Human Pathology (2019) **85**, 270–278

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

Management of patients with renal mass lesions based on renal biopsy cytology results☆,☆☆

Xiao Huang MD, PhD, Brannan Griffin MD, Xiaoqi Lin MD, PhD*

Northwestern University, Chicago, IL 60611, USA

Received 27 July 2018; revised 5 November 2018; accepted 7 November 2018

Keywords:
Kidney;
Biopsy;
Renal cell carcinoma;
Benign tumor;
Metastasis;
Clinical management

Summary The benefit of renal biopsy, especially in patients with a history of malignancy (HOM), has not been well-studied. We studied the clinical management of 339 renal masses after fine needle aspirate and/or core needle biopsy with touch preparation. Forty-one percent of patients had HOM, which did not increase the incidence of renal malignancy. The main reasons for renal biopsy were HOM and small renal masses (≤3 cm). The most common renal masses were clear cell renal cell carcinoma (32%). Thirty percent of renal masses metastasized. The overall accuracy of renal biopsy for subclassification was 76%. Nephrectomy was selected to manage 41% of renal masses, most for primary renal carcinoma. Chemoradiation was selected to treat 15% of patients, especially those with lymphoma (93%), metastatic malignancy (93%), and urothelial carcinoma (69%). Ablation was used to treat 6% of patients. Active surveillance was selected for 34% of patients, predominantly those with benign condition. Our results showed that renal biopsy was an easy and less aggressive tool for obtaining adequate diagnostic materials to render reliable and accurate diagnoses. Initial renal biopsy prevented unnecessary nephrectomy in patients with diagnoses of metastatic malignancy, lymphoma, and most benign tumors/lesions (for most but not all cases). Renal biopsy avoided chemoradiation against prior HOM in patients with diagnosis of benign tumors/lesions (22% of all patients) and primary renal carcinoma (38%). Therefore, renal biopsy significantly impacts the management of patients with renal mass, and any questionable renal mass should be biopsied before further management.

1. Introduction

Renal cancer is the 9th most common cancer in men and 14th in women [1]. The incidence of renal cell carcinoma (RCC) has increased worldwide in recent years, possibly due to an increased aging population and the liberal use of improved noninvasive radiologic imaging. Given the prevalence and clinical importance of renal tumors, evaluation and management become very important clinical issues in recent year. In addition, nonneoplastic lesions can occasionally present as a renal mass on imaging study, and at least 20% of small renal masses are benign neoplasms [2], which need to be distinguished from RCC. Traditionally, the standard clinical approach had been to surgically remove any renal mass that appeared to be predominately solid and primary and confined to the kidney, and pathologic diagnosis of renal lesions was established after total or partial nephrectomy. Currently, a

☆ Competing interests: All authors fully disclosed no financial conflicts of interest in the Support/Grant Information text box, as well as no ethical conflicts of interest.

☆☆ Funding/Support: This study was supported by the start-up fund of Dr Xiaoqi Lin from Department of Pathology, Northwestern University.

* Corresponding author at: Department of Pathology, Northwestern Memorial Hospital, Feinberg School of Medicine, Northwestern University, 251 E. Huron St, Galter Pavilion 7-132F, Chicago, IL 60611.
E-mail address: xlin@northwestern.edu (X. Lin).

https://doi.org/10.1016/j.humpath.2018.11.010
0046-8177/

greater proportion of the renal masses are diagnosed with computed tomography or ultrasound-guided fine needle aspiration (FNA) and/or core needle biopsy (CNB) biopsy to distinguish neoplasms from nonneoplasms, malignant neoplasms from benign neoplasms, lymphoma from nonhematopoietic malignancy, and primary tumors from metastatic malignancies to ensure that patients receive appropriate management. FNA has relatively greater sensitivity and utility for on-site evaluation, whereas CNB provides an additional sample for more specific RCC subclassification and ancillary studies and is, overall, more accurate [3,4]. The European Association of Urology (EAU) RCC Guideline Panel recommends renal tumor biopsy both before ablative therapy and systemic therapy without previous pathology and for patients likely to undergo active surveillance [5]. However, the benefit of renal biopsy for management of patients with renal mass lesions, especially those with previous malignancy history, is still not well studied.

An increasing challenge for pathologists occurs in biopsy specimens with the advent of therapies targeting molecular pathways known to be altered in specific RCC subtypes, typically tyrosine kinase inhibitors that are almost exclusively used to treat clear cell RCC (CCRCC) and papillary RCC (PRCC). Clinicians often need to know not just malignant versus benign or RCC versus other carcinoma subtype, but rather a precise diagnosis to the extent of specific RCC subtype to determine appropriate use of a target therapy.

Our retrospective study was designed to gain more information for the impact of renal biopsy on patients with renal masses to choose the most appropriate management.

2. Materials and methods

2.1. Case selection

This study has been approved by the institutional review board of Northwestern University. In total, 339 renal biopsy cases with FNA and/or CNB with touch preparation were retrieved from the Northwestern Memorial Hospital pathology database between 2002 and 2016. The renal neoplasms were classified according to the 2013 International Society of Urological Pathology Vancouver classification of renal neoplasia and the 2016 World Health Organization classification of tumors of the urinary system and male genital organs [6,7].

The following variables were recorded: cytology diagnosis, immunohistochemistry (IHC) stains, surgical pathology diagnosis, mass size, malignant history, therapy, and metastatic status.

