Risk Factors for Complications and Nondiagnostic Results following 1,155 Consecutive Percutaneous Core Renal Mass Biopsies

Natasza M. Posielski, Anthony Bui, Shane A. Wells,* Sara L. Best, Lori Mankowski Gettle, Timothy J. Ziemlewicz,† Meghan G. Lubner,‡ J. Louis Hinshaw, Fred T. Lee, Jr., Glenn O. Allen, Stephen Y. Nakada and E. Jason Abel§

From the Departments of Urology (NMP, AB, SLB, JLH, FTL, GOA, SYN, EJA) and Radiology (SAW, LMG, TJZ, MGL, JLH, FTL, SYN, EJA), University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

Abbreviations and Acronyms

ASA = aspirin

AUA = American Urological Association

BMI = body mass index

CT = computerized tomography

Hb = hemoglobin

INR = international normalized ratio

Accepted for publication December 29, 2018.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article.

* Financial interest and/or other relationship with Ethicon.

† Financial interest and/or other relationship with Ethicon and Histosonics.

‡ Financial interest and/or other relationship with Ethicon and Philips.

§ Correspondence: Department of Urology, University of Wisconsin School of Medicine and Public Health, 1685 Highland Ave., Madison, Wisconsin 53705 (telephone: 920-740-3911; FAX: 608-263-4563; e-mail: abel@urology.wisc.edu).

Editor's Note: This article is the first of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1216 and 1217.

Purpose: The purpose of this study was to evaluate patient, tumor and technical factors associated with procedural complications and nondiagnostic findings following percutaneous core renal mass biopsy.

Materials and Methods: We reviewed core renal mass biopsies from 2000 to 2017. Complications at 30 days or less were graded using the Clavien-Dindo system. Univariate and multivariable analyses were done to evaluate associations between clinical characteristics and the risk of complications or nondiagnostic findings.

Results: Of the 1,155 biopsies performed in a total of 965 patients procedural complications were identified in 24 patients (2.2%), including 5 (0.4%) with major complications (Clavien 3a or greater). No patients were identified with tumor seeding of the biopsy tract. Patient age, body mass index, gender, Charlson comorbidity index, smoking, mass diameter, nephrometry score, number of cores and prior biopsy were not associated with complication risk ($p = 0.06$ to 0.53). Complications were not increased for patients on aspirin or those with low platelets (25,000 to 160,000/μl blood) or a mildly elevated INR (international normalized ratio) (1.2 to 2.0, $p = 0.16$, 0.07 and 0.50, respectively). The complication risk was not increased during the initial 50 cases of a radiologist or when a trainee was present ($p = 0.35$ and 0.12, respectively). Nondiagnostic findings were present in 14.6% of biopsies. Independent predictors included cystic features, contrast enhancement, mass diameter and skin-to-mass distance ($p < 0.001$, 0.002, 0.02 and 0.049, respectively). Radiologist experience was not associated with the nondiagnostic rate ($p = 0.23$). Prior nondiagnostic biopsy was not associated with an increased nondiagnostic rate on subsequent attempts (19.2% vs 14.2%, $p = 0.23$).

Conclusions: Procedural complications following biopsy are rare even with low serum platelets, a mildly elevated INR or when the patient remains on aspirin. Cystic features, hypo-enhancement on imaging, a smaller mass diameter and a longer skin-to-tumor distance increase the risk of nondiagnostic findings.

Key Words: kidney neoplasms; carcinoma, renal cell; biopsy; aspirin; hemorrhage

Percutaneous renal mass biopsy may be helpful to evaluate patients with radiologically diagnosed renal masses. The AUA guidelines recommend discussing the procedural related risks with patients before obtaining

0022-5347/19/2016-1080/0
THE JOURNAL OF UROLOGY®
https://doi.org/10.1097/JU.0000000000000113
Vol. 201, 1080-1087, June 2019
Printed in U.S.A.

