Renal cell cancer treatment: an expert panel recommendation from the Latin American cooperative group-genitourinary and the Latin American renal cancer group: focus on surgery

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Abstract

Background: Renal cell cancer (RCC) is one of the 10 most common cancers in the world, and its incidence is increasing, whereas mortality is declining only in developed countries. Therefore, two collaborative groups, The Latin American Oncology Cooperative Group-Genitourinary Section (LACOG-GU) and the Latin American Renal Cancer Group (LARCG), held a consensus meeting to develop this guideline.

Methods: Issues (134) related to the treatment of RCC were previously formulated by a panel of experts. The voting panel comprised 26 specialists (urologists and medical oncologists) from the LACOG-GU/LARCG. A consensus was reached if 75% agreement was achieved. If there was less concordance, a new discussion was undertaken, and a consensus was determined by the most votes after a second voting session.

Results: The expert meeting provided recommendations that were in line with the global literature; 75.0% of the recommendations made by the panel of experts were evidence-based level A, 22.5% of the recommendations were level B, and 2.5% of the recommendations were level D.

Conclusions: This review suggests recommendations for the surgical treatment of RCC according to the LACOG-GU/LARCG experts.

Keywords: adjuvant treatment, cytoreductive nephrectomy, recommendations, renal cell cancer, small renal mass

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Introduction

Renal cell cancer (RCC) is one of the 10 most common cancers in the world, and there are indications that the incidence of this cancer is increasing, while its mortality rates have declined in most developed countries[1,2] but not in developing nations.[3] Global data for 2018 estimate 403,262 new cases of renal cancer in 2018/2019,[4] of which 6270 are expected to affect the Brazilian population.[5] However, mortality rates estimated by the

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number of cases are higher in underdeveloped countries, particularly in South America.[6] Estimates indicate that, by 2030, Brazil and Ecuador may show the greatest increase in the incidence of men and women with renal cancer, which justifies new knowledge and discussions about the subject to plan new resources for health.[1]

RCC encompasses a heterogeneous group of cancers with diverse clinical, pathological, and molecular characteristics, as well as distinct prognoses and therapeutic responses.[7] There are variables related to age, histological subtype, degree of differentiation, and tumor stage. Diagnostic and methodological innovations, medical consensus-based experiments, and the search for new clinical knowledge about this disease are important to improve clinical and surgical approaches. In most centers, RCC can be treated with partial or radical nephrectomy (RN),[8] ablation,[9] and active surveillance (AS).[10] However, after primary tumor treatment, approximately 30% of patients with RCC develop metastases,[11–14] a condition with high mortality.[15]

The incidence of RCC increases with age, and approximately 75% of cases occur in individuals over 60 years of age. There is a predominance in males (1.5:1).[6] In Brazil, according to the International Agency for Research on Cancer (IARC), the estimated age-standardized incidence rates for kidney cancer (both sexes, all ages) is 4.3 per 100,000 people in 2018.[16] The major risk factors for RCC include overweight, hypertension, and smoking. Other medical conditions that have been associated with RCC in epidemiological studies include chronic kidney disease (CKD), hemodialysis, renal transplantation, acquired renal cystic disease, and diabetes mellitus.[17] Many lifestyles, dietary, occupational, and environmental factors are also associated with RCC with varying levels of evidence.[18] Heredity plays a small role in RCCs, accounting for approximately 2–5% of cases.[19]

Considering the advances in biology, medicine, and diagnostics in the field of RCC, two collaborative groups have reviewed and detailed available clinical data on the management of RCC, and recommendations have been made. The Latin American Oncology Cooperative Group-Genitourinary Section (LACOG-GU) and the Latin American Renal Cancer Group (LARCG) have brought together experts on the topic and discussed small renal masses (SRMs), localized and locally advanced RCC, and adjuvant therapy. The results and recommendations are described throughout this manuscript, and all recommendations are based on clinical research evidence, preclinical data, or expert opinion.

Methods

A 1-day live meeting gathered experts from the LACOG-GU and the LARCG-Brazilian Branch to discuss many relevant clinical questions regarding surgery for renal cancer. The main objective was to suggest recommendations on the following subjects: SRMs, localized and locally advanced RCC, and adjuvant therapy.

