Guidelines on Renal Cell Cancer

Gerald Mickisch a, Joaquin Carballido b, Sverker Hellsten c, Harald Schulze d, Han Mensink e

a Erasmus University Rotterdam, The Netherlands; b University of Madrid, Spain; c University of Malmö, Sweden; d Academic Teaching Hospital Dortmund, Germany and e University of Groningen, The Netherlands

Abstract

Objectives: On behalf of the European Association of Urology (EAU), Guidelines for Diagnosis, Therapy and Follow-Up of Renal Cell Carcinoma Patients were established. Criteria for recommendations were evidence based and included aspects of cost-effectiveness and clinical feasibility.

Method: A systematic literature research using Medline Services was conducted. References were weighted by a panel of experts on renal cell carcinoma (RCC).

Results: RCC is characterised by a constant rise in incidence over the last 50 years, with a predominance of men over women and an incidence peak in the 6th and 7th decade. There is no risk factor established and the current TNM system (UICC, 1997) is endorsed for staging purposes. Clinical signs and symptoms of RCC are becoming less frequent, incidental discovery constitutes already a majority of cases. Diagnosis is established by ultrasound and abdominal CT, extension assessment in routine cases is done by chest X-ray. Additional examinations may be required in select cases. The therapy of choice in organ-confined RCC is surgery. Radical tumour nephrectomy is considered as a standard. Efficacy and side-effects of organ-sparing surgery, lymphadenectomy and inclusion/omission of ipsilateral adrenalectomy in selected cases is a matter of ongoing clinical research. In metastatic cases, tumour nephrectomy should only be considered in the context of modern systemic immunotherapy. A follow-up at regular intervals is recommended because certain cases of recurrences may be candidates for surgery and/or immunomodulating therapy.

Conclusion: A rise in incidence, improved diagnostic procedures, and evolving multimodality therapeutic concepts justify the need for rational guidelines on this most challenging urologic malignancy.

Key Words
Guidelines · Renal cell cancer · Diagnosis · Therapy · Follow-up
There are no generally accepted risk factors for RCC. There are some epidemiologic data indicating that a smoking habit, obesity or exposure to certain heavy metals such as cadmium may favour the development of RCCs.

**Diagnosis**

Clinical symptoms of RCC, such as haematuria, palpable tumour and flank pain, are becoming less frequent. Asymptomatic tumours are more commonly diagnosed [12]. Clinical examination has a limited role in diagnosing RCC, but it may be valuable in assessing co-morbidity [12]. In case of haematuria, additional tumours of the genitourinary tract should be excluded [13]. The most commonly assessed laboratory parameters are: Haemoglobin and erythrocyte sedimentation rate (prognosis); creatinine: (overall kidney function), and alkaline phosphatase (liver and bone metastases). Serum calcium is frequently included in the preoperative assessment because of its association with paraneoplastic manifestations, which may have clinical implications [14].

The majority of tumours are diagnosed by abdominal ultrasound performed for various reasons. A standard radiological procedure is an abdominal CT scan with and without contrast medium. It serves to document the diagnosis of RCC and provides information on the function and morphology of the contralateral kidney [15]. Additional diagnostic procedures, such as magnetic resonance imaging, angiography or fine needle biopsy, have a very limited role, but may be considered in selected cases [16].

**Extension Assessment**

An abdominal CT scan demonstrates primary tumour extension and provides information on venous involvement and metastatic spread to locoregional lymph nodes, adrenals, the contralateral kidney or to the liver, for example [15]. A chest X-ray is performed to assess pulmonary spread. If indicated by signs and symptoms, other diagnostic procedures may be applied, such as bone scan, brain CT or chest CT [12].

**Treatment**

Only radical surgery offers a reasonable chance of curing the disease [17]. The chances of cure by surgery most strongly depend on the stage (primarily) and grade (secondarily) of the disease (e.g. following TNM classification) [18]. A standard operative procedure is a radical nephrectomy including Gerota’s fascia [19]. There is no evidence to
favour a specific surgical approach. In selected cases of small (≤4 cm) peripheral lesions, an organ-sparing approach may be considered. Final evaluation of oncologic efficacy is pending [20, 21].

Adrenalectomy is generally recommended. The sparing of the ipsilateral adrenal gland in the case of a smaller tumour of the lower half of the kidney is currently being evaluated in ongoing clinical research [22]. A formal lymph node dissection is a valuable diagnostic tool (staging); however, therapeutic efficacy is unproven [23].

