

ACCURACY OF DIAGNOSIS BY GUIDED BIOPSY OF RENAL MASS LESIONS CLASSIFIED INDETERMINATE BY IMAGING STUDIES

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ABSTRACT

Objectives. To define the accuracy, safety, and impact of percutaneous biopsies of indeterminate mass lesions as an additional diagnostic tool. The vast majority of renal mass lesions are routinely diagnosed by radiographic features alone. However, with the increased use of computed tomography scanning and ultrasound, many smaller renal masses, which are "indeterminate" (refractory to categorization on the basis of imaging alone), are now being discovered.

Methods. We retrospectively reviewed 583 patients (364 male and 219 female) with indeterminate renal mass lesions diagnosed by imaging studies that were further investigated by percutaneous biopsy. Patients were followed up for at least 5 years if the biopsy result demonstrated a benign lesion, or they underwent surgical exploration if the biopsy result demonstrated a malignancy. Biopsy or aspiration material was assessed by histopathologic and cytologic evaluation and, when appropriate, with biochemistry, Gram stain, culture, and sensitivity. The biopsy site was localized by computed tomography, ultrasound, or fluoroscopy.

Results. Five hundred eighty-three patients with indeterminate renal mass lesions (representing 7.2% of all renal masses diagnosed from 1967 through 1996) were diagnosed by imaging studies complemented by guided biopsy. Sixty-six patients were lost to follow-up, leaving 517 patients who were analyzed. In 393 cases (76%), the imaging-guided biopsy provided a definitive diagnosis. The incidence of false diagnoses was 1.2% (7 biopsies). In 124 of the cases (21%), imaging-guided biopsy was unable to determine the etiology of the lesion with acceptable confidence; of these, 21 biopsies did not provide enough material to establish the diagnosis (16.9%).

Conclusions. Overall, percutaneous biopsy of the kidney has proved to be a safe and accurate diagnostic procedure, with impact on the management of cystic or solid renal lesions. UROLOGY 55: 348-352, 2000. © 2000, Elsevier Science Inc.

Most renal mass lesions are diagnosed by imaging techniques alone with acceptable confidence.¹ However, a group of indeterminate renal mass lesions remains and poses a vexing problem in terms of determining the underlying abnormality.²⁻⁸ For those, a clinical decision must be made concerning establishing the diagnosis, either by means of frequent follow-up examinations or by

intervention to provide a histopathologic diagnosis. Among these interventions, a choice between surgical exploration versus biopsy guided by imaging studies must be made.

We believe that renal biopsy guided by imaging has an impact on the management of renal mass lesions and is safe and minimally invasive. Surgical exploration can be reserved for those lesions that have defied characterization by biopsy or imaging.

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MATERIAL AND METHODS

From 1967 through 1996, 583 indeterminate renal mass lesions were subjected to biopsies, guided by imaging studies (Table I). They represent a small part (7.2%) of the 8140 renal mass lesions catalogued during that time. These procedures were performed at the following hospitals: Methodist Hospital, Indianapolis, Ind; University Hospital, Shreveport, La; Doctors' Hospital, Shreveport, La; Saint Jude Hospital, New Orleans, La; River Parish Hospital, La Place, La; Veterans Af-

TABLE I. Indeterminate renal masses—all modalities

Total (n)	Lost to Follow-up (n)	Total Analyzed (n)	Diagnosed Surgically (n)	Surgery with False Diagnosis (n)	Biopsy with False Diagnosis (n)	Diagnostic Accuracy (Surgery)	Diagnostic Accuracy (Biopsy)
583	66	517	124	2	7	98.3%	98.2%

fairs Medical Center, New Orleans, La; Hotel Dieu, New Orleans, La; Veterans Affairs Medical Center, East Orange, NJ; and University of Medicine and Dentistry, New Jersey, University Hospital, Newark, NJ.

From 1967 to 1976, intravenous urography, retrograde urography, gray-scale ultrasound, arteriography, and nuclear imaging studies were the primary methods used to assess kidneys and renal masses. Guided biopsies were reserved for indeterminate solid mass lesions and complex cysts.

From 1977 through 1996, the addition of computed tomography and more sophisticated forms of ultrasound resulted in improved diagnosis and categorization of renal mass lesions. The use of cyst puncture and aspiration for the diagnosis of renal cysts (even complex renal cysts) decreased, and guided biopsy was most often used to assess indeterminate solid mass lesions. Guided-biopsy procedures are now largely reserved for complex high-density cystic and solid renal mass lesions. Unlike the period before 1977, when most biopsies were carried out under fluoroscopic control, almost all biopsies after 1977 have been carried out with computed tomography (CT) guidance. A small number have been performed with ultrasound guidance.

