Stereotactic Body Radiation Therapy for the Definitive Treatment of Early Stage Kidney Cancer: A Survival Comparison With Surgery, Tumor Ablation, and Observation

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Abstract

Purpose: Partial nephrectomy is the preferred definitive treatment for early stage kidney cancer, with tumor ablative techniques or active surveillance reserved for patients not undergoing surgery. Stereotactic body radiation therapy (SBRT) has emerged as a potential noninvasive alternative for patients with early stage kidney cancer not amenable to surgery, with early reports suggesting excellent rates of local control and limited toxicity.

Methods and Materials: The national cancer database from 2004 to 2014 was queried for patients who received a diagnosis of T1N0M0 kidney cancer. Treatments were categorized as surgery (partial or total nephrectomy), tumor ablation (cryoablation or thermal ablation), SBRT (radiation therapy in 5 fractions or less to a total biological effective dose [BED10] of 72 or more), or observation. A propensity score was generated by multinomial logistic regression. A Cox proportional hazards model was fit to determine association between overall survival and treatment group with propensity score adjustments for patient, demographic, and treatment characteristics.

Results: A total of 165,298 received surgery, 17,196 underwent tumor ablation, 104 underwent SBRT, and 18,241 were observed. Median follow-up was 51 months. On multivariable analysis, surgery, tumor ablation, and SBRT were associated with a decreased risk of death compared with observation, with hazard ratios of 0.25 (95% confidence interval, 0.24-0.26, \( P < .001 \)), 0.36 (0.35-0.38, \( P < .001 \)), and 0.56 (0.39-0.79, \( P < .001 \)), respectively. When stratifying by BED10 and compared with observation, hazard ratio for risk of death for patients treated with SBRT to a BED10 \( \geq 100 \) (\( n = 62 \)) and a BED10 < 100 (\( n = 42 \)) was 0.34 (0.19-0.60, \( P < .001 \)) and 0.90 (0.58-1.4, \( P = .64 \)), respectively.

Conclusions: In this population-based cohort, patients undergoing high-dose SBRT (BED10 \( \geq 100 \)) for early stage kidney cancer demonstrated longer survival compared with patients undergoing observation. This may be a promising noninvasive treatment option for nonsurgical candidates with prospective efficacy and safety assessments merit ing study in future clinical trials.

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Introduction

Partial nephrectomy is the preferred definitive treatment for early stage kidney cancer, with tumor ablative techniques or active surveillance reserved for patients not undergoing surgery.1 With an increase in the number of incidentally diagnosed kidney cancers and in an increasingly elderly population who may not tolerate invasive procedures,2,3 stereotactic body radiation therapy (SBRT) has emerged as a potential noninvasive alternative for patients not amenable to surgery, with early reports suggesting excellent rates of local control and limited toxicity.4–5 This study uses a large national cancer registry to assess patterns of care and survival outcomes in patients with stage I kidney cancer treated with SBRT.

Methods and Materials

The national cancer database was queried from 2004 to 2014 for patients who received a diagnosis of T1N0M0 kidney cancer (7 cm or less with no nodal or distant metastases). Both clinical and pathologic staging was used to determine patient inclusion. Histologic subtypes were limited to clear cell carcinoma, papillary carcinoma, renal cell not otherwise specified (NOS), and carcinoma NOS. Exclusion criteria is listed in Figure 1. Treatments were categorized as surgery (including partial and total nephrectomy), tumor ablation (including cryoablation and thermal ablation), SBRT, or observation. SBRT was defined as radiation therapy in 5 fractions or less to a total biological effective dose (BED10) of 72 or more assuming a tumor α/β value of 10. Although there is limited research into the radiobiology of kidney SBRT, studies from non-small cell lung cancer suggest a BED10 of approximately 70 corresponds to the lower limit of what may be considered an acceptable tumor control probability.10–12 Because a BED10 of 100 has been shown to be an important cut point for outcomes in multiple other disease sites,13,14 patients receiving SBRT were dichotomized by those treated to a BED10 of <100 or ≥100. This project was reviewed by our institutional review board and found to be exempted.

