2004	Ref.	0.22	Ref.	0.13
2009	1.68 [0.73, 3.83]		2.08 [0.82, 5.29]	
Tumor Size				
4 cm	Ref.	0.02	Ref.	<0.01
>4-7 cm	0.16 [0.03, 0.78]*		0.10 [0.04, 0.29]	
Cell Type				
Clear Cell	Ref.	0.05	Ref.	0.02
Non-Clear Cell	0.49 [0.24, 1.00]		0.32 [0.13, 0.81]	
Charlson Comorbidity Score				
0	Ref.	0.04	Ref.	0.04
1	2.47 [1.06, 5.76]*		2.47 [1.06, 5.75]	
Hospital Residency Training				
Yes	Ref.	0.08	Ref.	<0.01
No/Unknown	0.48 [0.21, 1.10]		0.28 [0.13, 0.61]	

Notes. Abbreviations: OR=Odds ratio; CI=Confidence Interval; Ref.=Referent category; n/a=not applicable (was not included in final model).

^aEstimates based on patients with AJCC stage I tumors of size ≤7cm who underwent partial nephrectomy (including partial or subtotal nephrectomy) or radical nephrectomy (including complete/total/simple nephrectomy and radical nephrectomy) within 12 months after diagnosis. Multivariable model adjusted for age at diagnosis, year of diagnosis, tumor size, tumor cell type, Charlson Comorbidity Index, hospital residency training and SEER Registry.

Table 3

Multivariate regression analyses of factors associated with receipt of Laparoscopic Radical Nephrectomy vs. Open Radical Nephrectomy

Characteristic	Laparoscopic vs Open Radical Nephrectomy ^a (n=849)			
	Bivariate OR [95% CI]	p-value	Multivariate ^a OR [95% CI]	p-value
Age at Diagnosis, years				
<65	Ref.	0.72	Ref.	0.68
65	0.91 [0.54, 1.52]		1.18 [0.54, 2.57]	
Year of Diagnosis				
2004	Ref.	<0.01	Ref.	0.02
2009	2.08 [1.27, 3.41]		2.57 [1.15, 5.73]	
Sex				
Male	Ref.	0.06	Ref.	0.34
Female	0.62 [0.37, 1.03]		1.39 [0.71, 2.72]	
Tumor Stage				
I	Ref.	<0.01	Ref.	<0.01
II	0.47 [0.31, 0.73]		0.28 [0.12, 0.64]	
Cell Type				
Clear Cell	Ref.	0.06	Ref.	0.74
Non-Clear Cell	0.59 [0.35, 1.02]		0.88 [0.43, 1.83]	
Number Hospital Beds				
<300/OPD/Unk.	Ref.	<0.01	Ref.	0.07
300-499	1.94 [0.95, 3.97]		1.45 [0.42, 4.93]	
500	5.29 [2.86, 9.79]		3.20 [0.87, 11.83]	
Hospital Residency Training				
Yes	Ref.	<0.01	Ref.	0.08
No/Unknown	0.34 [0.20, 0.59]		0.51 [0.24, 1.09]	
No. Number Surgeons				
<6.57	Ref.	0.03	Ref.	0.15
6.57	3.32 [1.13, 9.72]		2.19 [0.75, 6.34]	

Notes. Abbreviations: CI=Confidence Interval; n/a=not applicable (was not included in final model); OPD=outpatient department; OR=Odds ratio; Ref.=Referent category; Unk=unknown.

^aEstimates based on patients diagnosed with stage I-II tumors who received radical nephrectomy via laparoscopic or open surgical techniques within 12 months after diagnosis. Multivariable model adjusted for age at diagnosis, year of diagnosis, sex, stage at diagnosis, tumor cell type, number of hospital beds, hospital residency training, number of surgeons per 10,000 population, and SEER Registry; tumor size was not included in this analysis.