2.2. FNA and CNB

Percutaneous FNA and CNB were performed under local anesthesia and guidance of computed tomography scan or ultrasound imaging using 22- or 20-gauge needles for FNA and/or 20-gauge core needle devices for CNB. The FNA smears or touch preparations of CNB were air-dried and stained with modified Giemsa (Diff-Quik, Polysciences, Inc., Warringtonn, PA) stain for on-site evaluation for adequacy and immediate interpretation by board-certified cytopathologists. Alcohol/methanol-fixed FNA smears were stained with Papanicolaou stain.

2.3. Histology and IHC

Cell blocks, CNBs, and total/partial nephrectomy tissues were formalin-fixed, paraffin-embedded, sectioned, and stained with hematoxylin and eosinE); for histomorphology examination [8].

IHC stains were performed on the sections of paraffin-embedded tissue with appropriate positive and negative controls (ie, positive controls expressed the immunoreagent and negative controls showed no expression) [8]. Antibodies directed against cytokeratin 7 (M7018; DakoCytomation, Carpinteria, CA), CA IX (SC-25599; Santa Cruz Biotechnology, Santa Cruz, CA), CD10 (NCL-L-CD10-270; Novocastra, United Kingdom), AMACR (p504s; M3616; DakoCytomation, Carpinteria, CA), CD117 (A4502; DakoCytomation, Carpinteria, CA), and vimentin (M0725; DakoCytomation, Carpinteria, CA) were used. IHC staining was graded in a semiquantitative manner and scored as either diffuse (>50% of tumor cells positive), focal (between 10% and 50% of tumor cells positive), or negative (<10% of tumor cells positive) [8].

2.4. Correlation of cytology and nephrectomy diagnosis

Diagnoses obtained from nephrectomy and diagnoses from CNBs for the cases without nephrectomy were together used as final diagnosis, and their corresponding agreement with cytology biopsy was reported as "accuracy 1" (Tables 3 and 4). If only diagnoses obtained from nephrectomy were used as final diagnoses, their corresponding agreement with cytology biopsy was reported as "accuracy 2" as comparison (Tables 3 and 4). The cytology diagnoses were categorized as accuracy (same diagnosis as final), misinterpretation (different diagnosis from final), unclassified (inability to subtype tumor), atypical (atypical cells present, quantitatively or qualitatively insufficient for definitive diagnosis), and unsatisfactory (insufficient material for definitive diagnosis). For analysis, the mass lesions were further classified into 3 categories: (1) primary renal carcinoma (PRCa) including all subtypes of RCC and urothelial carcinoma; (2) benign tumors including oncocytoma, angiomyolipoma, and metanephric adenoma; and (3) metastatic malignancy.

2.5. Clinical management of patients after renal mass after biopsy

We reviewed the electronic medical records for information on patients' management after biopsy. We divided management data into 5 categories: (1) total/partial nephrectomy, (2) chemoradiation, (3) ablation, (4) active surveillance, and (5) not available.

2.6. Statistical analysis

Student *t* test, χ^2 test, and Yate correct test were used for statistical analysis of the data, and results are reported in the article.

3. Results

3.1. Clinical information of patients

The diagnosis of renal mass lesions was rendered based on histology findings (Table 1 and representative pictures in Figure). Clinical information on the studied renal lesions was summarized in Table 1. The most common renal mass lesion was CCRCC (32%). There were 8 RCCs (2%) and 4 oncocytic neoplasms (1%) that could not be subclassified because specimens contained either too scant cellularity or with nonspecific cytohistomorphology and immunoprofiles. Unsatisfactory rate was about 6%, and atypical rate was only 0.6%. In these cases, no or too scant diagnostic materials were identified in specimens, and no subsequent nephrectomy was performed.

For total cases, the male-to-female ratio was 184:155 (Table 1). Angiomyolipoma was significantly female predominant, with male-to-female ratio of 1:7 ($P < .01$). All other lesions did not show any significant sex preference.

The age of the patients ranged from 22 to 88 years, with a mean ± SD of 62.0 ± 13.9 years (Table 1). Only patients with medullary RCC and Wilms tumor were statistically younger than those with other renal mass lesions, 30.3 ± 7.5 and 22.0 ± 0.0 years, respectively ($P < .05$).

In all, 139 (41%) patients with renal mass lesion had history of malignancy (HOM; Table 1). which is the one of the main reasons for renal biopsy to exclude metastasis. However, only 13 (4%) renal lesions were proved to be metastatic malignancies: 3 lung carcinomas, 3 lymphomas, 2 melanomas, 2 esophageal carcinomas, 2 adenoid cystic carcinomas, 2 breast carcinomas, and 1 myxoid leiomyosarcoma of the uterus. HOM incidence in cases of metastatic malignancy to the kidney was significantly higher than those of other renal lesions (100%; $P < .05$).

About 30% of renal masses metastasized to lymph nodes or other organs. Urothelial carcinoma and RCC with sarcomatoid differentiation had significantly higher metastatic rates than other malignant tumors, nearly double ($P < .05$; Table 1).

The tumor size ranged from 0.7 to 20 cm (Table 2). The high-grade malignancies tended to be larger than low-grade malignancy, benign tumors, and nonneoplastic lesions. In total, 49% of biopsied mass lesions were ≤3 cm, suggesting that small renal mass was one of the main reasons for renal biopsy.