A propensity score was generated by multinomial logistic regression, and a Cox proportional hazard model was fit to determine association between treatment group

CONSORT Diagram

[Diagram showing patient flow from diagnosis to treatment options with breakdown of patients and exclusion criteria]

Figure 1  Consort diagram displaying. Abbreviations: NCDB = National Cancer Database; SBRT = stereotactic body radiation.
Table 1  Patient and tumor characteristics

| Treatment          | Surgery | Tumor ablation | SBRT | Observation |
|--------------------|---------|----------------|------|-------------|
|                     | 165,298 (%) | 17,196 (%) | 104 (%) | 18,241 (%) |
| **Age (y)**         |         |                |      |             |
| Median              | 61      | 69             | 75   | 74          |
| 18-49               | 33,312  | 1165           | 6.8% | 1 1.0%      |
| 50-64               | 67,870  | 4860           | 28.3%| 24 23.1%    |
| >64                 | 64,116  | 11,171         | 65.0%| 79 76.0%    |
| **Race**            |         |                |      |             |
| White               | 122,024 | 13,230         | 76.9%| 75 72.1%    |
| Black               | 18,671  | 1765           | 10.3%| 15 14.4%    |
| Hispanic            | 20,055  | 1828           | 10.6%| 10 9.6%     |
| Other               | 4548    | 373            | 2.2% | 4 3.8%      |
| **Sex**             |         |                |      |             |
| Female              | 65,644  | 6411           | 37.3%| 37 35.6%    |
| Male                | 99,654  | 10,785         | 62.7%| 67 64.4%    |
| **Year of diagnosis** |       |                |      |             |
| 2004                | 11,597  | 436            | 2.5% | 0 0.0%      |
| 2005                | 12,400  | 735            | 4.3% | 0 0.0%      |
| 2006                | 13,488  | 1161           | 6.8% | 1 1.0%      |
| 2007                | 14,394  | 1416           | 8.2% | 5 4.8%      |
| 2008                | 14,753  | 1762           | 10.2%| 11 10.6%    |
| 2009                | 15,600  | 1905           | 11.1%| 9 8.7%      |
| 2010                | 15,190  | 1917           | 11.1%| 18 17.3%    |
| 2011                | 16,202  | 1864           | 10.8%| 14 13.5%    |
| 2012                | 16,991  | 1928           | 11.2%| 12 11.5%    |
| 2013                | 17,183  | 1964           | 11.4%| 21 20.2%    |
| 2014                | 17,500  | 2108           | 12.3%| 13 12.5%    |
| **Charlson-Deyo comorbidity score** |       |                |      |             |
| 0                   | 115,165 | 11,551         | 67.2%| 83 79.8%    |
| 1                   | 37,410  | 4029           | 23.4%| 18 17.3%    |
| 2                   | 9387    | 1182           | 6.9% | 2 1.9%      |
| 3                   | 3336    | 434            | 2.5% | 1 1.0%      |
| **Tumor stage**     |         |                |      |             |
| T1a                 | 110,014 | 15,188         | 88.3%| 63 60.6%    |
| T1b                 | 55,284  | 2008           | 11.7%| 41 39.4%    |
| **Tumor size (mm)** |         |                |      |             |
| Median              | 34.9    | 26.5           | 35.8 | 32.7        |
| 0-25                | 57,245  | 9397           | 54.6%| 29 27.9%    |
| 26-50               | 81,524  | 7527           | 43.8%| 65 62.5%    |
| 51-70               | 26,529  | 272            | 1.6% | 10 9.6%     |
| **Laterality**      |         |                |      |             |
| Left                | 79,987  | 8407           | 48.9%| 46 44.2%    |
| Right               | 85,080  | 8775           | 51.0%| 58 55.8%    |
| Unknown             | 231     | 14             | 0.1% | 0 0.0%      |
| **Histology**       |         |                |      |             |
| Clear cell carcinoma| 92,157  | 6779           | 39.4%| 37 35.6%    |
| Papillary carcinoma | 26,457  | 2465           | 14.3%| 13 12.5%    |
| Renal cell carcinoma NOS | 46,382 | 7545           | 43.9%| 47 45.2%    |
| Carcinoma NOS       | 302     | 407            | 2.4% | 7 6.7%      |
| **Tumor grade**     |         |                |      |             |
| 1                   | 23,580  | 2685           | 15.6%| 11 10.6%    |
| 2                   | 84,040  | 4330           | 25.2%| 23 22.1%    |
| 3                   | 30,161  | 612            | 3.6% | 0 0.0%      |
| 4                   | 2623    | 35             | 0.2% | 0 0.0%      |
| Unknown             | 24,894  | 9534           | 55.4%| 70 67.3%    |