PATIENTS

Five hundred eighty-three renal mass lesions were biopsied with imaging guidance. The patient age ranged from 14 to 91 years (mean 57). Three hundred sixty-four patients were male, and 219 were female. Sixty-six of the patients were lost to follow-up, leaving a total of 517 available for analysis. One hundred ninety lesions were biopsied under fluoroscopic control, 82 lesions under ultrasound guidance, and 245 lesions under CT guidance (Table I). For the present report, only biopsies performed with ultrasound or CT imaging were considered.

METHODS

The vast majority of biopsies were carried out using a coaxial system. This system was used to protect tissues outside Gerota's fascia against possible implantation of tumor cells and to facilitate a radical nephrectomy, if the diagnosis of a renal malignancy was established. A 19-gauge sheath was advanced through Gerota's fascia.

The lesion, solid or cystic, was then punctured with a 21 or 22-gauge Chiba or Franzen needle. A core biopsy was obtained with the 20 or 21-gauge Franzen needle, liquid aspirate with a 21 or 22-gauge Chiba needle, and a cytopathologic sample with a 22-gauge Chiba needle. The core biopsy specimens were sectioned, stained, and examined microscopically.

Aspiration samples were examined by cytopathologic techniques and sometimes by flow cytometry. Liquid aspirates were processed through a micropore filter, and the latter aggregate examined cytopathologically.

In about 10% of solid lesions, the core biopsy specimen was obtained with an 18-gauge biopsy gun. Specimens for culture and sensitivities were obtained in all lesions suspected of being infectious.

RESULTS

CT-guided biopsies were performed on 245 indeterminate lesions. In 214 patients, a diagnosis

was made (87%). These diagnoses were confirmed by long-term follow-up of 5 years in 213 patients. In 1 patient, who underwent surgical exploration, the biopsy diagnosis proved to be inaccurate (0.4% false-positive results). Thirty-one lesions (13%) could not be diagnosed on the basis of biopsy results alone and, thus, required surgical exploration.

Ultrasound-guided biopsies were performed in 82 patients, establishing a diagnosis in 54 patients (65.8%) of benign lesions. Of the 54, 52 diagnoses were confirmed benign during long-term follow up (greater than 5 years); 2 proved to be inaccurate (2.4% false-negative results). In 28 of those patients, a diagnosis was not achieved by biopsy alone (34.2%), and surgical exploration was necessary.

Overall, guided biopsies established a diagnosis in 76.4% of the lesions. Only in 1.4% of these cases did the diagnosis ultimately prove to be inaccurate. In 23.5%, the biopsied lesions could not be diagnosed, and surgical exploration was necessary.

IMAGING-GUIDED BIOPSIES COMBINED

Overall, in cystic lesions, the image-guided biopsy established a diagnosis in 84.6% (predicted and confirmed as benign cystic lesions). Fifteen percent of cystic lesions (47 patients) could not be diagnosed because of insufficient biopsy material in 10 and an inconclusive reading in 37. These patients underwent surgical exploration (Table II).

One patient, diagnosed with a hemorrhagic cyst, was found to have renal cell carcinoma, which was diagnosed on follow-up CT scanning. One cystic lesion in an adult diagnosed as benign on biopsy was found to be a Wilms' tumor during follow-up, resulting in a 0.6% false-negative rate of diagnosis.

In inflammatory lesions, image-guided biopsies established a diagnosis in 69.6% of the patients. One patient, who was diagnosed with xanthogranulomatous pyelonephritis, actually had renal cell carcinoma, which was diagnosed 6 months later because of an increase in the size of the lesion on CT scan after 6 months of follow-up. Surgical exploration established the diagnosis of renal cell carcinoma, a 1.8% rate of inaccurate diagnosis among the group of lesions diagnosed as inflammatory (Table II). Sixteen patients (22.2%) required surgical exploration to establish the diagnosis of an

TABLE II. Indeterminate renal mass lesions—etiology and diagnostic modality

Lesion Type	Diagnostic Modality	Analyzed (n)	Indeterminate on Biopsy (n)	Diagnosed (True Positive) (n)	Misdiagnosed (n)	Diagnostic Accuracy (%)
Cystic lesions	Surgery	47	0	47	0	100
	Biopsy	312	47	264	1	84.6
Inflammatory	Surgery	16	0	16	0	100
	Biopsy	56	16	39	1	69.6
Hemorrhage	Surgery	10	0	10	0	100
	Biopsy	34	10	20	4	58.8
Benign neoplasm	Surgery	14	0	13	1	92.9
	Biopsy	29	14	15	0	51.7
Malignant neoplasm	Surgery	37	0	36	1	97.3
	Biopsy	86	37	48	1	55.8

inflammatory lesion. The biopsy result was inconclusive in 12 cases, and in 4 cases, the biopsy material was insufficient to establish a diagnosis.

