Guidelines

EAU Guidelines on Renal Cell Carcinoma: The 2010 Update

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Article info

Abstract

Context and objectives: The European Association of Urology Guideline Group for renal cell carcinoma (RCC) has prepared these guidelines to help clinicians assess the current evidence-based management of RCC and to incorporate the present recommendations into daily clinical practice.

Evidence acquisition: The recommendations provided in the current updated guidelines are based on a thorough review of available RCC guidelines and review articles combined with a systematic literature search using Medline and the Cochrane Central Register of Controlled Trials.

Evidence synthesis: A number of recent prospective randomised studies concerning RCC are now available with a high level of evidence, whereas earlier publications were based on retrospective analyses, including some larger multicentre validation studies, meta-analyses, and well-designed controlled studies.

Conclusions: These guidelines contain information for the treatment of an individual patient according to a current standardised general approach. Updated recommendations concerning diagnosis, treatment, and follow-up can improve the clinical handling of patients with RCC.

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1. Introduction

The European Association of Urology (EAU) Guideline Group for renal cell carcinoma (RCC) has prepared the current guidelines to present evidence-based knowledge for the clinical management of the malignancy and to help clinicians incorporate the updated recommendations into their clinical practice. The update has been based on a structured literature search. Publications concerning RCC were found to be mostly retrospective, including some larger multicentre studies and well-designed controlled studies. The randomised controlled trials available have

provided high levels of evidence-based information, allowing high-grade recommendations. This review is an update of the 2007 guidelines review [1], which has been completely revised and supplemented with data on other tumours of the kidney with the exception of renal pelvic carcinoma. Further references and detailed information on the level of evidence and grades of recommendation are available at the EAU website (www.uroweb.org).

2. Epidemiology and aetiology

Renal cell carcinoma represented the ninth most common malignancy in Europe in 2008 [2]. Until recently, there was a worldwide and European annual increase in incidence of about 2%, except in Denmark and Sweden, where a decrease was observed [2]. In 2008, there were an estimated 88 400 new cases and 39 300 kidney cancer–related deaths from RCC in Europe [2]. Additionally, overall mortality rates in Europe increased until the early 1990s, with rates generally stabilising or declining thereafter [3]. This decline in mortality has been substantial in the Scandinavian countries since the 1980s, and since the 1990s, a significant decline has been observed in France, Germany, Austria, the Netherlands, and Italy.

There is a 1.5:1 predominance of new cases diagnosed in men over women, with peak incidence occurring between 60 and 70 yr of age. Identified aetiologic factors are mainly related to lifestyle, such as smoking, obesity, and hypertension [4–6]. For cigarette smoking and hypertension, a dose-related incidence is demonstrated [4,6]. Having a first-degree relative with kidney cancer is also associated with an increased risk of RCC [7]. Hereditary tumours can be found as part of the following entities: von Hippel-Lindau (VHL) syndrome (clear cell RCC [ccRCC]), hereditary papillary RCC (pRCC), Birt-Hogg-Dube syndrome (chromophobe RCC [chRCC]), hereditary leiomyomatosis, tuberous sclerosis, and constitutional chromosome 3 translocation [8]. The recommended prophylaxis is to avoid cigarette smoking and obesity.

3. Symptoms and diagnosis

Many renal masses remain asymptomatic and nonpalpable until the late stages of the disease. Currently, most RCCs are detected incidentally by the frequent use of imaging examinations for a variety of unrelated symptoms or diseases. Clinical symptoms, such as flank pain, gross haematuria, palpable abdominal mass, and paraneoplastic syndromes, or symptoms due to metastatic disease, such as bone pain or persistent cough, remain evenly distributed in patients diagnosed due to symptoms [9]. Physical examination has only a limited role in diagnosing RCC. However, it is important for the clinical evaluation, especially findings such as: a palpable abdominal mass, cervical lymphadenopathy, nonreducing varicocele, and bilateral lower extremity oedema suggesting venous involvement. The most commonly assessed laboratory parameters are serum creatinine, C-reactive protein, glomerular filtration rate, haemoglobin, erythrocyte sedimentation rate, alkaline phosphatase, and corrected serum calcium. Renal function should be estimated when there is a solitary kidney or bilateral tumours; when renal function is compromised, as indicated by increased serum creatinine; or when there is risk of future renal impairment from comorbid disorders affecting renal function [10]. An isotope renogram and a total renal function evaluation should be considered to optimise the treatment decision (eg, the need to preserve renal function).

