

Treatment and Overall Survival in Renal Cell Carcinoma

Mishari H. M. Alshyarba, MD, SB (URO), AB (URO)* Abdulaziz Alamri, MD, FRCSC (Canada)**
Jaber Madi M Assiri, MBBS*** Awadh Mohammed A. Alahmari, MBBS****

Background: Renal Cell Carcinoma (RCC) is the second cause of mortality from urological malignancies; it accounts for 2-3% of malignancies in adults. More than 50% of all diagnosed RCCs are in a localized stage. Partial nephrectomy (PN) has become the golden standard for treating renal masses ≤ 4 cm.

Objective: To evaluate the management of renal tumors and compare the overall survival for PN and radical nephrectomy (RN) for clinical stage 1 renal tumor patients.

Design: A Retrospective Study.

Setting: Aseer Central Hospital, Saudi Arabia.

Method: All patients who presented with solid renal masses over ten years (2008-2017) were reviewed. The clinical stage 1 group was divided into two: those who underwent PN and those who underwent RN. Kaplan-Meier analyses were used to estimate overall survival.

Result: Fifty-three RCC patients with complete data were included in the study. Flank pain and hematuria were the most common presentations, 24 (45%) and 19 (35%), respectively. Forty-nine (92%) patients underwent RN while 4 (8%) underwent PN. Histopathology reports were RCC in 43 (82%) patients and non-RCC malignant tumors in 3 (6%) patients.

Conclusion: Over-treatment of stage 1 RCC with RN was a trend. An extensive and continuous laparoscopic training for urologists in performing PN is extremely essential in reinforcing surgeon's expertise.

Bahrain Med Bull 2020; 42 (2): 113 - 115

Renal Cell Carcinoma (RCC) is the second cause of mortality from urological malignancies; it accounts for 2-3% of malignancies in adults¹. More than 50% of all diagnosed RCCs are in a localized stage². PN has become the golden standard for treating renal masses ≤ 4 cm^{3,4}.

In Saudi Arabia, the renal cancer incidence was 2.8% and was the tenth among the ten most common cancers in Saudi nationals⁵. Few national studies recently reported their experiences with renal tumors^{6,7}. We believe that PN has a survival advantage over radical nephrectomy (RN) for stage 1 renal tumor patients.

The aim of this study is to evaluate our management of renal tumors and compare the overall survival for PN and RN for clinical stage 1 renal tumors patients.

METHOD

All patients who presented with solid renal masses from January 2008 to December 2017 were reviewed. Personal

characteristics, clinical, management and outcome of our study group were documented. All radiologic images were reviewed by a single experienced radiologist to confirm the clinical tumor stage and minimize diagnosis bias. The pathology, the outcome, and complications, median follow-up, as well as the overall survival, were documented. The one year, two years and five years of survival for each stage were documented. The clinical-stage 1 group was divided into two; those who underwent PN and those who underwent RN. The overall survival in each group was compared.

Statistical analyses were performed using SPSS 22.0. Descriptive and inferential statistics were obtained. Value of $P < 0.05$ was considered statistically significant. Kaplan-Meier test was used to estimate the overall survival for all stages of our series and RN and PN patients of stage 1 group. The log-rank test was used to compare overall survival.

* Assistant Professor of Urology, College of Medicine, King Khalid University
Consultant Urologist, Aseer Central Hospital

** Assistant Professor
Department of Surgery (Urology Division), College of Medicine
King Khalid University
P.O. Box 641, Abha 61421

*** Consultant Urologist, Aseer Central Hospital
Resident
Department of Urology
Aseer Central Hospital

**** Intern
King Khalid University
Kingdom of Saudi Arabia
E-mail: mhalshyarba@kku.edu.sa

RESULT

Fifty-three renal tumor patients were surgically treated from January 2008 to December 2017. The mean age was 56.4 years (range, 1.3-95) years. Thirty-one (58%) were males and 22 (42%) were females; the male to female ratio was 1.4:1.0. Thirty-seven (69.8%) patients were above 50 years. Flank pain and hematuria were the most common presentations in 24 (45.2%) and 19 (35.8%) patients, respectively. Incidental renal tumor detection was found in 7 (13.2%) patients. Forty-four patients (83%) were having a normal renal function. Fifteen (28.3%) patients were hypertensive and 12 (22.6%) patients were diabetics, see table 1.