In hematomas or hemorrhagic lesions, imaging-guided biopsies established a diagnosis in 58.8%. During long-term follow-up, two lesions were found to be renal cell carcinoma, and one lesion was subsequently diagnosed as angiomyolipoma, resulting in 8.8% inaccurate diagnoses rendered by biopsy (Table II) because of sampling errors. Ten lesions (22.7%) could not be diagnosed by biopsy alone, because of inadequate material in 3 cases and an inconclusive reading in 7 cases, and were explored surgically.

In benign neoplasms, imaging-guided biopsies established the diagnosis in 15 (51.7%) of 29 patients, without any false-negative results during follow-up (Table II). Fourteen patients required surgical exploration to establish a diagnosis, because the biopsy result was inconclusive in 10 patients, and the material was insufficient in 4 patients.

In malignant neoplasms, imaging-guided biopsies established a diagnosis in 49 (55.8%) of 86 patients (Table II). One case revealed a renal abscess that had been initially diagnosed as renal carcinoma (1.1% false-positive result).

MISDIAGNOSIS BY IMAGING-GUIDED BIOPSIES

The presumptive diagnosis of hematoma, established in 3 patients by imaging-guided biopsy, had to be corrected to renal cell carcinoma in 2 patients and to angiomyolipoma in 1 patient. In each instance, the malignant or benign neoplastic lesion was associated with hemorrhage, which led to the misdiagnosis. However, during the follow-up period, progressive growth of the lesion triggered a

re-examination and ultimately surgical exploration. One lesion, diagnosed as an infarction by guided biopsy, continued to show growth on follow-up examinations and, likewise, proved to be renal cell carcinoma on surgical exploration.

One other lesion, diagnosed as a hemorrhagic cyst on guided biopsy, showed not only progressive growth of the primary tumor, but also metastases to the lung during the follow-up, and on surgical exploration was found to be renal cell carcinoma.

One patient, diagnosed with necrotic renal cell carcinoma on the basis of a grade IV cytologic finding obtained from imaging-guided aspiration, proved to have a renal abscess on exploration. However, another lesion diagnosed as xanthogranulomatous pyelonephritis showed progressive growth during follow-up and proved to be renal cell carcinoma.

It is interesting to note that the frozen-section diagnosis established in the 124 surgical specimens had to be corrected in 2 patients on the basis of the final histopathologic evaluation. In the first patient, the diagnosis was corrected from renal cell carcinoma to xanthogranulomatous pyelonephritis. In the second, the diagnosis of cystic nephroma was changed to Wilms' tumor. Ten of the patients who underwent surgery were lost to follow-up within a short period and confirmation of the primary diagnosis was therefore not achieved. Table III demonstrates the accuracy of diagnosis by fine needle aspiration for cystic and solid lesions individually.

COMMENT

The prevalence of renal cell carcinoma, 30,600 newly discovered cases in 1996,⁹ as well as the fact

TABLE III. False-positive and false-negative results of renal biopsy for cystic and solid renal lesions

	Cystic Lesions (n = 312)	Solid Lesions (n = 205)
Surgery performed for diagnosis (n)	47	77
Surgery for diagnosis and therapy (eg, neoplasm) (n)	49	126
Malignant (n)	26	86
Renal cell carcinoma	18	69
Lymphoma	3	3
Metastases	3	13
Transitional cell carcinoma	1	
Other	1	1
Benign (n)	286	119
False positive for malignancy at biopsy (n)	0 (0)	2 (1)
False negative for malignancy at biopsy (n)	2 (0.6)	4 (1.9)

Numbers in parentheses are percentages.

that 25% of these lesions are 3 cm or smaller and only 17% present with metastases,¹⁰ emphasizes the need for early identification of cancer to allow treatment and to prevent its progression. Although surgical exploration of all renal mass lesions was considered obligatory in the past, this concept has now been abandoned. Relatively high complication rates reported even for surgical exploration of renal cysts and the availability of other therapeutic alternatives for the management of both cystic and solid renal lesions has diminished the role for open surgery for diagnostic purposes.