3.1. Radiologic investigations

The current approach for detection and characterisation of renal masses is to use ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI; Table 1). Most renal masses are diagnosed accurately by using imaging alone. Imaging can be used to classify renal masses as solid or cystic (Table 1). For solid renal masses, the most important criterion for differentiating malignant lesions is the presence of enhancement [11]. Abdominal and chest CT provides information on primary tumour extension, morphology of the contralateral kidney, and evaluation of metastases [11]. For the evaluation of cystic renal masses, the Bosniak classification is recommended [12]. If CT results are indeterminate, MRI may provide additional information regarding the renal mass, local growth, and vena cava thrombus involvement. MRI is also indicated in patients who have contrast allergy or who are pregnant [13]. Evaluation of the tumour thrombus can also be performed with Doppler US [11]. The true value of positron emission tomography (PET) in RCC remains to be determined. Currently, PET is not a

Table 1 – Selected recommendations on diagnosis, classification, and imaging in patients with renal tumour masses

Recommendation	Grade
Chest CT is most sensitive and is recommended for assessment of the lung, but a plain chest x-ray can be sufficient in low-risk patients.	A
Abdominal CT or MRI are recommended for the workup of patients with RCC.	A
Evaluation of renal function is recommended before treatment planning.	B
Percutaneous biopsy is always indicated before ablative and systemic therapy without previous histopathology and in surveillance strategies.	B
Bosniak classification of renal cysts is advocated for the workup of cystic renal masses.	C
Except for angiomyolipomas, most uncommon renal tumours cannot be differentiated from RCC based on imaging.	C
The current TNM classification system is recommended for staging.	B
The Fuhrman grading system and RCC type classification should be used.	B
No molecular prognostic marker, at present, is recommended for routine clinical use.	B

CT = computed tomography; MR = magnetic resonance imaging; RCC = renal cell carcinoma.

standard investigative tool [14]. There is consensus that most bone and brain metastases are symptomatic at diagnosis, so bone or brain CT examination is indicated only if symptoms or laboratory signs are present.

3.2. Renal biopsy

Renal tumour biopsy is increasingly being used in diagnosis and is always indicated before ablative and systemic therapy without previous histopathology and in surveillance strategies to stratify follow-up [15]. Biopsy aims to determine malignancy and type and grade of the renal mass. In most series, a core biopsy demonstrates high specificity and high sensitivity for the presence of malignancy, although 10–20% of biopsies are inconclusive [16]. For large renal masses scheduled for nephrectomy, biopsies are not recommended (Table 1).

3.3. Histologic diagnosis

RCC is the most common solid lesion within the kidney and accounts for approximately 90% of renal malignancies. The Fuhrman histologic classification system is the most generally accepted classification of tumour grade. According to the World Health Organisation [17], there are three major histologic RCC types: ccRCC (80–90%), pRCC (10–15%), and chRCC (4–5%). These RCC types can be differentiated by histologic and molecular genetic changes, and pRCC can further be divided into two different subtypes, type 1 and type 2, the latter having a worse prognosis [18].

3.4. TNM stage classification

The current TNM stage classification system is recommended for clinical and scientific use [19]. The 2009 version introduced significant changes, including a tumour size stratification of T2 tumours, which defines a T2a tumour >7 cm but ≤10 cm and a T2b tumour as >10 cm limited to the kidney. In the current TNM version, T3a tumours also include RCCs with a tumour thrombus that extends into the renal vein only. Adrenal invasion is now classified within the pT4 tumours, because many studies have shown that adrenal invasion caries a very poor prognosis.

