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REVIEW ARTICLE

The role of biopsy in incidental renal tumours

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KEYWORDS

Renal cell cancer;
Small renal tumours;
Renal tumour biopsy

ABBREVIATION

FNA, Fine-needle aspiration

Abstract *Purpose:* Historically, the biopsy of renal masses was not advocated, and to date there remains some controversy on the role of biopsy for renal masses in making treatment decisions. With the widespread use of imaging methods, the incidental diagnosis of renal masses has increased, necessitating renal biopsies to better plan the management of these tumours. Here I review previous reports to define the role of biopsy in incidental renal tumours.

Methods: Data were obtained from English-language studies listed in PubMed on the use of renal biopsy for evaluating incidental solid small renal tumours.

Results: The biopsy of small renal tumours is increasingly accepted due to: the increase in the incidence of small renal tumours; the finding that a significant number of these tumours are benign; the availability of new management options, such as ablative therapy and surveillance strategies; that imaging alone is unable to predict the biological behaviour of these tumours; and advances in the pathological evaluation of the biopsies. The biopsy procedure has an acceptable complication rate but is not free of limitations. The current recommendations for the use of renal biopsy in small renal tumours are: to help in differentiating benign from malignant renal tumours; before or during ablative therapies and during the follow-up after ablative therapies, for defining treatment success or failure; and to exclude nonrenal cell primary tumours (metastasis and lymphoma) or benign conditions (abscess), which may not require surgery.

Conclusions: The biopsy of small renal tumours is a safe and accurate procedure, and can help in the planning of definitive patient management.

Introduction

Historically, the biopsy of renal masses was not advocated, and to date there remains controversy on the role of biopsy of renal masses for treatment decision-making. With the current widespread use of imaging methods the incidental diagnosis of renal masses has increased [1]. Most of these asymptomatic renal tumours are benign [2]. The highest incidence of incidentally detected small renal tumours was reported in elderly patients, who often present with several comorbidities [3]. Nephron-sparing surgery remains the standard of care for

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small RCC, but energy-ablative techniques and surveillance protocols have evolved as alternative management options [4]. This has lead to the reconsideration of renal biopsy in the management of incidentally discovered renal tumours. It was reported that biopsy could avoid unnecessary surgery in a third of incidental renal masses [5]. Some report that the role of percutaneous biopsy for renal masses is increasing, and in the future will provide important information about which masses are safe while under surveillance [6]. In this review I assess previous reports to define the role of biopsy in incidental renal tumours.

Methods

Medline and PubMed were searched from 1950 to January 2011 for English-language studies on the use of renal biopsy for evaluating incidental solid small renal tumours. In all, 46 articles were obtained that had a level of evidence of 2a, 2b and 3.

Role of biopsy in the evaluation of renal masses

Previously, the classic teaching has been against renal biopsy for the renal masses. This fear of renal tumour biopsy has increased for several reasons: (i) seeding of the puncture site with tumour [7]; (ii) the rate of obtaining adequate cytological material from fine-needle biopsies for analysis was 70–98%, leaving many biopsies as indeterminate [8]; and (iii) a negative biopsy would not exclude RCC and a positive biopsy might understage or undergrade the lesion [9]. False-negative biopsies are usually due to an insufficient amount of tissue, sampling of necrotic areas, or the presence of blood or normal kidney. In the preoperative renal biopsy the accuracy of grading is generally poorer than that of the histopathological diagnosis on the postoperative specimen, due to inter- and intra-observer variability and tumour heterogeneity. Grade heterogeneity in a single tumour has been reported, and in a preoperative renal biopsy, the biopsy underestimated the nuclear grade in 55% of the cases [10].

Preparation for renal mass biopsy

Procedures before the biopsy include a relevant history, platelet count, international normalized ratio and partial thromboplastin time (within 1 month of biopsy) [11]. Patients are advised to discontinue aspirin and NSAIDs 7–10 days, stop warfarin 5 days and stop heparin 4 h before the procedure. A careful review of the available imaging is necessary to choose the best suitable approach to the lesion. Biopsies are generally taken under CT or ultrasonographic guidance, and MRI is not often used. However, no study has compared the diagnostic success rate of renal tumour biopsy with different imaging techniques [11]. The advantages of CT guidance are: (i) gas and other structures do not obscure visibility; (ii) there is excellent spatial resolution; (iii) there is better needle visualization; (iv) it is easier to avoid necrotic areas; and (v) there is more rapid acquisition of skills. The disadvantages of CT guidance are higher cost and exposure to ionizing radiation [11].

Techniques of renal mass biopsy and complications

Core biopsies and fine-needle aspiration (FNA) can be done in the same sitting. FNA specimens can provide cytological details that are sometimes better than those seen in core biopsies. The needles used are 18 G for core biopsy (15–22 mm long) and 21 G for FNA. A core biopsy specimen of <10 mm long should be considered unsatisfactory, and areas of necrosis should be avoided [12]. It has been recommended to obtain one central and one peripheral biopsy in tumours of <4 cm, and two peripheral biopsies in larger tumours, due to the presence of central necrosis in larger tumours [13].

