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Review

The role of biopsy for small renal masses

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HIGHLIGHTS

- Small renal masses (SRMs) are defined as enhancing kidney tumours ≤4 cm that are usually incidentally detected. Most, but not all, are RCCs..
- SRMs are usually treated as presumed RCC. As a result, benign tumours and low grade RCCs of uncertain biology are being treated in over 20% of cases.
- Pretreatment renal tumour biopsy (RTB) can reduce potentially unnecessary treatment, but is not widely practiced yet.
- RTB is safe, **with only a 1% incidence of significant complications,** has a high diagnostic yield and accuracy, and is cost effective.
- RTB, together with molecular and genetic studies will improve our knowledge of SRMs and has the potential of risk-adapted personalized treatment

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ABSTRACT

The incidence of small renal masses (SRMs) has been increasing due to the more liberal use of abdominal imaging. This increased detection has driven the attention of clinicians to the characterization of these lesions and toward a better understanding of their natural history. To this end, renal tumour biopsies (RTBs) have a crucial role as they provide vital pathological information. The improved quality and accuracy of RTBs provide urologists with a very truthful tool to support and guide treatment decisions. The future of RTB will combine pathological, molecular and genetic information that will, improve our knowledge about these lesions and open the potential for risk-adapted personalized medicine.

1. Introduction

The incidence of renal cell carcinomas (RCCs) is increasing and it is now estimated that approximately 2–3% of all newly diagnosed cancers are RCCs [1]. This trend is thought to be mainly driven by the increase in incidental detection of small renal masses (SRMs) due in large part to a more broad use of abdominal imaging [2,3].

SMRs are classified as predominantly solid enhancing tumours measuring ≤4 cm in maximal diameter [4]. The current era of easy access to imaging studies places physicians in a difficult position, since the histology of most of these SRMs are not readily diagnosed by imaging [5]. Not all SRMs are malignant and those that are, demonstrate heterogeneous features with a significant proportion considered to be of low-malignant potential [6,7]. Despite these observations, the majority of SRMs are still being treated without a pretreatment diagnostic biopsy which results in potential over-treatment. Thus, renal tumour biopsies (RTBs) have being increasingly proposed to characterize the histology of these SRMs and to assist in treatment decisions [8,9].

The first RTB was performed in 1901 in New York City as part of a renal decapsulation procedure [10]. Since then, many innovations have been made in the technique, imaging guidance, pathological evaluation and more recently, genetic and molecular tests. Furthermore, as we learn more about the natural history of SRMs, pretreatment RTB may allow personalization of treatment to not only patient characteristics including renal function but by anticipated clinical behaviour.

In this report, we will review the natural history of SRMs as well as the safety, technical considerations, outcomes and roles of RTB in the management of SRMs.

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2. Natural history of small renal masses

We know that most SRMs are RCCs, and treatment results are excellent with >90% disease-specific survival at 5 year [4]. However, not all SRMs are malignant **[20–30% will be benign (e.g.: angiomyolipoma, oncocytoma, metanephric adenoma, etc]** and if they are, not all have similar growth potential. Increasingly, there is concern about the morbidities of treatment for potentially indolent lesions.

Although the incidence of kidney cancer is increasing, mortality has not increased proportionately [11]. One explanation is that many SRMs have a low malignant potential and therefore, may not need aggressive initial treatment. Understanding the biologic behaviour and natural history of SRMs will improve the prediction of local tumour growth or stage progression and metastatic potential which are usually but not always linked.

We are particularly interested in the natural history of SRMs that are histologically characterized. **Our original institutional surveillance cohort suggested that about one third of patients (11/32) presenting with a SRM, presumed to be a RCC, progressed (median follow-up of 28mo).** [12] **However, in an update of our series (n = 151), progression was lower with only 2 patients (1%) reported to have progressed to metastatic disease.** [4] **The observed overall growth rate was relatively slow (0.13 cm/yr), with two thirds of SRMs (100/151, median follow-up of 29mo) showing slow or no growth at all.** [4,12].

