Review Article

Saudi Oncology Society and Saudi Urology Association combined clinical management guidelines for renal cell carcinoma

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Abstract

This is an update to the previously published Saudi guidelines for the evaluation, medical, and surgical management of patients diagnosed with renal cell carcinoma (RCC). It is categorized according to the stage of the disease using the tumor node metastasis staging system 7th edition. The guidelines are presented with supporting evidence level, they are based on comprehensive literature review, several internationally recognized guidelines, and the collective expertise of the guidelines committee members (authors) who were selected by the Saudi Oncology Society and Saudi Urological Association. Considerations to the local availability of drugs, technology, and expertise have been regarded. These guidelines should serve as a roadmap for the urologists, oncologists, general physicians, support groups, and healthcare policy makers in the management of patients diagnosed with RCC.

Key Words: Cancer, carcinoma, cell, guidelines, kidney, management, renal, Saudi Oncology Society, Saudi Urological Association

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INTRODUCTION

Renal cancer represents the third common genitourinary cancer in Saudi Arabia after urinary bladder and prostate.[1] It accounts for 3.4% of all male cancers and 2.0% of all female cancers. In 2010, a total of 167 cases were diagnosed in males and 117 cases in females. The age-standardized rate

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in males was 2.9/100,000 and in females was 2/100,000 populations.

All cases of renal cell carcinoma (RCC) should preferably seen or discussed in a multidisciplinary forum.

1. Pretreatment evaluation
   - 1.1. Evaluation of suspicious renal mass:
     - 1.1.1. History and physical examination
     - 1.1.2. Blood count, renal, and hepatic profile
     - 1.1.3. Computed tomography scan of chest, abdomen, and pelvis
     - 1.1.4. Urine analysis
     - 1.1.5. Urine cytology should be done if urothelial cancer is suspected
     - 1.1.6. Indications of renal mass biopsy, suspicion of renal abscess, suspicion of metastases, suspicion of renal lymphoma, and prior to systemic therapy. Furthermore, strongly advocated before nonsurgical options (i.e., active surveillance, cryoablation, and radiofrequency ablation)
     - 1.1.7. Brain imaging and bone scan should be done only if clinically indicated.
2. Staging[2]

   The American joint commission on cancer staging tumor node metastasis 7th addition will be adopted [Appendix 1].
3. Treatment
   - 3.1. Localized disease (T1a):
     - 3.1.1. The recommended treatment is surgical excision preferably by partial nephrectomy (open, laparoscopic, or robotic) in all cases and especially in patients with solitary kidney, bilateral tumors, familial renal cell cancer, or renal insufficiency (evidence level-I [EL-1])[3-9]
     - 3.1.2. Radical nephrectomy (preferably laparoscopic) should be reserved for cases where partial nephrectomy is not technically feasible after consultation with an experienced surgeon (EL-1)[3-16]
     - 3.1.3. Nonsurgical options (i.e., active surveillance, cryoablation, and radiofrequency ablation) are all inferior to surgical excision in terms of oncological outcome and are not recommended except in patients with significant comorbidities that interdict surgical intervention (EL-2).[17-21]
   - 3.2. Localized disease (T1b)
     - 3.2.1. The recommended treatment is radical nephrectomy (preferably laparoscopic) (EL-1)[22-33]
     - 3.2.2. Partial nephrectomy may be an option, especially in a patient with a solitary kidney, bilateral tumors, familial renal cell cancer, or renal insufficiency. However, this should only be performed by experienced surgeon in a high-volume center (EL-1)[22-27]
     - 3.2.3. Nonsurgical options (i.e., active surveillance, cryoablation, and radiofrequency ablation) are not recommended.
   - 3.3. Localized disease (T2)
     - 3.3.1. The recommended treatment is radical nephrectomy (EL-1)[22-27]
     - 3.3.2. Partial nephrectomy and nonsurgical options (i.e., active surveillance, cryoablation, and radiofrequency ablation) are not recommended.
   - 3.4. Localized disease (T3)
     - 3.4.1. The recommended treatment is radical nephrectomy with complete excision of all venous thrombus in the renal vein, inferior vena cava, and right atrium (EL-2)
     - 3.4.2. These surgeries should only be performed in a tertiary care centers with the availability of cardiac, vascular or hepatic surgeon depending on the case (EL-2).[28,29]
   - 3.5. Excision of the ipsilateral adrenal gland
     - 3.5.1. Ipsilateral excision of the adrenal gland during radical nephrectomy is indicated in upper pole kidney tumors or in the presence of a concurrent radiologically detectable adrenal gland lesion (s) (EL-2).[30-33]
   - 3.6. Lymphnode dissection
     - 3.6.1. Resection of the regional lymphnodes (within Gerota's fascia) is an integral part of radical nephrectomy
     - 3.6.2. Resection of the nonregional lymphnodes provides no therapeutic advantages and it is used for staging purposes (EL-1).[34]
   - 3.7. When doing partial nephrectomy the surgeon should aim to obtain adequate surgical margin and avoid tumor inoculation except in patients with Von Hippel–Lindau syndrome[35-37]
   - 3.8. Postoperative follow-up after treatment we use the European Association Of Urology Guidelines [Appendix 1].
   - 3.9. Metastatic/advanced unresectable disease:
     - 3.9.1. Risk stratification for metastatic RCC
     - 3.9.2. The Memorial Sloan-Kettering Cancer Center (MSKCC) risk classification for metastatic disease:[38] Risk factors are:
     - 3.9.3. A Karnofsky performance status of <80%
     - 3.9.4. Serum lactic dehydrogenase level >1.5 times the upper limit of normal
     - 3.9.5. Corrected serum calcium >10 mg/dL (2.5 mmol/L)