To this end, a panel of experts used their clinical experience to vote and achieving consensus on 134 questions that were previously formulated by a competent committee. The 11 urologists and 15 clinical oncologists specialized in urologic oncology who formed the panel of experts received, prior to the meeting, studies related to the topics that would be addressed for voting.

Four or five alternatives were offered for each question, always including an 'abstention' alternative, which was not computed in the result but was necessary because it avoided undecided votes from those who had not mastered the subject (Figure 1).

To establish a consensus, at least 75% of the panel had to agree with an answer. Failure to achieve this percentage resulted in a new vote at the end of the session, always preceded by a discussion of the subject. Ultimately, a recommendation was suggested based on majority approval. The result of the percentage for each question raised can be fully appreciated in the supplementary material (Figure S1).

The recommendations presented and discussed in this article reflect the results of the first or second round of expert voting, and the level of evidence was elaborated according to the Oxford Centre for Evidence-based Medicine – Levels of Evidence.[20]

Ethical committee approval

Ethical board approval was not necessary for this study since it did not involve human or animal trials.

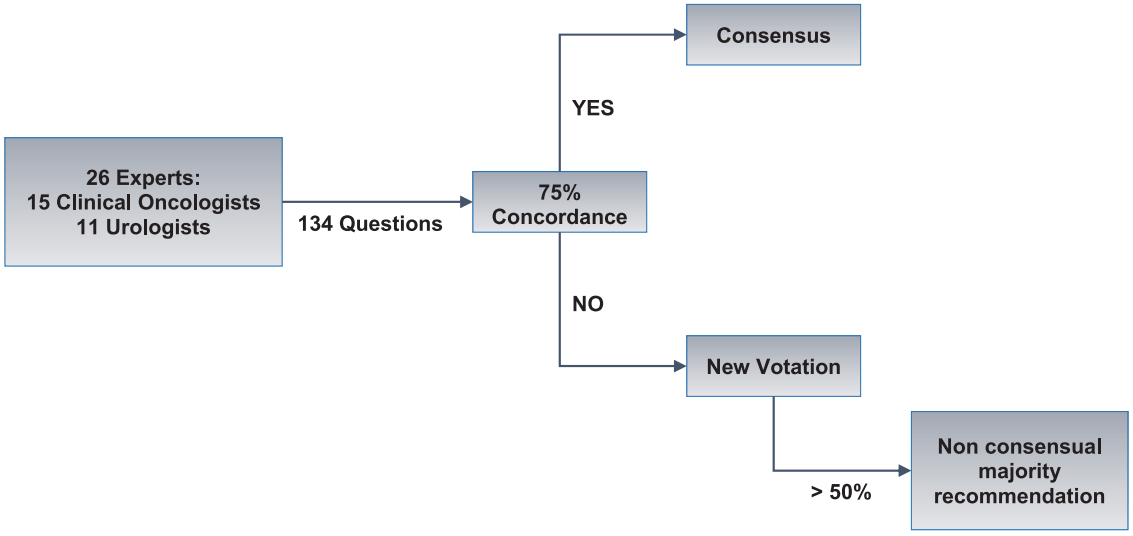

Figure 1. Strategy for formulating renal cell cancer recommendations.

Results

Management of SRMs

When and how to carry out biopsy? A biopsy may distinguish the histologic subtype and aggressiveness of a tumor and thus helps to decide the management.[21,22] Biopsy is indicated in situations where an SRM is suspected to be a metastatic lesion, a manifestation of lymphoma, or of infectious or inflammatory origin rather than a primary renal tumor.

Biopsy is also indicated for patients who will be managed with thermal ablation (TA), to provide a pathologic diagnosis, and to assist in guiding subsequent surveillance. Alternatively, biopsy is indicated whenever there is clinical diagnostic doubt or if the pathology of the renal lesion is unclear and ascertainment of the etiology of the mass will influence subsequent management (recommendation level A).[21–23]

Panelists also recommended biopsy when patients are candidates for AS or after a partial nephrectomy (PN) or a thermoablative procedure when there is suspicion of local recurrence (recommendation level A).[22,23]