4. Prognostic factors

Factors influencing prognosis can be classified into anatomic, histologic, clinical, and molecular. Anatomic factors are commonly gathered together in the TNM staging classification system, giving the most reliable prognostic information. Histologic factors include Fuhrman grade, RCC subtype, sarcomatoid features, microvascular invasion, tumour necrosis, and invasion of the collecting system. The Fuhrman nuclear grade system is affected by intra- and interobserver discrepancies but is an independent prognostic factor. The RCC type classification shows a trend in univariate analysis towards a better prognosis for patients with chRCC versus pRCC or ccRCC; however, this survival difference does not remain when stratified to TNM stage [20]. In pRCC, two

subgroups are shown with different clinical course: type 1, with low-grade tumours with a chromophilic cytoplasm, while type 2 pRCC are mainly tumours with an eosinophilic cytoplasm and a great propensity for developing metastases. This classification has been confirmed at the molecular level [21]. Clinical factors including patient performance status, localised symptoms, cachexia, anaemia, and platelet count have been shown to predict survival, especially in patients with metastatic disease.

Numerous molecular markers have also been investigated as prognostic variables, including carbonic anhydrase IX, vascular endothelial growth factor (VEGF), hypoxia inducible factor, Ki67 (proliferation), p53, phosphatase and tensin homologue, E-cadherin, and CD44 (cell adhesion) [22]. To date, none of these markers has been shown to improve the predictive accuracy of current prognostic systems, and they are not recommended in routine practice. Finally, gene expression profiling seems promising, but it has not helped so far to identify new relevant prognostic factors. Postoperative prognostic systems and nomograms that combine independent prognostic factors have been developed and externally validated [23]. These systems may be more accurate than TNM stage for predicting survival. An important advantage of nomograms is their ability to measure predictive accuracy, which enables all new predictive parameters to be objectively evaluated.

5. Other renal tumours

The common RCC types account for 85–90% of the renal malignancies. The remaining 10–15% of renal tumours include a variety of uncommon sporadic and familial carcinomas and a group of unclassified carcinomas as well as a number of benign tumours [17]. Collecting-duct carcinoma is a rare RCC type, often presenting at an advanced stage of disease and with adverse survival. Sarcomatoid RCC represents high-grade transformation in different RCC types without being a distinct histologic entity. Sarcomatoid changes in RCC carry a worse prognosis. Unclassified RCC is a diagnostic category for RCC that cannot be assigned to any other category of RCC-type carcinoma [17]. There are no strict histopathologic criteria for multilocular cystic RCC (cRCC), which is essentially a well-differentiated cRCC. Metastasis of this tumour type is not described in the literature. A similar imaging appearance might also be due to a mixed epithelial and stromal tumour of the kidney, a cystic nephroma, or a multilocular cyst, all of which are benign lesions. A number of less common renal tumour types are described. Most of these uncommon renal tumours cannot be differentiated from RCC on the basis of radiology and therefore should be treated in the same way as RCC.

Benign renal tumours include oncocytoma and angiomyolipoma. Imaging characteristics alone are unreliable when differentiating between oncocytoma and RCC (Table 1). Histologic diagnosis is the reference standard, but percutaneous biopsy has low specificity [16]. Watchful waiting can be considered in selected cases of histologically verified oncocytoma. Angiomyolipoma is composed of adipose tissue, muscle cells, and abnormal thick-walled blood vessels. CT

Table 2 – Selected recommendations on treatment of localised renal cell carcinoma

Recommendations	Grade
For T1 RCCs, nephron-sparing surgery should be performed whenever possible. Open partial nephrectomy currently remains the standard.	A
Laparoscopic radical nephrectomy is recommended in T2 renal cell cancer when nephron-sparing surgery is not suitable.	B
Extended lymphadenectomy does not improve survival and can be restricted to staging purposes.	A
Adrenalectomy is generally not recommended except when a normal adrenal gland cannot be excluded by imaging and palpation.	B
Embolisation can be a beneficial palliative approach in patients unfit for surgery and suffering from massive haematuria or flank pain.	C
Patients with small tumours and/or significant comorbidity who are unfit for surgery should be considered for an ablative approach (eg, cryotherapy and radiofrequency ablation).	A
RCC = renal cell carcinoma.	

and MRI mostly lead to diagnosis due to the presence of adipose tissue. Indications for intervention primarily include symptoms such as pain and bleeding or suspected malignancy. Treatment with a conservative nephron-sparing procedure can be considered for angiomyolipomas >4 cm, but a selective arterial embolisation can also be considered [24].

