Small Renal Masses

Editorial

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Abstract

Introduction and Objectives. Small renal cell masses (SRMs), are defined as enhancing tumors < 4 cm in diameter, with image characteristics constistent with stage T1aN0M0 renal cell carcinoma (RCC) This review aims to highlight the benefits and limitations on current diagnosis and treatment of SRMs.

Materials and Methods. We performed a current literature search, reviewed and discussed the evidence in the field of active surveillance and surgery for SRMs.

Results. Speed of growth can be correlated with malignant pathology, higher pathological stage and grade or the risk of metastasis.

Conclusions. There is emerging data demonstrating that initial active surveillance (AS) with delayed treatment appears to be a relatively safe management option for selected cases.

Key-words: active surveillance; renal cell carcinoma; renal mass; small renal mass

Introduction and Objectives

Small renal masses (SRMs), are defined as enhancing tumors < 4 cm in diameter, with image characteristics constistent with stage T1aN0M0 renal cell carcinoma (RCC). Incidental findings of renal masses less than 4 cm have increased with the routine use of ultrasound (US), computerized tomography (CT) and magnetic resonance imaging (MRI) in the work of nonspecific abdominal symptoms.[1] About 20% to 25% of SRMs are benign (renal oncocytoma, atypical angiomyolipoma, cystic nephroma, etc.). Most studies have reported that the rates of malignant pathology, higher pathological stage and grade, speed of growth and the risk of metastasis increase with tumour size.[2] Many investigators are searching for novel therapeutic combinations while keeping the risk of overtreatment to a minimum. This review aims to highlight the benefits and limitations on current diagnosis and treatment of SRMs.

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Materials and Methods

We performed a current literature search, reviewed and discussed the evidence in the field of the diagnosis and treatment (active surveillance and surgery) for SRMs.

Results and Discussions

Due to the increase in the incidence of SRMs and the heterogeneity of these tumors, there are currently multiple treatment options, including extirpation surgery (radical and partial nephrectomy), ablative therapies (cryotherapy, radiofrequency ablation) and active surveillance. Several studies indicate that AS is safe in the elderly and/or patients with extensive comorbidities precluding surgery, the main trigger for intervention being the tumor growth rate. [4]

In recent years, several retrospective studies on active surveillance (AS) have been collected for patients with SRMs, the information from prospective studies being limited. The Delayed Intervention and Surveillance for Small Renal Masses Registry, the largest prospective AS cohort for SRMs, reported that in a well selected cohort (497 patients enrolled), AS was not inferior to PI (primary intervention). In addition to tumor growth rate (> 0.5 cm / year), a significant proportion of patients undergo delayed surgical therapy due to patient preference or anxiety in the absence of clinical progression. [3]

Kato et al. observed a significantly higher growth rate in high-grade renal carcinoma compared to low-grade tumors (0.93 cm / year vs. 0.28 cm / year, p = 0.01). [9] Patients who developed metastasis while in the active surveillance program also had a high growth rate (1.3-2.9 cm / year). It should be remembered that a large number of studies have shown an absence or reduced growth rate (less than 0.5 cm / year) of malignant tumors, in addition, it is known that benign lesions (oncocytoma) can also have a fast growth rate. [4]

Recently, contrast-enhanced ultrasound (with microbubble contrast agents and complementary pulse sequences to highlight real-time parenchymal vasculature) has also shown promising results in differentiating various subtypes of RCC and benign lesions such as angiomyolipomas (AML) and oncocytomas. On contrast-enhanced CT, enhancement is considered significant if it is more than +15 HU. If the enhancement is between 10–15 HU, the mass is indeterminate. Renal masses with borderline enhancement on CT should be further evaluated with MRI or contrast-enhanced ultrasound. Several authors consider the value of 20 UH (as compared to 15 UH) to be correct, and this criterion has some limits in the detection of hypovascularized lesions and small cystic lesions. [5,6]

The EAU guidelines present a strong degree of recommendation for the use of multi-phasic contrast-enhanced CT of abdomen and chest for the diagnosis and staging of renal tumors. For imaging follow-up in active surveillance, it is recommended to perform a cross-sectional scanning (CT or MRI) within 6 months of AS to establish a growth rate, with continued imaging (US, CT or MRI) at least annually thereafter. In the case of T1 renal tumors, Percutaneous biopsy performed before initiation of treatment to identify benign vs. malignant kidney mass is considered to be safe and cost-effective. A recent meta-analysis, including 5228 biopsies, found that less than 1% of patients had complications (hemorrhage and seeding along the needle tract). [5,7,8]

For the first time, in 2009, the percentage of partial nephrectomies (PN) exceeded that of radical nephrectomies (for many decades, the main method of treatment of renal carcinoma) performed in patients with renal masses of less than 4 cm. A meta-analysis involving more than 40000 patients (31000 with radical nephrectomy and 9300 with partial nephrectomy), objected that partial nephrectomy for small kidneys led to a 19% decrease in overall mortality risk and 29% of the cancer-specific mortality risk. [10] A study by Hong evaluate the safety and functional outcome of nephrometry score-guided off-clamp technique (RENAL=Radius, Exophytic/Endophytic, Nearness to the colecting system, Anterior/Posterior, Location) in laparoscopic partial nephrectomy. Nephrometry score has an important role in reporting partial nephrectomy results because it indicates the degree of technical complexity and allows valid comparison between different cohorts (tumor complexity: low = 4-6, moderate = 7-9, increased = 10-12). [11]

Ablative therapies that spare nephrons and potentially avoid general anesthesia are gaining popularity. The most studied ablative treatments include radiofrequency ablation (RFA) and cryoablation (CA). New therapies include microwave ablation, irreversible electroporation, and high-intensity focused ultrasound (HIFU). [1] In a recent study involving 1424 patients, 1057 underwent PN, 180 underwent RFA and 187 underwent cryoablation, no significant difference in survival between PN, RFA and CA for T1a renal tumors was observed. In other studies that followed the postoperative evolution after cryoablation and RFA, there were

no differences in overall survival (OS), cancer specific survival (CSS) and relapse-free survival (RFS). [12]

In addition, microwave ablation, a method under investigation for the treatment of renal carcinoma, has been shown to have similar (surgical, oncological and functional) results to partial nephrectomy following a 36-month follow-up. [13] Irreversible electroporation for renal masses is a second ablative therapy under investigation, using electrical impulses created by a two-electrode mechanism, during a real-time scanning in an open CT scanner, the patient being merely sedated. [1] In relation to HIFU, a 2016 study using 6 animal models (pigs) concluded that contrast-enhanced MRI provides technical support for renal ablation through MRg-HIFU. The histopatholygic exam demonstrated coagulation necrosis, vascular damage and confirmed the volume of damage seen on MRI. [14]

Another element with obvious utility in the therapeutic decision are biomarkers. Following a recent study from 2015, in which two urinary biomarkers (aquaporin 1 and perpilin 2) were investigated, 99% sensitivity and 100% specificity were found in differentiating benign renal tumors from RCC. [15]

Conclusions

Taking into account the increased incidence of SRMs, and the technological advances regarding the correct diagnosis (differential diagnosis between benign/malign tumors) and the targeted treatment of these lesions, the physician should understand the contemporary management and the long-term outcomes of available management options. Based on current data, initial active surveillance (AS) with delayed treatment supervising local progression appears to be the relatively safe initial management options for selected patients.

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