(continued on next page)
and overall survival (OS) with propensity score adjustments for patient, demographic, and treatment characteristics, including age at diagnosis, race, sex, year of diagnosis, Charlson-Deyo comorbidity score, tumor size, laterality, histology, grade, insurance plan, rurality, median income, education, academic hospital, and distance traveled for treatment. The proportional hazard assumption was visually checked. To reduce lead time bias, patients were excluded if they died or were lost to follow-up before 2.67 months from diagnosis, corresponding to the time in which 90% of subjects had started definitive treatment. Approximately 3.5% of all patients (1.9% of surgery patients, 1.3% of tumor ablation patients, no SBRT patients, and 16.8% of observation patients) were excluded from analysis by this follow-up time constraint.

**Results**

A total of 200,839 patients were included, of whom 165,298 received surgery (median follow-up 57 months), 17,196 underwent tumor ablation (median follow-up 50

| Table 1 (continued) | Treatment | P value |
|----------------------|-----------|---------|
|                      | Surgery   | Tumor ablation | SBRT   | Observation |
|                      | 165,298 (%) | 17,196 (%) | 104 (%) | 18,241 (%) |
| Academic treatment facility |             |             |         | <.001       |
| Yes                  | 65,410 39.6% | 7362 42.8% | 49 47.1% | 6593 36.1% |
| No                   | 90,197 54.6% | 9560 55.6% | 54 51.9% | 11,346 62.2% |
| Unknown              | 9691 5.9% | 274 1.6% | 1 1.0% | 302 1.7% |

**Abbreviations:** NOS = not otherwise specified; SBRT = stereotactic body radiation therapy.

| Table 2 | Patient and tumor characteristics by radiation dose | SBRT dose | P value |
|---------|-----------------------------------------------------|-----------|---------|
|         |                                                     | BED <100  | BED ≥100 |
| Age (y) |                                                     | 42 (%)    | 62 (%)  | .47     |
| Median  |                                                     | 75        | 73      |
| Charlson-Deyo comorbidity score |             |           |         | .83     |
| 0       | 33 78.6% | 50 80.7% | .83     |
| 1       | 8 19.1%  | 10 16.1% |         |
| 2       | 1 2.4%   | 1 1.6%   |         |
| 3       | 0 0.0%   | 1 1.6%   |         |
| Tumor stage |             |           |         | .32     |
| T1a     | 23 54.8% | 40 64.5% | .32     |
| T1b     | 19 45.2% | 22 35.5% |
| Tumor size (mm) |             |           |         | .06     |
| Median  | 39.2      | 33.5      | .06     |
| Laterality |             |           |         | .57     |
| Left    | 20 47.6% | 26 41.9% | .57     |
| Right   | 22 52.4% | 36 58.1% |
| Histology |             |           |         | .16     |
| Clear cell carcinoma | 20 47.6% | 17 27.4% | .16     |
| Papillary carcinoma | 3 7.1%   | 10 16.1% |
| Renal cell carcinoma NOS | 17 40.5% | 30 48.4% |
| Carcinoma NOS | 2 4.8%   | 5 8.1%   |
| Most common fractionation (fx) schemes |             |           |         | N/A     |
| 40 Gy in 5 fx | 13 31.0% |            | N/A     |
| 39 Gy in 3 fx | 9 21.4%  |            |
| 36 Gy in 3 fx | 9 21.4%  |            |
| 48 Gy in 3 fx |            | 29 46.8% |         |
| 45 Gy in 3 fx |            | 9 14.5%  |         |
| 50 Gy in 5 fx |            | 8 12.9%  |         |

**Abbreviations:** BED = biological effective dose; NOS = not otherwise specified; SBRT = stereotactic body radiation therapy.
months), 104 underwent SBRT (median follow-up 37 months), and 18,241 were observed (median follow-up 19 months; Table 1). The most common fractionation schemes for patients receiving SBRT were 40 Gy in 5 fractionation for the BED10 < 100 cohort (42 patients) and 48 Gy in 3 fractionation for the BED10 ≥ 100 cohort (62 patients; Table 2).