Nevertheless, other studies have demonstrated that lesions between 3 cm and 4 cm in diameter can have aggressive pathologic features [13]. These results highlight the heterogeneous behaviour of SRMs. A number of clinical characteristics have been used to predict malignancy including initial tumour size [7,14–16], age [17] and growth rate [18]. Despite initial encouraging results in studies of these variables, their clinical utility has not been validated for clinical utility in the prediction of biologic behaviour of renal lesions. Currently, the best method to characterize SRMs in the absence of validated imaging or other biomarkers, is RTB. Not only are benign vs malignant tumours diagnosed, but RTB provides information about the heterogeneous patterns of behaviour before a treatment decision is made.

3. Current indications of renal tumour biopsies

The management of SRMs has evolved in recent years due to the increasing use of nephron-sparing surgery, ablation as well as the increasing acceptance and use of RTBs [19]. However, despite a growing body of evidence, the merits and safety of pretreatment RTB continues to be debated [8].

Due to concerns about perceived low diagnostic rates and poor correlation with surgical pathology (including mixed histology and grade), safety and controversy about clinical utility, the use of RTBs was traditionally reserved to diagnose secondary malignancy, metastatic renal tumours as well as benign non-tumour pathology such as renal abscess [20–22]. More recently, RTBs are being increasingly considered by the urologists in a variety of other situations including diagnosis of suspected recurrence post-ablative therapy and to characterize the RCC subtype in the setting of metastatic disease to select the optimal biological systemic therapy (particularly when a cytoreductive nephrectomy is not indicated) [21]. Although not universally accepted, there is increasing acceptance in many centres that RTBs should be offered to most, if not all patients presenting with a SRM in whom treatment is being considered to help guide clinical management.

There are relatively few contraindications for RTB. The absolute one is uncorrectable coagulopathy. Relative contraindications include patients with short life expectancy who are not candidates for any treatment, as the results would not alter the management strategy [21].

4. Renal mass biopsy: techniques, safety and accuracy

RTBs have evolved to a procedure with a high diagnostic rate and very low risk for significant complications [22]. Despite this success in centres with experience, RTBs appear to be rarely performed outside academic centres. To the contrary, in centres with experience, indications as well as diagnostic success are increasing [23].

4.1. Technique

4.1.1. Image-guidance

RTBs are generally performed as an outpatient or as a short-stay procedures under local anesthetic using either ultrasound or CT-guidance. There are currently no data supporting one procedure over another [8]. However, we usually favor ultrasound-guidance as our initial approach as it has the advantages of real-time visualisation of the tumour, lower cost and avoidance of ionizing radiation when compared to CT-guidance. Body habitus and tumour location are also considerations.

4.1.2. Fine needle aspiration (FNA) versus needle core biopsies

RTBs are classically performed using two methods, fine-needle aspiration (FNA) or needle core biopsy. With FNA, tumour cells are aspirated during multiple needle passes whereas a needle core biopsy is taken with a double action needle, usually through a coaxial sheath. Both sample one area of the tumour mass per pass and redirection of the needle is required for sampling other areas. FNAs have lower diagnostic rates and do not allow for the same histologic architectural examination as with core biopsies [24]. Needle cores are therefore the preferred form of biopsy.

4.1.3. Needle size and number of cores in core biopsies

Several studies have examined the effect of needle size on biopsy outcome. Breda et al. compared, in a prospective study, the accuracy of 14-, 18- and 20-gauge needle biopsies and concluded that larger bore needles (14- and 18-gauge) were the most accurate for histological diagnosis [25]. However, similar results were obtained with 14- and 18-gauge needles. Therefore, we perform our RTBs using 18-gauge needles.

The optimal number of cores to be taken at the time of biopsy has yet to be defined. However, it appears that increasing the number of cores may improve the diagnostic rate. Thus, expert opinion is that at least two cores should be taken during RTB with the aim to obtain optimal quality of tissue to maximize diagnostic yield [26].

Given the known heterogeneity of RCCs, it is not surprising that multi-quadrant biopsy of large lesions increases the diagnostic rate and the identification of aggressive pathologic features [27]. Whether these findings hold true among SRMs is yet to be proven but may become of greater importance in the near future. Furthermore, a single tumour biopsy, might not be considered representative of the landscape of genomic abnormalities in a tumour or may completely miss the heterogeneous area in the case of a hybrid/mixed tumour [21]. Perhaps, the adoption of a multi-quadrant biopsy scheme will help decrease this risk and may become of greater importance in the near future with the development of molecular and genetic studies. However, this remains to be validated.

4.1.4. Tumour characteristics associated with a diagnostic biopsy

Several tumour characteristics have been associated with a