Table 1: Group Characteristics (N=53)

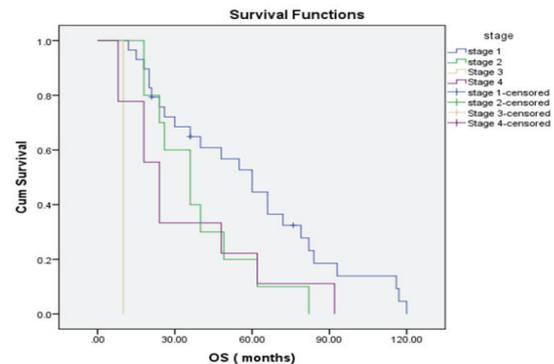
Variable	Number (%)
Age (years)	56.4 ± 17.7
Gender	
Male	31 (58%)
Female	22 (42%)
Presentation	
Flank pain	24 (45%)
Hematuria	19 (35.8%)
Incidental	7 (13.2%)
Renal profile	
Normal	44 (83%)
Abnormal	9 (17%)
Risk factors	
DM	13 (24.5%)
Hypertension	13 (24.5%)
Smoking	2 (4%)
Clinical stage	
Stage (1)	30 (56.6%)
Stage (2)	10 (18.8%)
Stage (3)	1 (1.8%)
Stage (4)	10 (18.8%)
Unknown	2 (3.7%)
Operative procedure	
Radical Nephrectomy (RN)	49 (92%)
Partial Nephrectomy (PN)	4 (7.5%)
Laparoscopic	4 (7.5%)
Robot-assisted	3 (5.6%)
Complications	
Bleeding	10 (18.8%)
30-days mortality	0
Positive surgical margin	0
RCC	
Clear cell	30 (56.6%)
Papillary	6 (11.3%)
Chromophobe	6 (11.3%)
Sarcomatoid	1 (1.8%)
Malignant non RCC	3 (5.6%)
Collecting duct carcinoma	1 (1.8%)
Extra-adrenal pheochromocytoma	1 (1.8%)
Nephroblastoma	1 (1.8%)
Benign renal tumors	7 (13.2%)
Angiomyolipoma	2 (3.7%)
Oncocytoma	2 (3.7%)
Fibroma	1 (1.8%)
Renal cortical adenoma	1 (1.8%)

Thirty (56.6%) patients were in clinical stage 1; 10 (18.8%) patients were in stage 2; one (1.8%) patient was in stage 3 and 10 (18.8%) were in stage 4. Two (3.7%) patients were of unknown stage as their imaging was done in another hospital and during the study were unavailable. Forty-nine (92.4%) patients underwent RN while 4 (7.5%) patients underwent PN. The laparoscopic and robotic-assisted approach was performed in 4 (7.5%) and 3 (5.6%) patients, respectively, see table 1.

Bleeding was the most common complication, 10 (18.8%); all patients were managed conservatively. Our patients had neither intraoperative nor surgery-related mortality. All PN cases had a negative surgical margin.

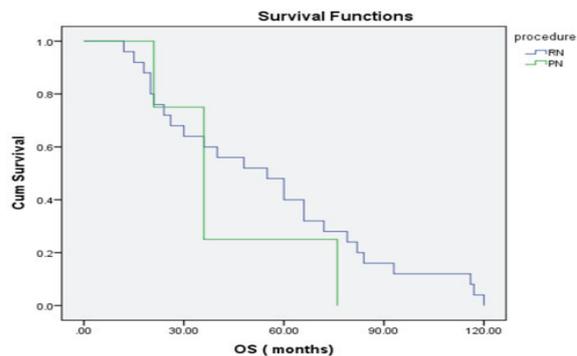
Histopathologically RCC was seen in 43 (81.1%) patients and non-RCC malignant tumors in 3 (5.6%) patients. The benign renal tumors were seen in 7 (13.2%) patients, see table 1.

Forty-two (79.2%) patients have had a follow-up. Eleven (20.7%) patients were either referred to higher center care for adjuvant therapy or lost for follow-up. The median follow-up was 24 months (range, 1-80 months). The mean overall survival (OS) was 44 months (range, 3-120). The stage-related OS showed a statistically significant 1, 2 and 5-year OS (97%, 73%, and 43%), respectively, for stage 1 compared with other stages. This was confirmed with Kaplan-Meier analyses (P-value ≤ 0.00001), see figure 1. We, however, did not find a significant overall survival advantage when we compared RN and PN patients of stage 1 in our study (P-value ≤ 0.406), see figure 2.



Log Rank (Mantel-Cox) , 0.00001 * Significant

Figure 1: Kaplan-Meier Estimates for Overall Survival per Stage in Renal Cell Carcinoma



Log Rank (Mantel-Cox), 0.406 * N.S

RN= Radical Nephrectomy , PN= Partial Nephrectomy

Figure 2: Kaplan-Meier Estimates with Log-Rank Test for Overall Survival in Stage 1 Renal Cell Carcinoma Patients

DISCUSSION

Renal cell carcinoma is the most fatal urological malignancy; it frequently appears in advanced ages. It is often diagnosed in the sixth to eighth decades of life⁸.

During the 10-year interval, we managed 53 patients with a renal tumor, with a frequency of approximately 5.3 cases per year. However, our study cohort showed a relatively younger mean age of 56.4 years at the diagnosis compared to other studies⁹. Furthermore, 67% of our patients were above 50 years. There was no significant gender predominance in our study.