6. Treatment of localised renal cell carcinoma

The treatment recommendation of RCC depends on the consideration of a variety of factors: tumour size and location, local or distant spread, renal function, comorbidities, and performance status (Table 2).

6.1. Surgery

Surgery is the only curative therapeutic approach for RCC (Table 2). Nephron-sparing surgery (NSS) for localised RCC has an oncologic outcome similar to that of radical surgery [25] and is generally recommended for T1 tumours. NSS is an option in T2 tumours (Table 3).

NSS is not suitable in patients with locally advanced tumour growth, unfavourable location, and/or significant deterioration of general health. In these situations, the curative therapy remains radical nephrectomy either by laparoscopic or open surgery [26].

Adrenalectomy is not indicated when imaging clearly shows a normal adrenal gland and operative findings do not give any indication of a nodule within the adrenal gland [27].

Lymph node dissection does not appear to improve long-term survival following nephrectomy [28]. For staging purposes, the lymph node dissection can be limited to the hilar region. In patients with palpable or CT-detected enlarged lymph nodes, resection should be performed to obtain adequate staging information. Extirpation of a tumour thrombus should always be considered.

6.1.1. Indications for nephron-sparing surgery

Indications for NSS are (1) absolute in cases with an anatomic or functional solitary kidney, (2) relative when the functioning opposite kidney is affected by a condition that might impair renal function in the future, and (3) elective in the presence of a healthy contralateral kidney. Another indication is patients with hereditary RCCs, who carry a high risk of developing additional kidney tumours. When compared with radical nephrectomy, NSS can achieve preserved renal function, decreased overall mortality and reduced frequency of cardiovascular events [29].

For elective indications, NSS for T1a tumours provides recurrence-free and long-term survival rates similar to those observed after radical surgery (Table 3). For larger tumours (T1b and T2), partial nephrectomy has demonstrated feasibility and oncologic safety in carefully selected patients [30]. The complication rates observed with NSS are slightly higher but are tolerable when compared with radical nephrectomy. In general, NSS carried out for absolute rather than elective indications has an increased complication rate and a higher risk of developing locally recurrent disease, probably due to the larger tumour size [31]. If the tumour is completely resected, the thickness of the surgical margin does not affect the likelihood of local recurrence [32].

6.2. Laparoscopic surgery

Laparoscopic surgery for RCC has become an established surgical procedure. Whether done retroperitoneally or transperitoneally, the laparoscopic approach follows established open surgical oncologic principles. Laparoscopic

Table 3 – Recommended surgical treatment strategy of patients with renal cell carcinoma according to clinical tumour stage

Stage	Surgery	Approach	Recommendations
T1	Nephron-sparing surgery	Open	Recommended standard
		Laparoscopic	Optional in experienced centres
	Radical nephrectomy	Laparoscopic	In patients not suitable for nephron-sparing surgery
		Open	Optional in patients not suitable for nephron-sparing surgery
T2	Radical nephrectomy	Laparoscopic	Recommended standard
		Open	Adequate and recommended but has higher morbidity
	Nephron-sparing surgery		Recommended in selected patients in experienced centres
T3, T4	Radical nephrectomy	Open	Recommended standard for most patients
		Laparoscopic	Feasible in selected patients

radical nephrectomy is the recommended standard of care for patients with T2 tumours and smaller renal masses not treatable by NSS. Long-term outcome data indicate that laparoscopic radical nephrectomy has equivalent cancer-free survival rates to those of open radical nephrectomy [33].

Laparoscopic NSS, in experienced hands and selected patients, is an alternative to open surgery. The optimal indication for laparoscopic NSS is a relatively small and peripheral renal tumour. The intraoperative ischaemia time is generally longer during laparoscopy than with open NSS [34]. Long-term renal function depends on the duration of the warm intraoperative ischaemia time. Laparoscopic NSS has a higher complication rate compared with open surgery. However, the oncologic outcome, in available series with limited follow-up, appears to be similar to the outcome achieved with open NSS. Robot-assisted partial nephrectomy is a novel technique that is still undergoing evaluation.