Potential complications of biopsy are tumour seeding along the needle tract, bleeding, arteriovenous fistula, infection and pneumothorax [5,12]. The overall estimated risk of tumour seeding along the needle tract is $<0.01\%$ [14] and the risk increases with the number of needle passes and with non-cutting needles. Urothelial carcinoma carries a higher risk of seeding than RCC and a percutaneous biopsy in the presence of radiological suspicion of renal pelvic tumour or positive urinary cytology should only be taken after careful consideration of the risks and benefits [11]. Contemporary series of renal mass biopsy show a minor complication rate of $<5\%$, with serious complications being exceedingly rare [15]. In a study of 1083 of renal mass biopsies, there were 1.4% minor and 0.46% major complications [16]. Most complications were related to bleeding and did not require a transfusion. Death after renal biopsy is an extremely unlikely event; in a large review of abdominal fine-needle biopsies the overall mortality rate was reported to be 0.031%, and attributed to hepatic haemorrhage and pancreatitis, which can be avoided in almost all cases of kidney biopsy. Hence the mortality rate from renal tumour sampling is considered to be even lower [17]. No cases of death after renal mass biopsy have been reported recently [18]. Finally, there is no evidence that needle biopsy complicates subsequent radical or partial nephrectomy [12]. The sensitivity and specificity of needle core biopsy is reported to be 70–100% and 100%, respectively, with an accuracy of $>90\%$ in all recent series [11].

Arguments against renal biopsy in incidental renal masses

Traditionally, a preoperative biopsy was rarely taken for solid renal masses; this contrasts with many other urological neoplasms, including prostate and bladder cancer, and is clearly related to the misperception that almost all solid renal masses in adults are malignant, whatever their size. Furthermore, it was thought that preoperative biopsy of renal masses lacks significant specificity and sensitivity. However, this conclusion has been largely based upon FNA with cytological assessment; without the tissue architecture as seen on core biopsy, FNA lacks sensitivity (70–90%), and 60% yield insufficient cellular material for diagnosis [19]. The study by Vasudevan et al. [5] shows that preoperative renal core biopsies taken with either ultrasonographic or CT guidance, using local anaesthetic and a 16 G core biopsy gun, and assessed by a specialist urological pathologist using Solufix [20] (a fixative designed to improve cytological detail, particularly in renal tumours) is, by contrast to FNA, highly accurate in diagnosing and characterizing renal masses. Another study [21] supported the superiority of core renal biopsy compared to FNA, with biopsy giving a specificity and sensitivity of 100% for a diagnosis of malignancy. False-negative results remain a concern, as there are reports of false-negative rates of up to 21% in core biopsies and 24% in FNA [19]. False-negative biopsies are usually due to an

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insufficient amount of tissue, sampling of necrotic areas, or the presence of blood or normal kidney. In the presence of negative or non-diagnostic biopsy and suspicious imaging, further biopsy or surgical exploration should be considered [22].

Wolf [23] reviewed all pertinent peer-reviewed articles published after 1985 on evaluating and managing all solid and cystic renal masses; he recommended renal biopsies in specific cases only, and not routinely for incidental cases. The current role of needle core biopsy and FNA of renal masses is primarily to exclude non-renal cell primary tumours (metastasis and lymphoma) or benign conditions (abscess), which might not require surgery. Biopsy has also been used to confirm the diagnosis and the histological subtype of renal primary lesion in patients with disseminated metastases or unresectable retroperitoneal masses [11].

Arguments in favour of biopsy for incidental renal tumours

Indications for renal mass biopsy

The current indications for renal mass biopsy are: to help in differentiating benign from malignant small renal tumours [24]; to separate indolent from aggressive tumours using molecular markers [25]; concomitant with ablative therapies [26]; and to exclude non-renal cell primary tumours (metastasis and lymphoma) or benign conditions (abscess) that might not require surgery. FNA and core renal mass biopsy in combination are found to be complementary [16], and a new terminology to facilitate the comparison of results from various studies and stimulate progress has been proposed, in which all biopsies are categorized as uninformative vs informative, with the latter being subclassified as confirmed accurate, presumed accurate or confirmed inaccurate [27].