If surgery cannot eradicate all tumour deposits, tumour nephrectomy remains palliative therapy and should be considered in the context of multimodality treatment (e.g., in conjunction with immunotherapy or experimental therapies) [24, 25].

In certain patients, e.g., in patients with bilateral tumours, a solitary tumour-bearing kidney, multifocal lesions, renal insufficiency, or in an occasional palliative situation, individual decisions not amenable to general guidelines, will be required.

Follow-Up

Rationale for Follow-Up

The follow-up of patients with RCC after surgical treatment is recommended to detect local recurrence and distant metastases as early as possible to enable additional treatment when indicated and if possible. Such therapy may include resection of a pulmonary metastasis or local recurrences; certain cases may also be candidates for immunomodulating therapy. With this background in mind, a regular postoperative follow-up of patients with RCC is suggested [26–28].

Principles

Prognostic factors and the type of surgical intervention (radical vs. partial or nephron-sparing surgery) are relevant in determining the most efficient follow-up regimen. The only established prognostic factor is tumour stage according to the TNM system [28]. After nephron-sparing tumour resection (either elective or mandatory), the local recurrence rate may vary between 0 and 10% [20, 27]. In a small proportion of patients with a genetic predisposition, a different follow-up procedure may be required [29, 30].

Follow-Up Procedures

The first assessment is at 4–6 weeks and includes: physical examination to exclude surgical complications; serum creatinine to assess the remaining kidney function, and haemoglobin to assess recovery of perioperative blood loss.

If these values are normal, repeat investigation is usually unnecessary. Urine analysis is not needed for routine follow-up.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Visit</th>
<th>Examination</th>
<th>Optional</th>
<th>Purpose</th>
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<tbody>
<tr>
<td>All T</td>
<td>4–6 weeks after surgery</td>
<td>physical exam</td>
<td>AP&lt;sup&gt;a&lt;/sup&gt;</td>
<td>exclude complications of surgery to check recovery of perioperative blood loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>creatinine Hb</td>
<td></td>
<td>establish remaining kidney function&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>T1, T2</td>
<td>every 6 months for 3 years</td>
<td>physical exam</td>
<td>AP&lt;sup&gt;b&lt;/sup&gt;</td>
<td>exclude complications of surgery and LR and LN metastases</td>
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<tr>
<td></td>
<td>every year from 3 to 5 years</td>
<td>chest X-ray</td>
<td>kidney imaging</td>
<td>exclude pulmonary metastases and LR after partial nephrectomy</td>
</tr>
<tr>
<td>T3, T4</td>
<td>every 6 months for 3 years</td>
<td>physical exam</td>
<td></td>
<td>exclude complications of surgery and LR and LN metastases</td>
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<tr>
<td></td>
<td>every year from 3 to 10 years&lt;sup&gt;c&lt;/sup&gt;</td>
<td>chest X-ray</td>
<td></td>
<td>exclude pulmonary metastases and LR after partial nephrectomy</td>
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<td></td>
<td></td>
<td>retroperitoneal imaging</td>
<td></td>
<td>to detect LR, contralateral metastases or neo-occurrence</td>
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</tbody>
</table>

<sup>a</sup> If elevated preoperatively (recurrent or persisting elevation suggests distant metastases or residual tumour), when bone pain is present or bone or liver metastases are suspected.<br><sup>b</sup> If the postoperative level is abnormal, it should be repeated at regular visits.<br><sup>c</sup> There is a small, but continuous, risk of recurrence or metastasis from 5 to 15 years.

AP = Alkaline phosphatase; LR = local recurrence; LN = lymph node.

If alkaline phosphatase is abnormal preoperatively, repeat measurement is recommended because recurrent or persistent alkaline phosphatase elevation after surgery suggests distant metastasis, or residual tumour [31, 32]. In patients with elevated alkaline phosphatase levels combined with bone pain a bone metastasis may be suspected. Elevated levels may also be found in patients with liver metastases or paraneoplastic manifestations.

A chest X-ray is recommended to detect pulmonary metastases, which occur most commonly within 3 years after surgery. Imaging of the contralateral kidney is advocated in case of enhanced risk of developing metachronous disease (as in familial papillary RCC or von Hippel-Lindau disease). Imaging of the retroperitoneum by abdominal CT or ultrasound is recommended only after nephron-sparing surgery or after radical surgery in locally advanced disease, e.g. T3, T4.

A recommended follow-up scheme is shown in table 1.

References