The advent of spiral CT and the meticulous assessment of renal mass lesions before enhancement and during the arterial and parenchymal phases of enhancement, with thin slices complemented by ultrasound and Doppler ultrasound, has greatly improved the diagnostic accuracy of imaging studies. The "Bosniak" classification, based on imaging analysis alone,¹¹ serves a useful purpose for the categorization of cystic renal mass lesions, although it has some major shortcomings.^{12,13} There is general agreement that Bosniak class I lesions (simple cysts) can be safely monitored and hence assigned to conservative management. Likewise, Bosniak IV lesions are virtually diagnostic of renal cell carcinoma and should be managed accordingly.¹¹⁻¹³ The problem lies in the Bosniak II or III lesions. High-density cysts, hemorrhagic cysts, in-

flammatory cysts, multilocular cysts, and cystic nephromas are considered Bosniak II lesions and theoretically could be followed up at intervals by CT and ultrasound. However, interobserver variation is marked on the assignment of these lesions to the subgroup of class II that can be safely monitored versus the subgroup of class II that perhaps warrants exploration.^{12,13} Wilson *et al.*¹² reported four malignancies in five lesions classified as Bosniak class II lesions; Cloix *et al.*¹⁴ found one malignancy in seven of those lesions. Aronson *et al.*¹³ found four neoplasms in seven lesions characterized as Bosniak class III. Wilson *et al.*¹² found four in four lesions classified as Bosniak class III, and Cloix *et al.*¹⁴ found four in 13 lesions classified as Bosniak III. These reports clearly indicate the need for a better and more diagnostic assessment. Our experience, identifying 227 such indeterminate class II and III cysts of a total of 312 reveals the magnitude of the problem. Of our patients with Bosniak II or III cystic lesions, 89.4% were definitively classified by CT-guided biopsy and assigned to appropriate management. Misclassification occurred in only 4 patients (2.25%) on the basis of imaging-guided biopsies. If the classification is based on imaging alone, misclassification to Bosniak II/III classified cysts occurs in up to 41% of cases.^{12,14}

We have routinely practiced aspiration and core biopsy of these lesions. Although published studies report varying rates of sensitivity and specificity in the detection of malignancy, the overall accuracy to detect malignancy appears to be greater than 95%. In the series by Torp-Pedersen *et al.*,³ comparing the usefulness of cytologic versus histopathologic evaluation, the false-positive rate of an aspiration was 15%, and biopsy with a 0.8-mm needle had no false-positive results. Some large series have shown no false-negative results and less than 1% false-positive results.⁵ Admittedly, other series do not concur and reported a high incidence of false-negative results, such as Juul *et al.*² with 25 false-negative diagnoses in 285 cases and Haubek *et al.*¹⁰ with 17 false-negative diagnoses in 161 cases. More recent data suggest that false-negative biopsies may be caused by insufficient material.¹⁵ The addition of CT-guided core biopsy to obtain material from questionable areas, such as thickened wall segments, thickened components of septa, enhancing wall segments, or nodules or areas of heterogeneous density and enhancement characteristics, should substantially increase the diagnostic accuracy and avoid false-negative biopsy results. The addition of biochemical assessment of the biopsy specimens, such as lactate dehydrogenase (LDH) and protein, furnishes additional criteria that can be used to help to differentiate neoplastic from inflammatory lesions.

Flow cytometry DNA analysis is another modality that may refine the diagnosis of aneuploid clones of renal cell carcinoma.¹⁶

Clinical management was correctly instituted in 87.1% of our patients on the basis of biopsy alone. Only 21% of patients had to be referred to surgery to establish the definitive diagnosis. The impact on clinical management is increasingly recognized. Wood *et al.*¹⁵ reported altered management in 41% of their patients on the basis of guided biopsies, although most of the lesions were solid.

The judicious use of imaging-guided biopsy and aspiration can establish a diagnosis with a minimal risk of complications. Surgery has a higher risk of complications (even the loss of the kidney during the exploration). Above all is the disadvantage of prolonged postoperative convalescence. The incidence of misdiagnoses by imaging-guided biopsies and aspiration is not significantly higher than the misdiagnoses on frozen section analysis during open surgery; both are around 2%. A confidence level of diagnosis similar to that ascertainable by frozen section during open surgery eliminates the argument that an inferior diagnostic modality is used. Strict adherence to technical criteria for obtaining such samples (such as site location of the sample and processing of the samples by histopathologic and cytopathologic examination, flow cytometry, biochemical analysis, and culture/sensitivity) is of paramount importance. Moreover, if a composite lesion features different imaging characteristics in different regions, multiple samples must be obtained to assess the lesion adequately.

A concern regarding percutaneous biopsies had been the potential for needle tract seeding of the tumor cells.^{17–20} However, the risk seems negligible compared with the risk of transitional cell carcinoma.^{17,18,20} We encountered no complications and, in particular, during a follow-up period of at least 5 years, found no evidence of tumor tract seeding in the biopsy tract, either on imaging or during surgery. We believe that the use of a coaxial system, which shields the tissue outside Gerota's fascia from implantation, has eliminated this rarely reported complication.^{15,17–19}

On the basis of our experience, we recommend CT-guided aspiration and biopsy of indeterminate renal mass lesions as a safe, reliable, and accurate modality that could substantially reduce the current existing management problems in this group of patients.

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