At a median follow-up of 51 months, 40,489 patients (20.2%) had died with 5-year OS estimate shown in Table 3 and Figure 2. On multivariable analysis with propensity score adjustment, patients undergoing surgery, tumor ablation, and SBRT were associated with a decreased risk of death compared with patients undergoing observation, with a hazard ratio (HR) of 0.25 (95% confidence interval [CI] 0.24-0.26, P < .001), 0.36 (0.35-0.38, P < .001), and 0.56 (0.39-0.79, P < .001), respectively. Compared with observation, HR for risk of death for SBRT patients treated to a BED10 < 100 and a BED10 ≥ 100 was 0.90 (0.58-1.4, P = .64) and 0.34 (0.19-0.60, P < .001), respectively (Table 4). A sensitivity analysis using Cox regression with propensity score adjustment stratified into quintiles provided similar results (Table 5).

Discussion

In this analysis, we show that SBRT for primary kidney cancer is an uncommon treatment in the United States despite an increasing number of diagnosed patients, emerging evidence for the safety and efficacy of the treatment, and recent technical improvements in radiation delivery.2–6 We demonstrate that this is a recently adopted treatment, with no reported cases of primary kidney SBRT in 2004 or 2005 and only one case in 2006. Moreover, we show that patients treated with SBRT, and in particular, those with a BED10 ≥ 100, demonstrated an improved OS at 5 years compared with those who were observed, even after adjusting for patient and tumor characteristics. This outcome may in part reflect patient selection based on clinical factors not available or measured in covariates. For example, the median size of tumors in the higher BED cohort was 33.5 mm compared with 39.2 mm in the lower BED group, which suggests that BED may in part be a surrogate for tumor size. Still, the improved survival in patients treated with SBRT to a BED10 ≥ 100 versus BED10 < 100 persisted after propensity-adjustments and generates the hypothesis that radiation treatment, particularly at highly ablative doses, may have the potential to significantly alter the disease course in treated patients. This analysis supports prior single center studies that generally explored SBRT for primary kidney cancer with highly ablative doses4–6 and ongoing prospective clinical trials.15

For patients who are not ideal candidates for surgical resection, potential options include tumor ablation with cryotherapy or radiofrequency ablation, SBRT, or observation. SBRT may be an attractive treatment option for many patients for several reasons. First, SBRT is able to treat tumors larger than 4 cm or tumors located near the renal pelvis, criteria which are generally unsuitable for interventional radiology–guided tumor ablation.16,17 In this analysis, nearly 40% of SBRT tumors were >4 cm, compared with just 12% of ablated tumors. Second, SBRT is a noninvasive treatment with no associated anesthesia risk or prolonged recovery time. Third, SBRT is convenient for the patient, with treatment generally completed in 5 days or less or, in many cases, in a single day.

Limitations include the small number of patients treated with SBRT compared with other cohorts and the potential for confounding factors. Without information on cancer specific mortality or cause of death, and in a disease where overall outcomes are expected to be favorable,18 it is unclear whether the observed differences are related to differences in treatment or patient selection. Our findings of improved OS in patients treated with BED10 ≥ 100 compared with <100 are surprising because the risk of distant metastases and cancer-specific death in patients with T1N0M0 kidney cancer is relatively low.19–22 Indeed, prior single institutional studies of kidney SBRT demonstrated very low rates of local failure.4–6 Even if higher BED10 leads to improved local control, it is unclear if this

| Table 3 Unadjusted 5-year overall survival estimates by treatment group |
|------------------------|------------------------|------------------------|------------------------|
| Patients | Patients | Patients | Patients |
| N | Events N | 5-year estimated OS | 95% CI | P value |
| All | 200,839 | 40,489 | 0.82 | (0.81, 0.82) | <.001 |
| Surgery | 165,298 | 26,768 | 0.86 | (0.86, 0.86) |
| Tumor ablation | 17,196 | 4180 | 0.77 | (0.76, 0.77) |
| SBRT, BED < 100 | 42 | 20 | 0.42 | (0.25, 0.59) |
| SBRT, BED ≥ 100 | 62 | 12 | 0.73 | (0.56, 0.84) |
| Observation | 18,241 | 9509 | 0.43 | (0.42, 0.43) |

Abbreviations: BED = biological effective dose; SBRT = stereotactic body radiation therapy.
would drive a survival benefit in this population during this period of follow-up.