6.3. Therapeutic approaches as alternatives to surgery

6.3.1. Embolisation
There is no general benefit of embolisation before routine nephrectomy [35]. In patients unfit for surgery or who present with nonresectable disease, embolisation can control symptoms such as gross haematuria or flank pain. Embolisation is recommended before the resection of hypervascular bone or spinal metastases because it can reduce intraoperative blood loss. In selected patients with painful bone or paravertebral metastases, embolisation can relieve symptoms [36].

6.3.2. Surveillance
In patients presenting with small renal masses who appear to have no local tumour progression and a decreased risk of metastatic disease, active surveillance might be an alternative. Both short- and intermediate-term oncologic outcomes indicate that an appropriate strategy is to initially monitor small renal masses, and if required, to treat for progression [37].

6.3.3. Minimally invasive approaches
Suggested alternatives to the surgical treatment of RCC include percutaneous radiofrequency ablation (RFA), cryoablation, microwave ablation, laser ablation, and high-intensity focused ultrasound ablation. Possible advantages of these minimally invasive techniques include reduced morbidity, outpatient therapy, and the ability to treat high-risk surgical candidates (Table 2). The recommended indications are small, incidentally found renal cortical lesions in elderly patients, patients with a genetic predisposition for developing multiple tumours, those with bilateral tumours, and patients with a solitary kidney who are at high risk of complete loss of renal function following NSS. In general, tumours >3 cm or located in the hilum, near the proximal ureter or the central collecting system, are not recommended for ablative techniques via a percutaneous approach. Absolute contraindications include irreversible coagulopathies and severe medical instability, such as sepsis.

Of the available ablative techniques, RFA and cryoablation are the most investigated approaches. Before an ablative approach, a pretreatment biopsy should be carried out to clarify the histology of the renal mass. The available literature indicates that the pathology is unknown in a significantly higher proportion of patients undergoing RFA (40%) versus 25% in patients undergoing cryotherapy. Compared with RFA, cryoablation is more likely to be performed laparoscopically. The laparoscopic approach is more effective but has a higher complication rate. Repeat ablation is necessary more frequently following RFA because recurrent tumour is more frequent with RFA than with cryotherapy. Local progression rates for cryotherapy and RFA are poorer than rates for surgical procedures [38].

6.4. Adjuvant therapy

Adjuvant therapy with cytokines and vaccines does not improve survival after nephrectomy for patients at high risk for metastases. Outside of controlled clinical trials, there is no indication for adjuvant therapy following surgery.

6.5. Surgical treatment of metastatic renal cell carcinoma (tumour nephrectomy)

Tumour nephrectomy is curative only if surgery can excise all tumour deposits. For most patients with metastatic disease, tumour nephrectomy is palliative, and complementary systemic treatments are necessary. In a meta-analysis of two randomised studies comparing nephrectomy combined with immunotherapy versus immunotherapy only, increased long-term survival was found in patients undergoing nephrectomy [39]. Nephrectomy in patients with metastatic disease is indicated for those who are suitable for surgery and who have good performance status. At present, only limited data are available addressing the value of cytoreductive nephrectomy combined with targeting agents.

6.5.1. Resection of metastases
Complete removal of metastatic lesions contributes to improvement of clinical prognosis [40]. In patients with synchronous metastatic spread, metastasectomy should be performed if disease is resectable and the patient has a good performance status. There is a definite role for metastasectomy in patients with RCC to improve prognosis. Therefore, the possibility of metastasectomy has to be continuously reevaluated, even with new treatment modalities.

6.6. Radiotherapy for metastases in renal cell carcinoma

Radiotherapy can be used for selected symptomatic patients with nonresectable brain or osseous lesions who do not respond to systemic treatment approaches.