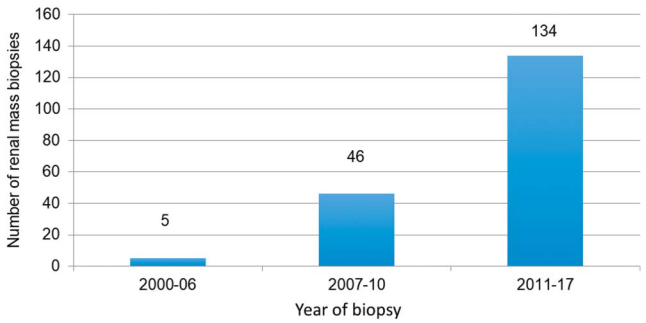
a biopsy.[1] Although the overall rate of biopsy related complications is low,[2,3] few studies have described the risks of biopsy in patients who remain on ASA or in those with mild coagulopathy. Bleeding complications such as hematoma, hemorrhage and hematuria are the most common adverse events following biopsy.[2] A discussion of risks related to bleeding is especially important, given the increasingly common use of anticoagulant and antiplatelet medications in urology cases.[4]

In addition to complications, the AUA recommends discussing the risk of nondiagnostic findings with patients before biopsy.[1] The incidence of biopsies with nondiagnostic results has been reported to be 10% to 22% in large series.[3,5,6] For locally advanced renal masses a multiquadrant biopsy technique may significantly decrease the nondiagnostic rate without increasing complications.[7] However, few groups have investigated whether obtaining multiple cores during biopsy impacts the complication rate of smaller tumors. Furthermore, it is possible that increasing institutional or individual experience may impact complication and nondiagnostic rates since at many centers the utilization of renal mass biopsy has increased (see figure).[8] It is possible that increasing institutional or individual experience may impact the complication and nondiagnostic rates.

The purpose of this study was to evaluate patient, tumor and technical factors associated with procedural complications and nondiagnostic findings in patients following renal mass biopsy.

METHODS

Using an Institutional Review Board approved protocol we reviewed clinical and radiological data on consecutive patients following percutaneous core renal mass biopsy at University of Wisconsin Hospital from January 2000 to December 2017 (IRB No. 2016-1258). Institutional guidelines allow biopsy in patients with an INR of 2.0 or less and a platelet count greater than 25,000/μl blood according to laboratory values measured within 6 months of the procedure if the patient is not on warfarin as well as continuation of ASA therapy during biopsy. All procedures were performed by fellowship trained radiologists with or without the presence of a trainee (a fellow or a resident).



Average number of renal mass biopsies per year increased from 2000 to 2017 at University of Wisconsin Hospital.

The indication for renal mass biopsy was discussed individually with patients. Biopsy was offered if results were thought to potentially impact shared decision making for treatment. Biopsy procedures were performed using moderate conscious sedation and local anesthesia. Ultrasound or CT fluoroscopy was utilized for guidance.

An 18-gauge core biopsy instrument was used for most biopsy procedures. The radiologist determined core biopsy length passes (13 to 33 mm) based on tumor diameter and the proximity of nontarget anatomy. Fine needle aspiration was not performed alone or in conjunction with any renal mass biopsy procedure. Biopsies during thermal ablation procedures were excluded from analysis. CT contrast enhancement was defined as greater than 20 HU.

Complications which developed within 30 days of the procedure were identified and reported using the Clavien-Dindo system.[9] Patients were routinely observed following the procedure to assess for immediate complications and they were telephoned 48 hours postoperatively to screen for complications. The Charlson comorbidity index was evaluated without points for age or renal cancer diagnosis. Nondiagnostic biopsy was defined to include all cases in which a renal mass biopsy was ordered but did not provide diagnostic information to guide treatment, including when the pathologist described insufficient tissue for evaluation, fibrosis only, necrosis only or normal renal parenchyma.

The patient, tumor and procedural factors evaluated included age, gender, BMI, the Charlson comorbidity index, prebiopsy serum laboratory values (Hb, creatinine, platelet count and the INR), systolic and diastolic blood pressure recorded on the day of biopsy prior to the procedure, bleeding disorder history, smoking status, tumor diameter, nephrometry score, prior biopsy history, presence of cancer on final biopsy pathology findings, size of the biopsy needles, the number of cores obtained, the type of imaging guidance (CT or ultrasound), presence of a trainee, uninterrupted aspirin use during biopsy and the administration of blood thinning medications prior to biopsy. Radiologist experience was quantified as the number of procedures performed. Renal mass biopsy specimens were evaluated by genitourinary pathologists.