Biopsy is generally not indicated in young and healthy patients who will be submitted to surgery routinely, after ablative procedures without suspicion of recurrence, or during AS (after being in surveillance, without any trigger of biopsy), or in complex cysts with solid areas smaller than 2 cm (recommendation level A).[21–23]

The biopsy can be performed as an outpatient procedure under computed tomography (CT) or ultrasound guidance with conscious sedation or local anesthesia, or both.[22] Percutaneous biopsy is generally safe, with a very low risk of clinically significant bleeding or seeding of the needle tract with malignant cells.[24] At least two fragments should be collected from each biopsy to ensure the quality of the procedure, and biopsy should be performed of both the central and peripheral areas of the lesion (recommendation level A).[21,22,24]

When and how to perform a PN? The surgical removal of the tumor with preservation of the normal parenchyma of the kidney is one option for managing SRMs that are suspicious for malignancy in patients who are candidates for definitive treatment. PN is associated with favorable oncologic outcomes and diminishes CKD and progressive CKD risks (recommendation level A).[25] Preferentially, PN should be performed in situations in which there might be a loss of renal function from inefficient kidneys or in cases that put the patient at risk of losing renal function, such as CKD, known familiar RCC syndromes, proteinuria, imminence of renal insufficiency, potentially kidney destroying-function comorbidities, bilateral tumors, and multifocal masses.[24]

PN, when compared with other management options, presents risks of complications such as perioperative bleeding (1–2%) or fistula or urinoma formation (3–5%). Such complications are almost always successfully manageable with conservative measures.[22] Therefore, the risks of such complications are low and manageable, and the clinician should always consider this procedure as a therapeutic option.

Both open and laparoscopic/robotic techniques are utilized, and result in comparable outcomes.[26,27] Although laparoscopic PN (L-PN) is technically challenging, robotic-assisted L-PN (RAL-PN) has evolved as a technique that offers similar oncologic outcomes and has less impact on renal function, as it minimizes the time of ischemia, especially in tumors with high nephrometric complexity.[28]

Panelists did not reach a consensus on the standard technique for performing PN, and this choice should take into account the surgeon's experience and preference (recommendation level A).[29] Although the panelists recognized that there are advantages of RAL-PN, there were no recommendations regarding these advantages, as 50% of the specialists' panel indicated that shorter perioperative time and diminished complications (bleeding and infections) justify the indication of RAL-PN, and the other 50% indicated not. Experts agree (not consensually) with data from a meta-analysis study that compared the two techniques by compiling data from 2000 patients over 20 years and concluded that RAL-PN provided superior, and at least equivalent, results compared with those of open and L-PN.[30]

It is also recommended that most cases should be submitted to warm ischemia, and the ideal time for ischemia is up to 25 min. Cold ischemia should be considered for an ischemia time over 25 min and elevated morphometric scores (recommendation level A).[21] Only the renal artery should be clamped in most cases, and intraoperative frozen-section analysis of surgical margins is not recommended routinely (recommendation level A).[21]

Regarding the surgical technique, the specialists do not recommend the use of intravenous heparin, osmotic diuretics, or furosemide. Hemostatic and sealant agents can be used at the discretion of the surgeon. The specialists do recommend the use of prophylactic heparin (recommendation level A).[21]

Enucleation consists of removal of the tumor with minimal dissection of the renal parenchyma.[29] This procedure has better results than PN in clear cell carcinomas T1 and T2, with a lower incidence of positive margins. However, PN appears to be more indicated in specific situations, such as for a solitary kidney, bilateral tumors, T3 tumors, and nonclear cell histology cases.[31–33] The recommendation of the panelists is to proceed with PN whenever possible (recommendation level A).[21,34]

RN: what is its role in SRMs? When a renal mass is suspected of being a RCC and is limited to the kidney, a RN results in a 5-year cancer-specific survival rate between 80% and 90%.[25,35] However, as a result of the procedure, patients could be at risk of long-term renal dysfunction, with the reported risk exceeding 30%.[36] Hospitals and surgeons performing a higher volume of nephrectomies report lower mortality rates than do institutions with lower volumes.[37]