Flank pain and hematuria were the most common presentations in our study. Incidental renal tumor detection was in 7 (13%) patients. This is considerably lower than those reported in other studies. Gupta et al in a comparative study found an increase of incidental renal tumor from 10.67% to 27.63% over 10 years interval ($P=0.001$)⁹. Metastatic renal tumors at presentation were seen in 19% in our study. Another recent study from Jeddah by Altayib revealed a slightly higher incidence compared to ours (26.6%)⁷.

In our study, 92% of patients underwent RN while 7.5% of patients underwent PN. Forty-four (82%) had a normal renal function at presentation. Some of our patients were neither ready to take the risk of the complications nor local recurrence risk of PN. We started PN particularly with the introduction of laparoscopy and robotics to our institute. Our practice was confirmed by Al-Othman et al who reviewed the pattern of urologic cancer management among practicing urologists in Saudi Arabia¹⁰. They found that only 9% of respondents preferred to perform PN for patients with small renal tumors ≤ 4 cm.

In our study, RCC was seen in 81% of the patients with clear cell type predominance (70%). This was consistent with similar studies^{9,11}. Benign renal tumor was seen in 13% of our patients. Our incidence of benign renal tumors was comparable with other studies^{12,13}.

The median follow-up of our patients was 24 months, the mean cumulative overall survival (OS) in this study was 44.7 months. This is consistent with the findings of Pierorazio et al in their review of 60 months for RN, 30 months for PN¹⁴. On stratification of our patients' stage per survival, we found a statistically significant survival advantage for the early-stage tumor over advanced-stage tumors. We did not find a significant survival benefit of RN over PN for clinical stage 1.

Our study had several limitations. First is the retrospective design. Second, only 4 patients underwent PN. Third, some patients were referred to other centers for adjuvant therapy, which implied a failure to measure cancer-specific and progression-free survivals.

CONCLUSION

An extensive and continuous laparoscopic training for young urologists is essential in reinforcing the surgeon's expertise.

A large prospective randomized double blind controlled study is advised.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design,

analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 23 November 2019.

Ethical Approval: Approved by the Research Ethics Committee, Aseer Central Hospital, Saudi Arabia.

REFERENCES

1. Jemal A, Bray F, Center MM, et al. Global Cancer Statistics, *CA Cancer J Clin* 2011; 61 (2): 69-90.
2. Altekruse SE, Huang L, Cucinelli JE, et al. Spatial Patterns of Localized-Stage Prostate Cancer Incidence among White and Black Men in the Southeastern United States, 1999-2001. *Cancer Epidemiol Biomarkers Prev* 2010; 19(6): 1460-1467.
3. Campbell SC, Novick AC, Beldegrun A, et al. Guideline for Management of the Clinical T1 Renal Mass. *J Urol* 2009; 182(4): 1271e1279.
4. Ljungberg B, Bensalah K, Canfield S, et al. EAU Guidelines on Renal Cell Carcinoma: 2014 Update. *Eur Urol* 2015; 67 (5): 913e924.
5. Bazarbashi S, Al Eid H, Minguet J. Cancer Incidence in Saudi Arabia: 2012 Data from the Saudi Cancer Registry. *Asian Pacific Journal of Cancer Prevention* 2017; 18(9): 2437.
6. Alkhateeb SS, Allothman AS, Addar AM, et al. Kidney Cancer in Saudi Arabia: A 25-Year Analysis of Epidemiology and Risk Factors in a Tertiary Center. *Saudi Medical Journal* 2018; 39(5): 459.
7. Tayib A. Renal Tumors in Adults: The Clinical Experience of 124 Patients. *Journal of King Abdulaziz University Medical Sciences* 2011; 98(281): 1-16.
8. Li W, Cheng Y, Cheng Y, et al. Clinical Efficacy of Radical Nephrectomy versus Nephron-Sparing Surgery on Localized Renal Cell Carcinoma. *Eur J Med Res* 2014; 19(1): 58.
9. Gupta NP, Ishwar R, Kumar A, et al. Renal Tumors Presentation: Changing Trends Over Two Decades. *Indian Journal of Cancer* 2010; 47(3): 287.
10. Al-Othman K, Al-Hathal N. Pattern of Management of Urologic Cancer in Saudi Arabia. *Urology Annals*, 2010; 2(1): 21.
11. Störkel S, Ebie JN, Adlakha K, et al. Classification of Renal Cell Carcinoma: Workgroup No. 1 Union Internationale Contrele Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer* 1997; 80: 987-989.
12. Mohsin R, Hashmi A, Sultan G, et al. Renal Tumors in Young Adults: A Single-Center Experience from a Developing Country. *Urol J* 2012; 9:373-80.
13. Yıkmaz TN, Baş O, İhsan Arık A, et al. The Relationship between Histopathology and Age Factor in Patients Who Were Operated for Renal Masses. *Turk Uroloji Dergisi*, 2015; 41(2): 57-60.
14. Pierorazio PM, Johnson MH, Patel HD, et al. Management of Renal Masses and Localized Renal Cancer: Systematic Review and Meta-Analysis. *Journal of Urology*, 2016; 196(4): 989-999.