3.2. Cytology biopsy results of renal masses

The overall diagnostic accuracy of the renal biopsy was 76% (accuracy 1, Table 3). The accuracy of renal biopsy in patients with nephrectomy showed similar findings (accuracy 2, Table 3). Seven cases (2%) were misinterpreted as follows: 3 CCRCC, 1 chromophobe RCC (ChRCC), 1 PRCC, 1 clear

Table 1 Clinical information of renal lesions

Lesions	No. (%)	Male/Female	Age (y)	HOM (%)	Metastasis (%)
CCRCC	110 (32)	60/50	64.8 ± 12.3	46 (42)	34 (31)
ChRCC	18 (5)	12/6	61.6 ± 10.9	10 (56)	3 (17)
PRCC	35 (10)	23/12	65.5 ± 12.5	12 (34)	12 (34)
CCPRCC	7 (2)	4/3	63.1 ± 11.0	0 (0)	0 (0)
RCC, sarcomatoid	11 (3)	6/5	54.9 ± 14.9	2 (18)	8 (73)*
RCC, medullary	4 (1)	0/4	30.3 ± 7.5*	0 (0)	2 (50)
MCRNLMP	1 (0.3)	0/1	74.0 ± 0.0	1 (100)	0 (0)
RCC, unclassified	8 (2)	6/2	61.5 ± 16.0	2 (25)	4 (50)
Wilms tumor	1 (0.3)	1/0	22.0 ± 0.0*	0 (0)	0 (0)
Hybrid oncocytic tumor	6 (2)	3/3	53.8 ± 16.0	2 (33)	0 (0)
Oncocytoma	29 (9)	17/12	66.4 ± 5.9	17 (59)	0 (0)
Unclassified oncocytic tumor	4 (1)	2/2	72.3 ± 14.6	1 (25)	0 (0)
Urothelial carcinoma	16 (5)	11/5	65.2 ± 13.5	7 (44)	13 (81)*
Lymphoma	14 (4)	8/6	55.3 ± 19.3	10 (71)	9 (64)
Metastatic malignancy	13 (4)	3/10	59.0 ± 12.0	13 (100)	13 (100)
Angiomyolipoma	8 (2)	1/7*	58.8 ± 8.2	1 (13)	0 (0)
Metanephric adenoma	1 (0.3)	0/1	52.0 ± 0.0	1 (100)	0 (0)
Atypical	2 (0.6)	1/1	70.0 ± 7.1	0 (0)	0 (0)
Infection or inflammation	30 (9)	16/14	53.8 ± 17.2	9 (30)	0 (0)
Unsatisfactory	21 (6)	10/11	64.0 ± 12.7	15 (71)	2 (10)
Total	339	184/155	62.0 ± 13.9	139 (41)	100 (30)

* $P < .05$, Yate correction test or Student *t* test.