RN encompasses the ligation of the renal artery and vein, removal of the kidney and Gerota's fascia, and occasionally of the ipsilateral adrenal gland. It is recommended for highly complex tumors and if the patient has normal kidney function in the contralateral kidney (recommendation level A).[21] If the patient presents with proteinuria or has CKD, the panelists did not reach a recommendation to perform RN (recommendation level D).[21]

RN can be performed by the open route or laparoscopically/robotically, and the choice of surgical technique should be based on patient-specific considerations (e.g. tumor size/morphometry) and the technical expertise available. Regardless of the technique used, the surgeon should focus every effort to remove the specimen intact (recommendation level A).[38]

Ablative techniques: when should they be considered? Ablative techniques (AT) (cryotherapy or radiofrequency ablation) are alternatives to PN for patients who do not desire, or do not tolerate, definitive surgery and have SRMs smaller than 3 cm (recommendation level B).[39] Although laparoscopic or percutaneous approaches are possible, the percutaneous technique is generally preferred due to its lower morbidity.[21] Published data show that the 5-year lesion recurrence-free rate is 93.5% with AT, and that the most common complication is a ureteral lesion.[39,40] However, recurrence/persistence after initial AT can often be

managed with repeated ablation. When considering these reablations, the outcomes for SRM ablation show results similar to those obtained with surgery.[39] The panel recommends AT procedures for elderly individuals or patients with comorbidities, but does not recommend such procedures in young or healthy patients; furthermore, these procedures should not be performed for central lesions or for lesions that are near the collector system or near vascular structures (recommendation level B).[39,40]

A series of different extracorporeal ablative modalities are also being studied, including stereotactic body radiation therapy (SBRT), microwave therapy, and irreversible electroporation, but data regarding these modalities are not available, and they are still considered investigational approaches.[41]

AS: for whom is it indicated? The panel of experts recommends AS as an alternative for suspicious masses, particularly those smaller than 3 cm (recommendation level A).[10,42] AS is preferred whenever the risks associated with intervention or the competing risks of death outweigh the potential oncologic benefits of active treatment.[10,42] This should be considered clinical practice for elderly individuals or patients with life expectancy lower than 5 years, especially those with frailty, multiple comorbidities, marginal renal function, tumor growth of less than 5 mm in diameter per year, or well differentiated histology (recommendation level A).[10,42]

AS protocols have yet to be validated, but recommendations for surveillance include initial high-quality axial imaging and baseline metastatic evaluation. Serial imaging [CT, magnetic resonance imaging (MRI), or ultrasound] of the renal lesion every 3–6 months for 2 years is used to establish an acceptable linear growth rate ($<$0.5 cm per year). Subsequently, annual imaging every 6–12 months (recommendation level A) is applied.[10,42]

Renal biopsy indication in AS protocols remains a debatable topic. Although not mandatory for all patients, renal biopsy might be considered in specific clinical situations, such as in cases with hematologic, metastatic, or infectious lesions. Potential risks, benefits, and nondiagnostic rates associated with renal biopsy should be considered in patients considering AS (recommendation level B).[42]

Localized and locally advanced RCC

RCC can be classified as follows:

(1) Localized disease. This includes stage I and II of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, Eighth Edition.[43]
(2) Locally advanced disease. This includes tumor invading fat, veins, lymph nodes; beyond Gerota's fascia; or extending into the ipsilateral adrenal gland (T4), as well as metastatic disease (M1). Either of these findings constitutes stage III or IV of RCC.[43]

Definitive treatment. Surgery is curative in the majority of patients with RCC who do not have metastases. Surgery is therefore the preferred treatment for patients with stages I, II, and III disease (recommendation level A).[21] Treatment may require RN, although PN to preserve the renal parenchyma is also possible, and is preferred for appropriately selected patients. The choice of surgical procedure depends upon the extent and burden of disease, as well as patient-specific factors such as age and comorbidity.[21]

When to perform an RN? RN is recommended for patients with localized tumors in which nephron-sparing procedures are not feasible due to tumor size or to a highly complex anatomy. In addition, RN should be performed in clinical T3 and T4 cases, such as tumors with suspected lymph node involvement, tumors with associated renal vein or inferior vena cava (IVC) thrombus, direct extension into the ipsilateral adrenal gland, or surgeons' choice (recommendation level A).[21,34,44–46]