Other limitations include the potential for discrepancies between staging technique between treatment cohorts (ie, patients treated with SBRT are staged only clinically, compared with those undergoing surgery who are staged pathologically). In addition, this analysis grouped together patients treated with both total and partial nephrectomy, although these are distinct treatments with likely distinct outcomes. Furthermore, we excluded any patients who received systemic therapy as a component of initial treatment, which may erroneously
Table 4 Cox proportional hazards regression for overall survival with propensity score adjustments*

| Treatment                | HR (95% CI) | P value |
|--------------------------|-------------|---------|
| Observation              | 1           |         |
| Surgery                  | 0.25 (0.24, 0.26) | <.001   |
| Tumor ablation           | 0.36 (0.35, 0.38) | <.001   |
| SBRT                     | 0.56 (0.39, 0.79) | <.001   |
| BED <100                 | 0.9 (0.58, 1.4) | .64     |
| BED >100                 | 0.34 (0.19, 0.6) | <.001   |

Age (y)                  
- 18-49                   | 1           |         |
- 50-64                   | 1.75 (1.66, 1.84) | <.001   |
- >64                     | 2.85 (2.71, 2.99) | <.001   |

Race                     
- White                   | 1           |         |
- Black                   | 0.99 (0.96, 1.02) | .5      |
- Hispanic                | 0.88 (0.85, 0.91) | <.001   |
- Other                   | 0.8 (0.74, 0.86) | <.001   |

Sex                      
- Female                  | 1.16 (1.13, 1.18) | <.001   |
- Male                    | 1           |         |

Year of diagnosis         
- 2004-2009               | 1           |         |
- 2010-2012               | 0.89 (0.87, 0.91) | <.001   |
- 2013-2014               | 0.88 (0.85, 0.92) | <.001   |

Charlson-Comorbidity Score
- 0                       | 1           |         |
- 1                       | 1.38 (1.35, 1.41) | <.001   |
- 2                       | 1.97 (1.91, 2.04) | <.001   |
- 3                       | 2.56 (2.45, 2.68) | <.001   |

Tumor size                
- 0-25 mm                 | 1           |         |
- 26-50 mm                | 1.21 (1.19, 1.24) | <.001   |
- 51-70 mm                | 1.56 (1.52, 1.61) | <.001   |

Laterality                
- Left                    | 1           |         |
- Right                   | 0.98 (0.96, 1.00) | .09     |

Histology                 
- Clear cell carcinoma    | 1           |         |
- Papillary carcinoma     | 1.01 (0.98, 1.04) | .67     |
- Renal cell carcinoma NOS| 1.13 (1.11, 1.16) | <.001   |
- Carcinoma NOS           | 1.33 (1.25, 1.42) | <.001   |

Grade                     
- 1                       | 1           |         |
- 2                       | 1.05 (1.01, 1.08) | .007    |
- 3, 4                    | 1.27 (1.23-1.33) | <.001   |

Although such exclusion criteria may limit capture of perioperative or treatment-related mortality, perioperative mortality after nephrectomy or partial nephrectomy is low.23 Finally, this study does not include cases treated in the past several years given the nature of national cancer database reporting and the lag between treatment and data collection and distribution.

Conclusions

SBRT for early stage kidney cancer may be a promising noninvasive treatment option for nonsurgical patients. Despite the small number of patients treated with SBRT and potential for unmeasured confounding factors, a national registry study such as this may be the only current viable way to compare outcomes after SBRT in early stage kidney cancer given its extremely limited utilization at present. The efficacy and safety of this approach is being evaluated in ongoing prospective clinical trials.15