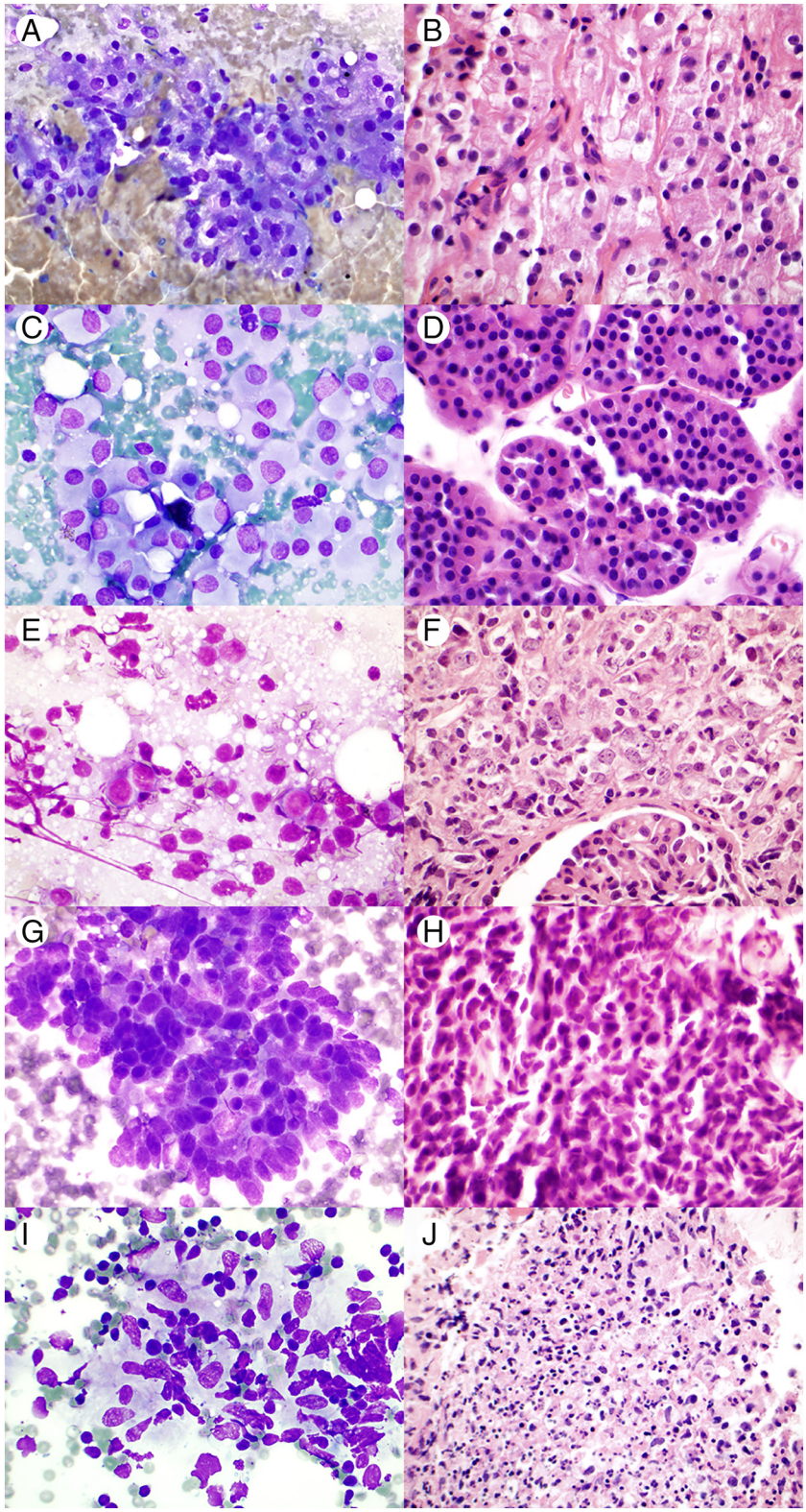

Figure Cytology (A, C, E, G, and I, Diff-Quik stain, original magnification ×600) and histology (B, D, F, H, and J, hematoxylin and eosin stain, ×600) of representative renal lesions. A and B, CCRCC. C and D. Oncocytoma. E and F, Lymphoma. G and H, Metastatic carcinoma. I and J, Granulomatous inflammation, infection.

Table 2 The size of renal masses

Lesions	No.	Range (cm)	Mean ± SD (cm)	≤3 cm (%)
CCRCC	110	0.9-18.0	4.7 ± 3.8	46 (43)
ChRCC	18	1.5-20.0	5.5 ± 4.7	7 (39)
PRCC	35	1.0-15.0	4.1 ± 2.9	13 (37)
CCPRCC	7	2.0-4.5	2.8 ± 0.9	5 (71)
RCC, sarcomatoid	11	2.5-15.0	8.8 ± 4.4	1 (9)
RCC, medullary	4	4.0-9.7	5.4 ± 2.9	0 (0)
MCRNLMP	1	2.1	2.1	1 (100)
RCC, unclassified	8	1.6-10.0	5.0 ± 2.9	3 (38)
Wilms tumor	1	3.5	3.5	0 (0)
Hybrid oncocytic tumor	6	1.1-4.0	2.2 ± 1.2	4 (67%)
Oncocytoma	29	1.0-5.0	2.8 ± 1.1	20 (69)
Unclassified oncocytic tumor	4	2.0-5.4	4.1 ± 1.5	1 (25)
Urothelial carcinoma	16	1.2-10.5	4.9 ± 2.6	2 (13)
Lymphoma	14	2.5-13.5	4.8 ± 3.3	6 (43)
Metastatic malignancy	13	0.7-7.0	3.4 ± 2.0	8 (62)
Angiomyolipoma	8	1.0-7.5	3.2 ± 2.1	6 (75)
Metanephric adenoma	1	12.0	12.0	0 (0)
Atypical	2	2.5-5.5	4.0 ± 2.1	1 (50)
Infection or inflammation	30	1.0-9.2	2.7 ± 1.6	24 (80)
Unsatisfactory	21	1.0-8.0	2.7 ± 1.8	17 (81)
Total	339	0.7-20		165 (49)

cell PRCC (CCPRCC), and 1 hybrid oncocytic tumor. Twenty-three cases (7%) could be not classified, including 7 unclassified RCC and 4 unclassified oncocytic tumors, because of no postbiopsy, potentially clarifying nephrectomy. Seven cases (2%) were classified as "atypical" including 2 cases without postbiopsy nephrectomy, 1 multilocular cystic renal neoplasm of low malignant potential (MCRNLMP), 1 oncocytoma, and 3 urothelial carcinomas. In addition, 46 cases

Table 3 Cytology biopsy results of renal lesions

Lesions	No. (%)	Accuracy 1 [a] (%)	Misinterpreted (%)	Unclassified (%)	Atypical (%)	Unsatisfactory (%)	Accuracy 2 [b] (%)
CCRCC	110 (32)	93 (85)	3 (3)	2 (2)		12 (11)	53/61 (87)
ChRCC	18 (5)	15 (83)	1 (6)	1 (6)		1 (6)	8/9 (89)
PRCC	35 (10)	28 (80)	1 (3)	3 (9)		3 (9)	20/22 (91)
CCPRCC	7 (2)	6 (86)	1 (14)				3/4 (75)
RCC, sarcomatoid	11 (3)	11 (100)					5/5 (100)
RCC, medullary	4 (1)	2 (50)		1 (25)		1 (25)	2/2 (100)
MCRNLMP	1 (0.3)				1 (100)		1/1 (100)
RCC, unclassified	8 (2)			7 (88)		1 (13)	0/0
Wilms tumor	1 (0.3)	1 (100)					1/1 (100)
Hybrid oncocytic tumor	6 (2)	1 (17)	1 (17)	4 (67)			1/6 (17)
Oncocytoma	29 (9)	26 (90)			1 (3%)	2 (7)	4/4 (100)
Unclassified oncocytic tumor	4 (1)			4 (100)			0/0
Urothelial carcinoma	16 (5)	10 (63)		1 (6)	3 (19)	2 (13)	7/9 (78)
Lymphoma	14 (4)	12 (86)				2 (14)	0/0
Metastatic malignancy	13 (4)	12 (92)				1 (8)	0/0
Angiomyolipoma	8 (2)	8 (100)					1/1 (100)
Metanephric adenoma	1 (0.3)	1 (100)					1/1 (100)
Atypical	2 (0.6)				2 (100)		0/0
Infection or inflammation	30 (9)	30 (100)					8/8 (100)
Unsatisfactory	21 (6)					21 (100)	0/0
Total	339	256 (76)	7 (2)	23 (7)	7 (2)	46 (14)	115/134 (86)