When to perform a PN? PN is recommended in patients with a tumor of at least 7 cm in size when it is technically feasible to preserve renal function, especially in patients with a solitary kidney; multiple, small, and bilateral tumors; patients with, or at risk for, CKD; tumors over 7 cm in diameter but anatomically simple to remove and in uncommon and highly selected metastatic tumors, if technically simple, as part of a cytoreductive surgery, in selected cases (recommendation level A).[25,47,48]

Lymphadenectomy: when to do it? Lymph node dissection at the time of RN is recommended by the panel of experts for patients with clinically suspected retroperitoneal or perihilar lymph node involvement (recommendation level B).[49,50] For

patients with cT1, cT2, cT3, or cT4 without clinical suspicion of lymph node involvement, the experts do not recommend routine lymph node dissection (recommendation level B).[49,50] During cytoreductive nephrectomy, routine lymph node dissection is not recommended, except if nodal involvement is suspected during the procedure (recommendation level B), and the use of nomograms should not be used to guide decision making.[49,50]

The recommendation for surgical boundaries is the interaortocaval sulcus as the medial limit, the superior mesenteric artery as the cephalic limit and the inferior mesenteric artery as the lower limit for lymphadenectomy (recommendation level B).[51] This approach allows a better staging of the tumor but does not represent therapeutic benefit (recommendation level B).[52]

Adrenalectomy: when is it indicated? Panelists recommend adrenalectomy at the time of nephrectomy for patients with solitary ipsilateral adrenal metastases identified by preoperative imaging studies (CT or MRI) or in direct involvement detected during surgery (recommendation level A).[53] Nevertheless, an adrenalectomy should not be routinely performed in patients who might be at risk for direct extension into the adrenal gland, such as invasion of fat tissue surrounding kidney, T3 tumors or larger, lymph node involvement or upper-pole lesions larger than 7 cm (recommendation level A).[53] The suspicion, without verifying imaging studies or intraoperative confirmation, should not indicate adrenalectomy since there is no gain in survival terms, and it may add morbidity to the surgical procedure (recommendation level A).[53]

Special situations

Renal vein or cavoatrial thrombus involvement: what should be done? RCC is complicated by renal vein involvement in fewer than 10% of cases, by vena cava involvement in 4% of cases and by atrial invasion in 1% of cases.[54] When the surgeon is facing such a situation, the group of experts recommends proceeding with thrombectomy at the time of RN (recommendation level A).[55] This approach should be performed only by experienced surgeons and should be limited to patients without evidence of distant disease.[55]

There are four stages of cavoatrial tumor involvement: Level I (thrombi do not surpass 2 cm above the renal vein), level II (thrombi are below the intrahepatic vena cava region), level III (thrombi involve the intrahepatic vena cava below the diaphragm), and Level IV (thrombi involve the atrium).[56,57]

Panelists recommend that the extent of thrombectomy associated with nephrectomy depends on the extent of tumor involvement:[54,57,58]

(1) For patients with thrombi extending up to the major hepatic veins, a simple thrombectomy is indicated.
(2) For those thrombi that extend above the major hepatic veins, cardiopulmonary bypass with or without hypothermic circulatory arrest might be required to achieve a complete resection. The participation of a cardiovascular surgical team is strongly recommended in these situations.
(3) For thrombi above level II, hepatic mobilization or the Pringle maneuver may be necessary.
(4) Thrombi in the renal vein have surgical indications, but if small and anatomically favorable, they can be managed by minimally invasive techniques.
(5) Presurgical embolization of the renal artery should not be performed.
(6) Neoadjuvant therapy for thrombi was not indicated by the experts.

All recommendations above are level A.[54,57,58]

Adjuvant therapy: when should it be performed?

The panel of experts was questioned about the use of adjuvant therapy, sunitinib, sorafenib, pazopanib or axitinib, with full or reduced doses in patients at intermediate, high, or very high risk; in patients with clear and nonclear-cell carcinomas; and in young patients. However, the experts do not recommend adjuvant therapy outside of a clinical trial (Recommendation level A).[59–64]

In highly selected cases when adjuvant therapy with TKI is considered, the panel indicates only patients with clear cell carcinomas, only sunitinib, only starting with full doses, and a treatment duration of 1 year. If the patient presents with any grade III toxicity or dose reduction, the panel recommends treatment discontinuation.