7. Systemic therapy for metastatic renal cell carcinoma

Until recently, treatment of metastatic renal cell carcinoma (mRCC) has been rather unsuccessful. Chemotherapy as

Table 4 – Selected recommendations on treatment with systemic therapy in patients with metastatic renal cell carcinoma

Recommendation	Grade
Targeting agents increase progression-free survival and overall survival as first- and second-line treatment of mRCC. Detailed recommendations of targeting agents are shown in Table 5.	A
Outside of controlled clinical trials, at present, there is no indication for adjuvant therapy following surgery.	A
Monotherapy with IFN-α or high-dose bolus IL-2 as a first-line treatment for mRCC is optional only in selected cases with clear-cell histology and good prognostic factors.	C
IFN = interferon; IL = interleukin; mRCC = metastatic renal cell carcinoma.	

monotherapy is not recommended. For immunotherapy, interferon-α (IFN-α) has proven superiority for survival over hormonal therapy, also compared with placebo. IFN-α provided a response rate of 6–15% and a modest survival benefit of 3–5 mo [41]. The best response was achieved in patients who had good risk Motzer criteria, ccRCC and lung metastases only. Interleukin-2 (IL-2) has also been documented with response rates ranging from 7% to 27% [41]. Long-term complete responders have been achieved with high-dose bolus IL-2 but only in ccRCC. IL-2 has not been validated in controlled randomised studies (Table 4).

7.1. Targeting agents

Recent advances in molecular biology have led to the development of novel agents for the treatment of mRCC. In ccRCC, HIF accumulation due to VHL inactivation results in overexpression of VEGF and platelet-derived growth factor (PDGF), both of which promote neoangiogenesis [42]. This process substantially contributes to the development and progression of RCC. At present, several targeting drugs have been approved both in the United States and in Europe for the treatment of mRCC (Table 5). A number of other agents targeting angiogenesis are under investigation as well as combinations of agents with each other or with cytokines. The role of the new drugs is still under development. There are no data to indicate that the new agents have a curative effect; rather, they appear to stabilise mRCC.

Sorafenib, an oral multiple tyrosine kinase (TK) inhibitor, was in a phase 3 trial compared with placebo in patients in

whom prior immunotherapy failed or who were unfit for immunotherapy. The trial reported a 3-mo improvement in progression-free survival in favour of sorafenib [43]. Survival seems to improve in patients who crossed over from placebo to sorafenib treatment.

Sunitinib is also a TK inhibitor. In a phase 3 first-line trial comparing sunitinib with IFN-α, sunitinib achieved a longer progression-free survival than IFN-α (11 vs 5 mo), although this benefit was restricted to low- and intermediate-risk patients [44]. Overall survival was 26.4 and 21.8 mo in the sunitinib and IFN-α arms, respectively, when there was crossover but was 28.1 mo with sunitinib versus 14.1 mo with IFN-α in patients who did not receive any poststudy treatment ($p = 0.003$).

Pazopanib is an oral angiogenesis inhibitor targeting VEGF receptor, PDGF receptor, and c-KIT. In a recent prospective randomised trial of pazopanib versus placebo in treatment-naive or cytokine-treated mRCC patients, there was a significant improvement in progression-free survival and tumour response (9.2 vs 4.2 mo) [45].

In a phase 3 trial, bevacizumab plus IFN-α was compared with IFN-α monotherapy [46]. The median overall response was 31% versus 13% for IFN-α only ($p < 0.0001$). Median progression-free survival increased significantly from 5.4 mo with IFN-α to 10.2 mo for bevacizumab plus IFN-α ($p < 0.0001$) but only in low-risk and intermediate-risk patients. No benefit was seen in high-risk patients.

Temsirolimus is a specific mammalian target of rapamycin (mTOR) inhibitor [47]. Patients with high-risk mRCC were randomised to receive first-line treatment with temsirolimus or IFN-α monotherapy or temsirolimus + IFN-α. In the temsirolimus group, overall survival was 10.9 mo versus 7.3 mo in the IFN-α group ($p < 0.0069$). In patients treated with combined temsirolimus plus IFN-α, overall survival was not significantly improved [47].

Everolimus is an oral mTOR inhibitor. A phase 3 study in 2008 compared everolimus versus placebo in mRCC patients also treated with best supportive care and who had failed previous targeting treatment. Median progression-free survival was 4 mo with everolimus versus 1.9 mo with placebo ($p < 0.001$) [48].