Factors in support for the use of renal mass biopsy

There are many factors in favour of using biopsies in small renal tumours including: the high incidence of benign tumours; the emergence of new minimally invasive and surveillance treatment options; increasing accuracy of pathological evaluation of biopsies; and inability of imaging alone to predict the biological behaviour of renal tumours. The high proportion of benign lesions in small (<4 cm) renal masses has been reported to be as high as 30% [28], with 87% of RCCs being of low grade, and this encouraged Neuzillet et al. [12] to advocate the routine use of needle biopsies before surgery to characterize the histology of renal masses of <4 cm. This policy allowed them to avoid surgery in 16% of patients who were found to have benign disease at biopsy. In addition, Wood et al. [16] avoided surgery in 44% of patients after a proper diagnosis of renal lesions by needle biopsy. With modern techniques, core biopsy and FNA of renal masses now provide adequate tissue for diagnosis in >90% of cases [12,19]. In clinical practice genetic profiling might be able to better differentiate renal tumours with varying grades of aggressiveness and metastatic potential, therefore allowing clinicians to distinguish tumours that are likely to progress and require immediate treatment from those with an indolent course that might benefit from conservative management, thereby avoiding unnecessary surgery [11]. Biopsy can be used to obtain a definitive tissue diagnosis to direct future therapy in patients with inoperable disease, because of locally advanced RCC and the presence of metastatic disease and comorbidities [29].

Minimally invasive ablative methods such as radiofrequency ablation and cryotherapy have shown great promise in the treatment of small renal masses, and it is well understood that biopsy might provide the only chance for a tissue diagnosis in such cases [8]. Helical CT guidance can help to direct the biopsy needle accurately, avoiding necrotic areas [12]. Vasudevan et al. [5] showed that 33% of the 70 renal biopsies taken for incidental asymptomatic renal masses of <5 cm, considered malignant on radiological features, ultimately proved to be benign. Richter et al. [30] assigned a definitive diagnosis to 76% of renal mass lesions diagnosed as indeterminate by imaging methods. Vasudevan et al. [5] proposed that core biopsies should be considered in the preoperative evaluation of incidentally detected small renal masses of <4–5 cm. Furthermore, the discovery of an incidental renal mass of >5 cm, if not clearly characterized as malignant by radiological features, might also require biopsy. However, it could be argued that for lesions of <1 cm in diameter the overwhelming majority are simple cysts, unless the patient is predisposed to developing RCC [31]. However, for observation of renal tumours, a safe threshold size of <3 cm has been suggested, below which the metastatic potential of observed lesions is low [32].

Nature and behaviour of small incidental renal masses

It is important to differentiate between indolent and potentially aggressive small renal tumours. Results can be improved by using core biopsy in preference to FNA cytology, or a combination of both techniques [21]. Renal core biopsy and FNA can provide essential information on molecular or genomic characterization for making decisions about treatment, and should therefore be considered in the diagnostic evaluation of all small renal masses [33]. This can provide not only better architectural information, but also tissue for additional histopathological and biochemical procedures. Lactate dehydrogenase and protein assessment of the biopsy specimens can be used to differentiate neoplastic from inflammatory lesions [30]. In some cases, the distinction between chromophobe RCC, oncocytoma and even clear-cell RCC (eosinophilic variant) can be problematic. Shah et al. [29] advised using Hale's colloidal iron and a contemporary immunohistochemical panel in all such cases, to define the morphology. Biopsy can thus reliably identify patients with high-risk histological subtypes of RCC, such as papillary RCC, and help in deciding the treatment options. The risk of tumour seeding is greater in patients with TCC, and most recent studies of RCC reported no such complication even after a long follow-up [5].

Conclusions

Renal mass biopsy has an increasing role as long as clear indications are present, and the limitations and complications of the biopsy are appreciated. Patient education, the availability of helical CT for biopsy guidance and the presence of a good cytopathologist are important prerequisites for success. With advances in imaging techniques and molecular biology it is convincing that renal mass biopsy should be considered for selected patients with small renal masses in whom it might

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influence the clinical management. However, young healthy patients who will not accept the ongoing uncertainty and low-level risk of renal mass biopsy, should be managed proactively, preferably by partial nephrectomy, which essentially represents an excisional biopsy that is both diagnostic and therapeutic.

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Editorial comment

Incidental small renal masses are frequently detected in elderly patients and have very heterogeneous biological behaviour. Many of these masses are benign or low-grade malignant tumours. Generally, tissue diagnosis is required before extirpation of any malignancy. Renal biopsy can significantly decrease the number of unnecessary surgical procedures and assist in decision-making, especially for elderly and unfit patients who are candidates for active surveillance or ablative therapies. Renal biopsy enhanced by molecular profiling [1] might be our future tool for decision making to conserve,

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ablate, excise or observe [2,3] these incidentally discovered small renal masses.

Concerns about renal biopsy are probably unfounded. Studies supporting these concerns are mostly old; as reported by Al-Marhoon, with the advances in imaging and methods of pathological evaluation, morbidity is minimal, seeding does not occur and the pathological evaluation is acceptably accurate [4].

This 'mini-meta-analysis' reported by Al-Marhoon questions the current practice and under-use of renal biopsy in the management of renal masses. I agree with the author that renal biopsy is an area that should be revisited, re-evaluated and kept as a top priority in future research.

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