Discussion

The present article represents the treatment recommendations with a focus on the surgical approach to RCC patients based on the experience of 26 specialists in urological surgery and clinical oncology from LACOG-GU and LARCG. These recommendations were based on the best possible clinical research evidence, preclinical data, or expert opinion, all aimed to improve patient outcomes in an ever-changing oncologic scenario. Medical research is of critical importance for advances in daily practice and improving clinical care worldwide. To achieve this goal, several medical societies and consensus groups constantly update their recommendations and make various efforts to spread new knowledge.[20]

The incidence of RCC is increasing, in part due to the development and widespread use of imaging technologies. Most renal tumors are detected incidentally as SRMs. A minority of these masses, presumably RCC, grow significantly over time, but the majority grow at a slow or undetectable rate.[65,66] Several SRM management options can be performed as surgical excision in the form of RN or PN, ablative techniques, and AS. The best management option in these cases requires careful consideration of patient and tumor characteristics.[67]

An important step is to decide when and how the renal biopsy should be performed in patients with SRMs. The recommendations here are consistent with the global literature and suggest that renal biopsy should be implemented in some cases, guided by an imaging method such as ultrasound and tomography, under the urologist or oncologist discretion and the availability of the method and the radiologist involved. In addition, it is recommended that the removal of two fragments, one central and one peripheral, is sufficient for the biopsy due to the risk of insufficient material, necrosis, or intratumoral heterogeneity, for example. Exceptions for this practice were also noted, and renal biopsy for SRMs was not recommended for patients with good performance status and no comorbidities who are candidates for surgery before the procedure, as a routine follow up for patients during AS, patients with complex renal cysts with solid areas less than 2 cm and in patients in the follow up after ablative procedures without suspicious lesions.[21–23]

PN is the gold standard in the treatment of SRMs in most centers.[68] Studies have shown that the preservation of renal parenchyma has decreased the development of postoperative CKD.[35,69–71] The recommendations of this article suggest that PN should be applied in most patients with an SRM, such as tumors with a high nephrometric score and patients with preexisting CKD, among others. However, there are cases where PN is not indicated and should be replaced by AT, either radiofrequency or cryoablation. These minimally invasive procedures should be applied in patients with medically high risk, comorbidities, and in the elderly. RN may also be indicated, and most people do fine with only one kidney.[67] The main recommendations are for highly complex cases, patients with normal contralateral kidney function (eGFR $> 45\,ml/min/1.73\,m^2$) and patients with comorbidities that prohibit renal artery clamping or pose a high risk to nephrectomy. However, this practice should not be applied in patients with a high risk of postoperative CKD or in end-stage renal disease.[25,72]

The surgical technique used in RN or PN should follow surgeons' experience and preference. Warm ischemia should be performed with the shortest possible time.[21] However, this time can, and should, be adequate for each situation. A longer ischemia time rather than an RN should always be chosen, as studies have shown that ischemia of up to 60 min does not cause damage to the patient.[67,73]

AS was also considered for SRMs by our experts, obviously with specific indications. Meta-analysis, prospective, and retrospective studies have indicated that the risk of metastatic progression during AS is less than 2%.[10,66,74–77] The main recommendations are for elderly patients, suspicion of RCC, life expectancy less than 5 years, and multiple comorbidities, that is, for very ill patients at high risk of death. These recommendations are in line with the 2009 American Urologic Association (AUA).[68] In addition, retrospective studies have indicated a 0–5.7% risk of progression to metastasis during AS, while prospective studies and meta-analyses have shown an overall metastasis rate of 1%.[10,66,74–77] AS should be accompanied with ultrasound, MRI or CT every 3–6 months in the first 2 years.[10,42] Experts recommend that intervention be performed in cases of increased mass, changes in biopsy characteristics, symptoms of disease progression, and patient's desire or anxiety.[10,42]