References

1. Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. *Eur Urol*. 2015;67:913-924.
2. King SC, Pollack LA, Li J, King JB, Master VA. Continued increase in incidence of renal cell carcinoma, especially in young patients and high grade disease: United States 2001 to 2010. *J Urol*. 2014;191: 1665-1670.
3. Saad AM, Gad MM, Al-Husseini MJ, et al. Trends in renal-cell carcinoma incidence and mortality in the United States in the last 2 decades: A SEER-based study. *Clin Genitourin Cancer*. 2019;17:46-57.e5.
4. Funayama S, Onishi H, Kuriyama K, et al. Renal cancer is not radioresistant: Slowly but continuing shrinkage of the tumor after stereotactic body radiation therapy. *Technol Cancer Res Treat*. 2019;18: 1533033818822329.
5. Ponsky L, Lo SS, Zhang Y, et al. Phase I dose-escalation study of stereotactic body radiotherapy (SBRT) for poor surgical candidates with localized renal cell carcinoma. *Radiother Oncol*. 2015;117:183-187.
6. Siva S, Pham D, Kron T, et al. Stereotactic ablative body radiotherapy for inoperable primary kidney cancer: A prospective clinical trial. *BJU Int*. 2017;120:623-630.

7. Siva S, Kothari G, Muacevic A, et al. Radiotherapy for renal cell carcinoma: renaissance of an overlooked approach. *Nat Rev Urol*. 2017;14:549-563.

8. Correa RJM, Louie AV, Zaorsky NG, et al. The emerging role of stereotactic ablative radiotherapy for primary renal cell carcinoma: A systematic review and meta-analysis. *Eur Urol Focus*. 2019;5:958-969.

9. Siva S, Louie AV, Warner A, et al. Pooled analysis of stereotactic ablative radiotherapy for primary renal cell carcinoma: A report from the International Radiosurgery Oncology Consortium for Kidney (IROCK). *Cancer*. 2018;124:934-942.

10. Mehta N, King CR, Agazaryan N, Steinberg M, Hua A, Lee P. Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control. *Pract Radiat Oncol*. 2012;2:288-295.

11. Macià I, Garau M. Radiobiology of stereotactic body radiation therapy (SBRT). *Rep Pract Oncol Radiother*. 2017;22:86-95.

12. Park S, Urm S, Cho H. Analysis of biologically equivalent dose of stereotactic body radiotherapy for primary and metastatic lung tumors. *Cancer Res Treat*. 2014;46:403-410.

13. Ohri N, Tomé WA, Méndez Romero A, et al. Local control after stereotactic body radiation therapy for liver tumors. *Int J Radiat Oncol Biol Phys*. 2018;S0360-3016(17), 34525-X.

14. Onishi H, Araki T, Shirato H, et al. Stereotactic hypofractionated high-dose irradiation for stage I non-small cell lung carcinoma: Clinical outcomes in 245 subjects in a Japanese multiinstitutional study. *Cancer*. 2004;101:1623-1631.

15. Siva S, Chesson B, Bressel M, et al. TROG 15.03 phase II clinical trial of Focal Ablative Stereotactic Radiosurgery for Cancers of the Kidney: FASTRACK II. *BMC Cancer*. 2018;8:1030.

16. Maria T, Georgiades C. Percutaneous cryoablation for renal cell carcinoma. *J Kidney Cancer*. 2015;2:105-113.

17. Wah TM, Irving HC, Gregory W, et al. Radiofrequency ablation (RFA) of renal cell carcinoma (RCC): Experience in 200 tumours. *BJU Int*. 2014;113:416-428.

18. Gill IS, Aron M, Gervais DA, Jewett MA. Clinical practice. Small renal mass. *N Engl J Med*. 2010;362:624-634.

19. Crispen PL, Wong YN, Greenberg RE, Chen DY, Uzzo RG. Predicting growth of solid renal masses under active surveillance. *Urol Oncol*. 2008;26:555-559.

20. Jewett MA, Mattar K, Basiuk J, et al. Active surveillance of small renal masses: Progression patterns of early stage kidney cancer. *Eur Urol*. 2011;60:39-44.

21. McIntosh AG, Ristau BT, Ruth K, et al. Active surveillance for localized renal masses: Tumor growth, delayed intervention rates, and >5-yr clinical outcomes. *Eur Urol*. 2018;74:157-164.

22. Smaldone MC, Kutikov A, Egleston BL, et al. Small renal masses progressing to metastases under active surveillance: A systematic review and pooled analysis. *Cancer*. 2012;118:997-1006.

23. Pereira J, Renzulli J 2nd, Pareek G, et al. Perioperative morbidity of open versus minimally invasive partial nephrectomy: A contemporary analysis of the National Surgical Quality Improvement Program. *J Endourol*. 2018;32:116-123.