[a] Accuracy of the cytology biopsy in patients without nephrectomy (CNB diagnosis as final).
[b] Accuracy of the cytology biopsy in patients with nephrectomy (nephrectomy diagnosis as final).

Table 4 Management of patients with renal mass lesions based on renal biopsy cytology results

Lesions	No. (%)	Nephrectomy (%)	Chemoradiation (%)	Ablation (%)	Active surveillance (%)	N/A (%)
CCRCC	110 (32)	72 (66)	4 (4)	7 (6)	21 (19)	6 (6)
ChRCC	18 (5)	11 (61)	0 (0)	2 (11)	3 (17)	2 (11)
PRCC	35 (10)	23 (66))	4 (11)	2 (6)	5 (14)	2 (6)
CCPRCC	7 (2)	4 (57)	0 (0)	1 (14)	2 (29)	0 (0)
RCC, sarcomatoid	11 (3)	5 (46)	2 (18)	0 (0)	2 (18)	2 (18)
RCC, medullary	4 (1)	3 (75)	1 (25)	0 (0)	0 (0)	0 (0)
MCRNLMP	1 (0.3)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
RCC, unclassified	8 (2)	0 (0)	3 (38)	2 (25)	3 (38)	0 (0)
Wilms tumor	1 (0.3)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Hybrid oncocytic tumor	6 (2)	6 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Oncocytoma	29 (9)	3 (10)	0 (0)	1 (3)	24 (83)	1 (3)
Unclassified oncocytic tumor	4 (1)	2 (50)	0 (0)	0 (0)	2 (50)	0 (0)
Urothelial carcinoma	16 (5)	4 (25)	11 (69)	0 (0)	1 (6)	0 (0)
Lymphoma	14 (4)	0 (0)	13 (93)	1 (7)	0 (0)	0 (0)
Metastatic malignancy	13 (4)	0 (0)	12 (93)	1 (8)	0 (0)	0 (0)
Angiomyolipoma	8 (2)	0 (0.0)	0 (0)	0 (0)	8 (100)	0 (0)
Metanephric adenoma	1 (0.3)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Atypical	2 (0.6)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)
Infection or inflammation	30 (9)	4 (13)	0 (0)	1 (3)	25 (83)	0 (0)
Unsatisfactory	21 (6)	0 (0)	1 (5)	2 (10)	17 (81)	1 (5)
Total	339	140 (41)	51 (15)	20 (6)	114 (34)	15 (4)

Abbreviation: N/A, not available.

(14%) were interpreted as "unsatisfactory." These results suggested that renal biopsy was an easy and less aggressive tool for obtaining adequate diagnostic materials to render reliable and accurate diagnosis.

3.3. Management of patients after biopsy

By reviewing our institution's electronic medical records, the clinical management of the patients after cytologic biopsy was recorded (Tables 4 and 5). Clinical management was not available in 15 cases (4%; Tables 4 and 5).

Overall, 41% of patients with renal mass were treated with nephrectomy (Table 4). Nephrectomy was more commonly used to treat patients with malignant tumors or tumors with malignant potential, ranging from 46% for RCCs with sarcomatoid differentiation to 100% for MCRNLMP, Wilms tumor, and hybrid oncocytic tumors (Table 4). On the other hand, nephrectomy was less commonly used in benign neoplasms and nonneoplastic lesions ranging from 0% for angiomyolipoma to 13% of infection or inflammation. One metanephric adenocarcinoma was resected because of the large tumor size, 12 cm.

Fifteen percent of patients with a renal mass received chemoradiation for malignant diagnoses, especially lymphoma (93%), metastatic malignancy (93%), and urothelial carcinoma (69%; Table 4). One case with both a cytology diagnosis of unsatisfactory and HOM received chemoradiation. Moreover, chemotherapy was used to treat 4% CCRCC, 11% PRCC, 18% RCC with sarcomatoid differentiation, 25% medullary RCC, and 38% RCC with unclassified type.