In the case of localized RCC, curative surgery remains the basis of treatment, although RN is no

longer the gold standard of treatment. This surgical technique is related to morbidity that can lead to renal failure and dialysis, and recovery usually requires a longer time. Alternatives such as PN may be used for tumors smaller than 7 cm, a solitary kidney, or patients at risk for CKD to avoid the negative consequences of RN. However, in more severe cases, such as those with a high risk of retroperitoneal lymph node involvement, there is an indication of lymphadenectomy associated with RN, whereas patients with solitary ipsilateral adrenal metastases (mainly, we suggested CT or MRI) should be submitted to adrenalectomy at the time of nephrectomy.[49,50,53]

As for adjuvant therapy after complete surgical resection of RCC, the available studies are controversial, but the majority of them are negative. Therapy involving vascular endothelial growth factor (VEGF) inhibitors have not demonstrated any improvement in overall survival (OS) in the adjuvant setting, with a high incidence of side effects and a negative impact on quality of life,[59–62] although therapy with sunitinib (VEGFR inhibitor) has been approved for this scenario in high-risk patients by the FDA.[61]

The ASSURE trial, which included intermediate, high, and very high-risk patients, failed to demonstrate disease-free survival (DFS) and OS benefits when using sunitinib or sorafenib in the adjuvant setting.[59] It also demonstrated an increase in grade 3/4 toxicities[64] compared with placebo. The PROTECT trial evaluated the use of pazopanib, another VEGFR inhibitor, as adjuvant therapy and did not prove beneficial in terms of DFS, showed high toxicity, and needed more time to evaluate OS.[60] The S-TRAC trial, which included only high-risk clear-cell carcinoma patients to receive sunitinib (50 mg/day for 4 weeks out of each 6-week cycle for 1 year) or placebo, proved a DFS benefit [59.3% *versus* 51.3% disease-free at 5 years, hazard ratio (HR) 0.76, 95% confidence interval (CI) 0.59–0.95] and did not prove an OS benefit. Toxicity was significantly increased with sunitinib compared with placebo, especially palmar-plantar erythrodysesthesia and hypertension. The quality of life was evaluated and decreased significantly in patients receiving sunitib.[61] On the other hand, patients with RCC who underwent nephrectomy and had no evidence of macroscopic residual or metastatic disease were submitted to a double-blind, randomized, phase III clinical study to compare axitinib *versus* placebo. During the ATLAS trial, a total of 724 patients received axitinib or placebo for less than 3 years. As a result, there was no significant difference in DFS (HR = 0.870; 95% confidence interval: 0.660–1.147; $p = 0.3211$). However, subgroup results based on risk groups were explored, wherein a reduction in the risk of an event was observed in the subpopulation at the highest risk of recurrent RCC but not in the lower-risk subpopulation. No new safety signs were observed in patients at high risk of recurrent RCC treated with adjuvant axitinib.[62] Another phase III trial using girentuximab (an antibody targeting carbonic anhydrase IX) failed to demonstrate any benefit in either DFS or OS.[63] For all these contradictions observed in the literature, the panel of experts does not recommend the use of adjuvant therapy in patients who are not participating in clinical trials.

In summary, it is important to keep in mind that the recommendations suggested by the panel of specialists aim to guide the actions to be taken, but not to replace the knowledge and experience of each physician. It is also important to highlight that the aim of the actual panel is to perform regular meetings every 2 years in order to update the recommendations. In addition, it is advised that complex cases should be submitted to a multidisciplinary discussion to better define the treatment to be applied based on the available experience, literature and technology.

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Conflict of interest statement

Adriano Gonçalves e Silva, Speaker Fee: Janssen, Pfizer, Bayer, AstraZeneca, Astellas, Pierre-Fabre, Sanofi, Roche, Merck Sharp & Dohme, Bristol-Myers Squibb. Advisory Board: Astellas, Janssen, Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Pfizer, Sanofi.

André Deeke Sasse, Honoraria: Janssen, Astellas, Roche, Merck Sharp & Dohme. Advisory Board: Janssen, Astellas, Roche, Merck Sharp & Dohme, Bristol-Myers Squibb. Events Sponsorship: Janssen, Roche.

André P. Fay, Honoraria: Pfizer, Astellas, Bristol-Myers Squibb, Novartis, Roche, AstraZeneca, Merck Sharp & Dohme. Advisory Board: Janssen, Novartis, Roche, Pfizer, Ipsen. Research Funding: CAPES, CNPq, Bristol-Myers Squibb, AstraZeneca, Roche, Merck Sharp & Dohme, Pfizer.