Differences in patient, tumor and procedural factors were evaluated by the Wilcoxon rank sum or Fisher exact test as appropriate. Univariate logistic regression models were constructed to evaluate the association of the risk of complications with variables of interest. Multivariable models were not used because of the low event rate and the lack of significant predictors on univariate analysis. Multivariable logistic regression analysis was done to evaluate the association of nondiagnostic findings with known independent predictors of nondiagnostic biopsies[6] and with radiologist biopsy experience. All analyses were performed with Stata/SE®, version 15.0.

RESULTS

A total of 1,155 renal mass biopsies were done in 965 patients at University of Wisconsin Hospital from

January 2000 to December 2017. Table 1 shows patient and mass characteristics according to whether a procedural complication was identified. There was significant variation in the nondiagnostic rate among the individual radiologists who performed renal mass biopsy (p = 0.02, table 2).

Biopsy Related Complications

In 24 of the 965 patients (2.2%) who underwent a total of 1,155 biopsies complications were identified within 30 days postoperatively, symptomatic hematoma in 6 (0.5%), gross hematuria in 8 (0.7%), pain requiring intravenous narcotics in 4 (0.3%), urinary tract infection in 3 (0.3%), and hypotension, pseudoaneurysm and urinary retention in 1 patient each. Major complications requiring a secondary procedure (Clavien 3a or greater) were identified in 5 patients (0.4%) and 11 (1.0%) were admitted to the hospital. Two patients were treated with selective renal arterial embolization and in 1 percutaneous drainage of an abscess was done. Two patients were admitted to the intensive care unit with sepsis related to urinary infection. No case of tumor seeding from the biopsy was identified. There were no deaths related to renal mass biopsy in our cohort. Table 3 shows factors associated with procedural complications.

Anticoagulation Status

Biopsy was performed in 441 patients (38.1%) on ASA and 176 (15.2%) with 160,000 platelets or less per μl blood. The lower limit of normal at the hospital was 160,000 platelets per μl blood. ASA use was not associated with a complication risk following biopsy (p = 0.18). A platelet count of 160,000/μl blood or less was also not associated with a complication risk (p = 0.15). Mild INR elevation to 1.2 to 2.0, which was identified in 57 patients (4.9%) at the time of the procedure, was not associated with a complication risk (p = 0.47). When considering only bleeding related complications such as hematoma, hematuria or pseudoaneurysm, no association was identified with a mild INR elevation

Table 1. *Patient and tumor characteristics*

	No Complications	Complications	p Value
No. pts	1,131	24	—
Median age (IQR)	65.6 (58.0—72.2)	66.4 (53.8—70.1)	0.54
Median kg/m^2 BMI (IQR)	29.7 (26.0—34.8)	31.5 (26.6—36.8)	0.35
Median cm tumor diameter (IQR)	3 (2.1—5)	3.8 (2—7.1)	0.46
Median nephrometry score (IQR)	7 (5—9)	8 (6—10)	0.24
Median Charlson comorbidity index (IQR)	1 (0—2)	0 (0—2.5)	0.18
Median serum Hb (IQR)	13.2 (11.6—14.5)	12.5 (10.6—14.2)	0.40
Median serum creatinine (IQR)	1 (0.8—1.2)	1 (0.8—1.6)	0.75
Median mm Hg procedure blood pressure (IQR):			
Systolic	132 (121—145)	139 (124—150)	0.36
Diastolic	74 (66—82)	77 (68—84)	0.51
No. current smoker (%)	151 (13.8)	2 (8.3)	0.76
No. male gender (%)	737 (65.2)	11 (45.8)	0.06
No. prior bleeding disorder (%)	14 (1.3)	0	—
No. biopsy yr (%):			0.18
2000—2006	34 (3)	1 (4.2)	
2007—2010	185 (16.3)	1 (4.2)	
2011—2017	912 (80.6)	22 (91.7)	
No. repeat biopsy for nondiagnostic results (%)	79 (7.6)	1 (4.3)	1.00
No. biopsy needle gauge (%):			—
18 or Less	1,014 (94.7)	24 (100)	
20 gauge	40 (3.7)	0	
22 or Greater	17 (1.6)	0	
No. cores obtained (%):			0.20
1	234 (20.8)	3 (13.0)	
2	403 (35.9)	6 (26.1)	
3 or Greater	486 (43.3)	15 (60.9)	
No. guidance (%):			—
CT	105 (9.3)	0	
Ultrasound	1,022 (90.7)	24 (100)	
No. pts on aspirin during biopsy (%)	435 (38.8)	6 (25.0)	0.21
No. pts on blood thinner prior to biopsy (%)	230 (45.5)	6 (25.0)	0.62
No. platelet count less than 160,000/μl blood (%)	175 (15.8)	1 (4.2)	0.16
No. INR 1.2—2.0 (%)	55 (5.0)	2 (8.3)	0.35
No. Ca diagnosed (%)	731 (82.4)	14 (73.7)	0.36
No. trainee present (%)	945 (83.7)	17 (70.8)	0.10
No. radiologist 1st cases (%):*			
25	298 (28.0)	2 (9.1)	0.05
50	590 (55.6)	10 (45.5)	0.39