Ablation was used to treat 6% of patients with renal mass, mostly for malignant tumors, including 1 metastatic malignant tumor, 6% CCRCC, 11% ChRCC, 6% PRCC, 14% CCPRCC,

Table 5 Management of patients with renal mass lesions based on renal biopsy cytology results

Lesions	No. (%)	HOM (%)	Nephrectomy (%)	Chemoradiation (%)	Ablation (%)	Active surveillance (%)	N/A (%)
PRCa	216 (71)	84 (38)	124 (57)	25 (12)	14 (6)	37 (17)	12 (6)
Metastatic malignancy	22 (7)	22 (100)	0 (0)	21 (95)	1 (5)	0 (0)	0 (0)
Benign tumors/lesions	68 (22)	28 (41)	8 (12)	0 (0)	2 (3)	57 (84)	1 (1)
Total	306	134 (46)	132 (43)	46 (15)	17 (6)	94 (31)	13 (4)
P1		<.01	<.01	<.01		<.05	
P2			<.01	<.01		<.01	
P3		<.01		<.01		<.01	

NOTE. χ^2 Test for statistics.

Abbreviations: N/A, not available; P1, comparison of PRCa with metastatic malignancy; P2, comparison of PRCa with benign tumors and lesions; P3, comparison of metastatic malignancy with benign tumors and lesions.

and 25% unclassified RCC (Table 4). Interestingly, 1 lymphoma case, 1 infection/inflammation, and 1 oncocytoma were also treated with ablation. Ten percent of patients with cytology biopsy diagnosis of unsatisfactory were also treated with ablation.

Active surveillance was selected for 34% of patients (Table 4), predominantly due to the nature of the renal masses (eg, diagnosis of a low-grade malignant tumor, benign tumor, or infection/inflammation), patients' complex conditions (eg, limiting comorbidities, inability to tolerate operation, etc), and personal preference. Malignant tumors selected for active surveillance included 19% CCRCC, 17% ChRCC, 14% PRCC, 29% CCPRCC, 18% RCC with sarcomatoid differentiation, and 38% unclassified RCC. Active surveillance was selected for most oncocytomas (83%) and all angiomyolipomas (100%).

We then divided all renal masses into PRCa, metastatic malignancies including renal involvement by lymphoma, and benign conditions (benign neoplasm and infection/inflammation), excluding atypical, unsatisfactory, and unclassified oncocytic tumors (Table 5). The results showed that most renal masses (71%) were PRCa, 7% were metastatic malignancies, and 22% were benign tumors/lesions. Thirty-eight percent of PRCa had HOM. However, HOM in PRCa was not statistically significant from that in benign tumors/lesions (41%), indicating that HOM did not increase incidence of renal malignancy. All patients with metastatic malignancy had HOM (100%) that was significantly different from that in PRCa or benign tumors/lesions ($P < .01$; Table 5).

In total, 43% of patients were treated nephrectomy. Nephrectomy was selected to treat 57% PRCa, which was statistically significantly different from that of metastatic malignancies or benign tumors/lesions ($P < .01$). There was no significant difference in nephrectomy between metastatic malignancies and benign tumors/lesions ($P > .05$). The data suggest that nephrectomy was the still the primary therapy for PRCa including those with HOM. Only 12% of patients with benign tumors/lesions received nephrectomy because of failure of renal functions (50%), oncocytoma (37.5%), unclassified oncocytic neoplasms (25%), or large size (12.5%). In addition, patients avoided nephrectomy when diagnosed with metastatic malignancy, lymphoma, and the majority of benign tumors/lesions.

Forty-three percent of the patients with PRCas did not receive surgical management because of many reasons: (1) advantage stage/metastasis (39.1%); (2) concurrent other malignancy, which needed priority treatment (18.5%); (3) low-grade cancer (CCPRCC; 13.0%); (4) severe underlying and comorbid medical condition (ie, not surgery candidates; 7.6%); (5) nephrectomy history concurrently with limited renal function (7.6%); (6) "unsatisfactory sample for diagnosis" (4.3%); (7) elderly patients (3.3%); (8) small tumor (≤3 cm; 3.3%); and (9) unavailable/unknown.

Chemoradiation was mainly selected to treat metastatic carcinoma and lymphoma (95%), which was statistically significantly more frequently than both PRCa (12%) and benign tumors/lesions (0%; Table 5). A significant significance of chemoradiation as a treatment modality was also seen between PRCa and benign tumors/lesions ($P < .01$). These data suggest that chemoradiation is still the first choice for metastatic malignancy and lymphoma, as well as a small portion of PRCa. All patients with benign tumors/lesions avoided treatment with chemoradiation, although 41% of them had HOM. Although 38% of patients diagnosed as having PRCa had HOM, only 12% of these patients received chemoradiation therapy against PRCa rather than against previous malignancy.

Ablation was selected for 6% of patients with renal mass. There was statistical significance among PRCa, metastatic malignancy, and benign tumors/lesions ($P < .01$ or $P < .05$; Table 5).

Active surveillance was selected predominantly for patients with benign tumors/lesions (84%), which was significantly more frequent than either PRCa (17%) or metastatic malignancy (0%; $P < .01$; Table 5). Selection of active surveillance in PRCa cases was significantly more frequent than in metastatic malignancy ($P < .05$). Reasons indicating active surveillance for PRCas were as follows: (1) old age, (2) poor health conditions, (3) late-stage disease, and (4) low-grade entities (eg, CCPRCC).

4. Discussion

The role of FNA and CNB in the workup and diagnosis of renal mass lesions remains controversial. Our study showed that FNA and CNB have high accuracy to make definitive diagnosis, assist urologists to make appropriate treatment decision (nephrectomy, chemoradiation, ablation, or active surveillance), and can significantly decrease the number of unnecessary surgeries and/or chemoradiation, especially for patients with HOM.