Andrey Soares, Speaker Fee: Janssen, Pfizer, Bayer, Novartis, AstraZeneca, Astellas, Pierre-Fabre, Merck-Serono, Sanofi, Roche. Events sponsorship: AstraZeneca, Pfizer, Astellas, Bristol-Myers Squibb, Bayer, Roche, Janssen, Merck Serono, Sanofi, Ipsen. Advisory Board: Astellas, Janssen, Roche, Bayer, Lilly, AstraZeneca, Novartis, Merck Sharp & Dohme, Bristol-Myers Squibb. Research Funding: Bristol-Myers Squibb.

Denis Leonardo Jardim, Speaker Fee: Roche, Janssen, Astellas, Merck Sharp & Dohme, Bristol-Myers Squibb and Libbs. Advisory Board: Janssen, Bristol-Myers Squibb and Libbs.

Deusdedit Cortez Vieira da Silva Neto, Speaker Fee: Janssen, Astellas, Pfizer. Advisory Board: Janssen.

Diogo Assed Bastos, Research Funding: Janssen, Astellas, Pfizer, Merck Sharp & Dohme. Honoraria/Advisory Board: Janssen, Astellas, Bristol-Myers Squibb, Merck Sharp & Dohme, Roche, Pfizer, Novartis, Bayer.

Diogo Augusto Rodrigues da Rosa, Research Funding: Roche, Bristol-Myers Squibb, Janssen, Lilly, AstraZeneca, Merck Sharp & Dohme. Speaker Fee: Janssen, Pfizer, AstraZeneca, Astellas, Roche, Amgen, Dr Reddy's, Merck Sharp & Dohme. Events Sponsorship: Janssen, AstraZeneca, Astellas, Bristol-Myers Squibb, Bayer, Roche, Janssen, Ipsen. Advisory Board: Janssen, Bayer, AstraZeneca.

Evanius Wierman, Honoraria: Janssen, Libbs. Advisory Board: Janssen.

Fabio Kater, Speaker Fee: Janssen, Roche, Amgen, Merck Sharp & Dohme, AstraZeneca, Astellas. Events Sponsorship: Roche, Janssen.

Fabio A. Schutz, Advisory Board: Bristol-Myers Squibb, Merck Sharp & Dohme, Ipsen, Pfizer. Speaker's bureau: Roche, Novartis, Pfizer, Bristol-Myers Squibb, Merck Sharp & Dohme, Janssen, Astellas.

Felipe de Almeida e Paula, None.

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Fernando Korkes, None.

Fernando Nunes Galvão de Oliveira, Speaker Fee: Astellas, Janssen, Merck Sharp & Dohme, Bayer, Roche, AstraZeneca, Libbs. Advisory Board: Merck Sharp & Dohme, Janssen, Ferring.

Fernando Sabino Marques Monteiro, Speaker and Advisory Board: Bristol-Myers Squibb.

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José Augusto Rinck Júnior, Speaker Fee/Events sponsorship: Pfizer, Astellas, Bristol-Myers Squibb, Merck Sharp & Dohme, Bayer, Roche, Janssen, Aché.

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Lucas Nogueira, Speaker Fee: Janssen, Pfizer, Bayer, Astellas, Pierre-Fabre, Roche, Merck Sharp & Dohme. Events Sponsorship: Astellas, Bayer, Janssen. Advisory Board: Astellas, Janssen, Merck Sharp & Dohme.

Manuel Caitano Maia, Speaker Fee: Pfizer. Events Sponsorship: Pfizer, Astellas, Bristol-Myers Squibb, Bayer, Roche, Janssen, Libbs.

Roni de Carvalho Fernandes, Events Sponsorship: Astellas, Janssen, Handle/Cook. Speaker Fee: Janssen, Aché. Advisory Board: Janssen.

Rodolfo Borges dos Reis, Speaker Fee: Janssen, AstraZeneca. Advisory Board: Janssen, Astellas. Research Funding: AstraZeneca. Events Sponsorship: Janssen, Pfizer, Astellas, Roche.

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Walter Henriques da Costa, None.

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Supplemental material

Supplemental material for this article is available online.

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