3.9.6. Hemoglobin concentration below the lower limit of normal
3.9.7. No prior nephrectomy (i.e., no disease-free interval)
3.9.8. Each of the above gives a score of one. Patients will be classified according to the total score as follow:
3.9.9. 0: No risk factors: Good risk group
3.9.10. 1, 2: Risk factors: Intermediate risk
3.9.11. 3, 4, 5: Risk factors: High risk
3.9.12. Heng criteria validates component of the MSKCC with the addition of
3.9.13. Neutrophils greater than the upper limit of normal
3.9.14. Platelets greater than the upper limit of normal.[39]

Several scenarios could be faced in patients with metastatic disease. Accordingly the following should be considered:

3.9.15. Potentially resectable primary with solitary metastasis or multiple resectable lung metastasis: Those patients should undergo primary nephrectomy and resection of the metastatic lesion/s (EL-2).[40-42] Following complete resection no further therapy or "adjuvant therapy" is indicated (EL-3)
3.9.16. Potentially resectable primary and multiple nonresectable metastasis: Those patients should undergo resection of the primary tumor if in good performance status (EL-1),[43-52] then should start systemic therapy according to the following guidelines:
3.9.16. 1. Clear cell histology, good, and intermediate risk: Options of therapy include systemic therapy with either sunitinib (EL-1), bevacizumab and interferon α-2a or pazopanib (EL-1). High dose interlukin-2 in highly selected patients and centers
3.9.16. 2. Clear cell histology with poor risk: Temsirolimus is the preferred treatment (EL-1). Alternative options include sunitinib (EL-2)
3.9.16. 3. Nonclear cell histology: Options of therapy include temsirolimus (EL-2), sunitinib (EL-2), or sorafenib (EL-2). Medullary and collecting duct carcinoma should be treated with platinum-based chemotherapy (EL-3).
3.9.17. Unresectable primary with or without metastatic disease: Those patients with good performance status should be offered systemic therapy according to their histology and MSKCC risk group as in item 4.8.2
3.9.17. 1. Recurrent disease postprimary nephrectomy: Treatment will depend if resectable or not:
3.9.17. 1.1. If resectable solitary metastasis: Surgical resection should be attempted (EL-2). No systemic therapy is of benefit following complete resection (EL-3)
3.9.17. 1.2. If nonresectable recurrence: Patient should be treated as metastatic disease according to their histology and MSKCC risk group and Heng criteria as in Item 3.9.1-3.
3.9.18. Second line therapy posttyrosine kinase inhibitors (TKIs) failure: Patients who fail 1st line TKI's should receive second-line therapy if in reasonable performance status, options of second line agents include everolimus (EL-1) or axitinib (EL-1)
3.9.19. Third line: Consider everolimus.

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Conflicts of interest

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APPENDIX

Appendix 1: Surveillance following surgery adapted from European Association of Urology

Risk profile	Treatment	Surveillance						
		6 months	1 year	2 years	3 years	4 years	5 years	After 5 years
Low	RN/PN	US	CT	US	CT	US	CT	Discharge
Intermediate	RN/PN/cryoablation/RFA	CT	US	CT	US	CT	CT	CT alternate 2 years
High	RN/PN/cryoablation/RFA	CT	CT	CT	CT	CT	CT	CT alternate years

CT: Computed tomography, RN: Radical nephrectomy, PN: Partial nephrectomy, RFA: radiofrequency ablation, US: Ultrasound