There is a general recommendation for therapy with targeting agents in patients with mRCC. A substantial improvement of progression-free and overall survival has been achieved after treatments with these targeting agents. First-line and second-line treatments are recommended while further sequential therapies are used clinically in selected groups of patients. For sequential treatment, clinical

Table 5 – Evidence-based treatment algorithm for first- and second-line systemic therapy in patients with metastatic renal cell carcinoma. European Association of Urology recommendation 2010 (grade A).

Treatment	Risk or prior treatment	Recommended agent
First line	Low- or intermediate-risk mRCC	Sunitinib Bevacizumab plus IFN-α Pazopanib
	High-risk mRCC	Temsirolimus
Second line	Prior cytokine therapy	Sorafenib Pazopanib
	Prior VEGFR therapy	Everolimus
	Prior mTOR inhibitor therapy	Clinical trials (Grade C)
IFN = interferon; mRCC = metastatic renal cell carcinoma; mTOR = mammalian target of rapamycin; VEGFR = vascular endothelial growth factor receptor.		

Table 6 – Example of a proposed follow-up algorithm for surveillance after treatment for renal cell carcinoma with combined patient risk profile and treatment efficacy

Risk profile and treatment/schedule	Risk profile		
	Low-risk RN/PN only	Intermediate-risk RN/PN or Cryo/RFA	High-risk RN/PN or Cryo/RFA
6 mo	CXR and US	CT	CT
1 yr	CXR and US	CXR and US	CT
2 yr	CXR and U/S	CT	CT
3 yr	CXR and US	CXR and US	CT
4 yr	CXR and US	CXR and US	CT
5 yr	CT	CT	CT
Following	Discharge	Yearly CXR and US	CXR/CT in alternate years

CT = computed tomography of chest and abdomen; CXR = chest x-ray; cyro = cryotherapy; PN = partial nephrectomy; RFA = radiofrequency ablation; RN = radical nephrectomy; US = ultrasound of kidneys and renal bed.
Note: This is not a European Association of Urology follow-up recommendation.

research is ongoing, but at present, solid evidence-based data are lacking and must be evaluated.

8. Surveillance following nephrectomy or ablative therapies

Surveillance after treatment for RCC allows us to monitor or identify postoperative complications, renal function, local recurrence after partial nephrectomy or ablative treatment, recurrence in the contralateral kidney, and development of metastases. There is no general consensus on surveillance after treatment for RCC, and in fact, no evidence exists that early versus later diagnosis of recurrence improves survival. However, follow-up is important to increase knowledge of the clinical treatment. Evaluation of postoperative complications and renal function are of direct clinical concern. Another reason for surveillance is to identify local recurrence or metastases early, especially in cases of resectable and preferably solitary lesions. Surveillance is particularly important after ablative therapies such as cryotherapy and RFA that have a higher local recurrence rate than conventional surgery because cure can be achieved by repeat ablative therapy or radical surgery.

8.1. Which investigations for which patients, and when?

Intensive radiologic surveillance for all patients is unnecessary. It is reasonable to stratify follow-up based on risk of progression [49]. When the risk of relapse is intermediate or high, more intense imaging surveillance is advocated. Depending on the availability of new effective treatments, more strict follow-up schedules may be required, particularly because there is a higher local recurrence rate after cryotherapy and RFA. Additionally, the optimal duration of follow-up is controversial. Several scoring systems and nomograms have been designed to quantify the likelihood of tumour recurrence, metastases, and subsequent death [50]. Using prognostic variables, several stage-based surveillance regimes have been proposed. There is a need for a surveillance algorithm to monitor patients after treatment for RCC, recognising both the patient risk profile and the efficacy of the treatment (Table 6). We recommend that the intensity of the follow-up programme for an individual

patient be adapted according to the risk of tumour recurrence and the type of treatment performed (grade C).

9. Conclusions

This guideline is intended to help clinicians gain knowledge of the current evidence-based management of patients with RCC according to a standardised general approach. Structured literature searches using an expert consultant were designed for each section. Searches were carried out in different databases for systematic reviews and clinical trials. Grade of recommendation was assigned based on the underlying evidence.

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