Current recommendations by the American Urological Association (AUA), EAU, and National Comprehensive Cancer Network provide guidelines regarding management strategies that include active surveillance, surgical extirpation, and ablation [9]. Current guidelines recommend partial nephrectomy as the preferred surgical management in patients with a clinical T1 renal mass [5,10]. A long-term comparison of patients treated with partial nephrectomy versus total/radical nephrectomy for tumors ≤5 cm reported equivalent cancer-specific survival and local recurrence rates at 9 years of active surveillance [11-14]. Partial nephrectomy is a viable treatment option for larger renal tumors (T1b), as it offers acceptable surgical morbidity, equivalent cancer control, and better preservation of renal function, with potential for better long-term survival [15]. For T2 tumors, partial nephrectomy use should be more selective, and specific patient and tumor factors should be considered [15]. However, optimal management choice is still unclear for individual patients between surgical treatment and nonsurgical treatment. Our study showed that nephrectomy was selected to treat 41% of renal masses, predominantly

PRCa (57%), indicating that nephrectomy was only used for a little more than half of patients with PRCa. Forty-three percent of the patients with PRCas did not receive surgical management because of many reasons: (1) advantage stage/metastasis (39.1%); (2) concurrent other malignancy, which needed priority treatment (18.5%); (3) low-grade cancer (13.0%); (4) severe underline medical condition (not surgery candidates; 7.6%); (5) previous nephrectomy history (7.6%); (6) unsatisfactory (4.3%); (7) elderly patients (3.3%); (8) small tumor size (3.3%); and (9) unavailable. Only 12% of patients with benign tumors/lesions received nephrectomy as therapeutic intervention for failure of renal functions (end-stage renal disease, acute renal failure, severe infection; 50%), oncocytoma (37.5%), unclassified oncocytic neoplasms (25%), or large size (12.5%). Our data also indicated that the nonsurgery managements were used for most of benign renal lesions. Therefore, renal biopsy is a critical, valuable tool to guide urologists in individualizing the treatment for patients with renal mass.

Management of patients with stage IV malignancy history or hematopoietic malignancy has not been standardized yet. Chemoradiation is the main therapy not only for metastatic malignancy and lymphoma but also for some patients with nonresectable or advanced-stage PRCas. At our institution, one of the main reasons to perform renal biopsy was to exclude metastatic malignancy, as 41% of patients receiving biopsy had HOM. In this study, we found that only 9% of patients with HOM (4% of total patients) were proven to have metastatic malignancy. Chemoradiation was selected to treat 95% of metastatic malignancy, 93% of lymphoma, and 12% of PRCa. Interestingly, our study showed that 38% of patients with biopsy-diagnosed PRCa had prior HOM, whereas 41% of patients with biopsy-proven benign tumors or infection/inflammation had HOM ($P > .05$). Therefore, prior HOM did not increase incidence of PRCa, unlike primary lung adenocarcinoma, for which incidence increases with a history of extrapulmonary malignancy [16]. Biopsy can accurately distinguish metastatic malignancy from primary renal lesions in patients with HOM, which significantly change clinical management for those patients with HOM, such as chemoradiation therapy for T4 metastatic malignancy versus suitable treatment of primary renal mass lesions.

Thermal ablation therapies, including cryoablation and radiofrequency ablation, have emerged as potential treatment options in select elderly or comorbid patients [17,18]. AUA and EAU guidelines recommend considering ablative approaches in patients who are at risk of increased surgical morbidity [9]. It should be noted, however, that there are insufficient data on long-term oncologic outcomes to recommend ablative therapies as a preferred modality [10,17,18]. Our study showed that ablation was used to treat 6% of renal masses as follows: mostly PRCa (14 cases; 6% of PRCa), 1 oncocytoma (3% of oncocytoma), and 1 metastatic malignancy (8% of metastatic malignant cases). Interestingly, 1 lymphoma (7% of lymphoma cases) was also treated with ablation. Biopsy results effectively assisted the urologist in clinical decision making, especially for elderly and nonsurgical candidate patients who were possible candidates for minimally invasive radiofrequency ablation.

AUA and EAU guidelines recommended that active surveillance be included in the discussion with every patient, especially elderly or comorbid patients [9,10]. Five-year overall survival was worse in the active surveillance group (75% versus 92% for those treated at 5 years), but cancer-specific survival was equivalent [18]. Our study showed that active surveillance was used to manage 34% of patients with renal mass, predominantly benign tumors and infection/inflammation, but also PRCas. The reasons for active surveillance used for PRCas in our study were as follows: (1) old age, (2) poor health conditions, (3) late-stage disease, and (4) low-grade entities.

Recent studies suggested that renal mass biopsy is recommended in every case of SRMs [19] because of the high diagnostic yield of FNA and CNB (sensitivity and accuracy >90%), high grading and subtyping prediction, and low associated morbidity (major bleeding <1%) [3,4,19,20]. Our data showed that small mass size was one of the main reasons to perform renal biopsy in our institute, as 49% of biopsied renal lesions were ≤ 3 cm. The total accuracy of our experience was 76%, slightly lower than these previous studies [3,4,19,20]. This phenomenon is most likely that we subclassified the renal lesions into more subtypes based on the 2016 WHO classification of renal tumors [7] rather than just separating RCC from benign lesions. Seven cases were misinterpreted because of the overlapping features of cytomorphology, histology, and immunoprofile of CCRCC, ChRCC, PRCC, oncocytoma, and hybrid tumor, and also because of scant cellularity in some cases. Twenty-six cases (8%) were unclassifiable because of nonspecific IHC results (64%), scant cellularity (29%), and nonspecific cytohistomorphology (7%). Seven cases were called atypical because of the scant cellularity, predominantly extensive necrosis, and cystic contents, which made the further definitive diagnosis difficult.

The unsatisfactory rate of our study was 14%, similar to the previously published false-negative diagnosis rate that was predominantly due to technical factors (up to 16%) [20]. The reasons for 46 cases to be interpreted as unsatisfactory were missing targeted lesions (52%), scant cellularity including predominantly extensive necrosis (48%), and sampling errors, similar to previous publications [20,21].

The evaluation and management of renal masses have been discussed over the past few years, and the survival benefit of nonsurgical interventions for diagnosis and treatment has been noted. Our study suggested that renal biopsy especially along with IHC has high diagnostic accuracy for subclassification of renal mass lesions. Therefore, FNA and/or CNB can be useful and reliable tools when evaluating renal mass lesions in several different clinical scenarios, guiding clinicians, and patients to choose suitable individualized treatments: total/partial nephrectomy, chemoradiation, ablation, or active surveillance. This measure will significantly impact patients' care.

References

[1] Moch H, Amin MB, Argani P, et al. Renal cell tumours—introduction. In: Moch J, Humphrey PA, Ulbright TM, Reuter VE, editors. WHO Classification of Tumours of the Urinary System and Male Genital Organs. Lyon: International Agency for Research on Cancer; 2016. p. 14-7.

[2] Remzi M, Ozsoy M, Klingler HC, et al. Are small renal tumors harmless? Analysis of histopathological features according to tumors 4 cm or less in diameter. J Urol 2006;176:896-9.

[3] Parks GE, Perkins LA, Zagoria RJ, Garvin AJ, Sirintrapun SJ, Geisinger KR. Benefits of a combined approach to sampling of renal neoplasms as demonstrated in a series of 351 cases. Am J Surg Pathol 2011;35:827-35.

[4] Veltri A, Garetto I, Tosetti I, et al. Diagnostic accuracy and clinical impact of imaging-guided needle biopsy of renal masses. Retrospective analysis on 150 cases. Eur Radiol 2011;21:393-401.

[5] Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 2015;67:913-24.

[6] Srigley JR, Delahunt B, Eble JN, et al. The International Society of Urological Pathology (ISUP) Vancouver classification of renal neoplasia. Am J Surg Pathol 2013;37:1469-89.

[7] Moch H, Humphey PA, Ulbright TM, Reuter VE. WHO Classification of Tumours of the Urinary System and Male Genital Organs. Lyon: International Agency for Research on Cancer; 2016.

[8] Lin X. Cytomorphology of clear cell papillary renal cell carcinoma. Cancer 2017;125:48-54.

[9] Motzer RJ, Jonasch E, Agarwal N, et al. Kidney cancer, version 3.2015. J Natl Compr Canc Netw 2015;13:151-9.

[10] Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. J Urol 2009;182:1271-9.

[11] Nieder AM, Taneja SS. The role of partial nephrectomy for renal cell carcinoma in contemporary practice. Urol Clin North Am 2003;30:529-42.

[12] Poulakis V, Witzsch U, de Vries R, Moeckel M, Becht E. Quality of life after surgery for localized renal cell carcinoma: comparison between radical nephrectomy and nephron-sparing surgery. Urology 2003;62:814-20.

[13] Van Poppel H, Joniau S. Is surveillance an option for the treatment of small renal masses? Eur Urol 2007;52:1323-30.

[14] Thompson RH, Boorjian SA, Lohse CM, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. J Urol 2008;179:468-71 [discussion 472-463].

[15] Mir MC, Derweesh I, Porpiglia F, Zargar H, Mottrie A, Autorino R. Partial nephrectomy versus radical nephrectomy for clinical T1b and T2 renal tumors: a systematic review and meta-analysis of comparative studies. Eur Urol 2017;71:606-17.

[16] Zhu B, Dalal S, Kamp DW, Lin X. Warranting investigation of primary lung adenocarcinoma in patients with an extrapulmonary malignancy and lung nodules due to high frequency. Am J Clin Pathol 2014;141:429-36.

[17] Welch BT, Brinjikji W, Schmit GD, et al. Evaluation of the charges, safety, and mortality of percutaneous renal thermal ablation using the nationwide inpatient sample. J Vasc Interv Radiol 2015;26:342-7.

[18] Leone AR, Diorio GJ, Spiess PE, Gilbert SM. Contemporary issues surrounding small renal masses: evaluation, diagnostic biopsy, nephron sparing, and novel treatment modalities. Oncology (Williston Park) 2016;30:507-14.

[19] Richard PO, Jewett MA, Bhatt JR, et al. Renal tumor biopsy for small renal masses: a single-center 13-year experience. Eur Urol 2015;68:1007-13.

[20] Andonian S, Okeke Z, VanderBrink BA, et al. Aetiology of non-diagnostic renal fine-needle aspiration cytologies in a contemporary series. BJU Int 2009;103:28-32.

[21] Phe V, Yates DR, Renard-Penna R, Cussenot O, Roupret M. Is there a contemporary role for percutaneous needle biopsy in the era of small renal masses? BJU Int 2012;109:867-72.