* Comparison of complications limited to biopsies done by 12 radiologists who performed most renal mass biopsies.

Table 2. *Individual complication and nondiagnostic rates by number of biopsies and cores*

	Radiologist No.											
	1	2	3	4	5	6	7	8	9	10	11	12
No. biopsies	62	68	68	72	75	84	91	95	98	111	122	138
Mean No. cores/biopsy	2.7	2.0	2.4	2.4	2.4	2.8	2.1	2.3	2.3	2.8	2.5	3.1
% Complication:												
Overall	1.6	2.9	2.9	1.4	1.3	3.6	1.1	0	2.0	2.7	0.8	2.2
Major	1.6	0	0	0	0	1.2	0	0	0	0.9	0.8	0
% Nondiagnostic:												
Overall	10.7	14.5	16.4	14.9	23.9	13.9	14.5	13.8	10.3	15.2	15.0	13.5
Less than 4 cm	8.3	11.9	20.9	16.0	27.5	19.2	15.4	17.8	12.5	18.8	15.6	17.5

(p = 0.19) or a low platelet count (p = 0.35). Preoperative Hb, creatinine and systolic blood pressure at the time of the procedure were not associated with complications (p = 0.45, 0.54 and 0.51, respectively, table 3). Of the patients 14 (0.9%) had a history of a bleeding disorder but none experienced a complication.

Table 3. *Univariate logistic regression analysis of factors associated with risk of any grade complication after renal mass biopsy and multivariable analysis of factors associated with nondiagnostic biopsy findings*

	OR (95% CI)	p Value
Univariate		
Age	0.97 (0.95–1.00)	0.09
BMI	1.04 (0.99–1.08)	0.10
Female gender	2.21 (0.98–4.98)	0.06
Tumor diameter (continuous)	1.05 (0.95–1.17)	0.35
Biopsy yr:		
2000–2006	Referent	—
2007–2010	0.18 (0.01–3.01)	0.24
2011–2017	0.82 (0.11–6.26)	0.85
No. cores:		
1	Referent	—
2	1.16 (0.29–4.69)	0.83
3 or Greater	2.40 (0.69–8.40)	0.17
On aspirin during biopsy	0.53 (0.21–1.34)	0.18
Prebiopsy blood thinner use	1.11 (0.61–2.02)	0.73
Less than 160,000 platelets/μl blood	0.23 (0.03–1.73)	0.15
INR 1.2–2.0	1.73 (0.40–7.54)	0.47
Serum Hb	0.93 (0.77–1.12)	0.45
Serum creatinine	1.13 (0.73–1.73)	0.54
Charlson comorbidity index	0.85 (0.65–1.13)	0.27
Trainee present	0.47 (0.19–1.15)	0.10
Blood pressure during procedure:		
Systolic	1.01 (0.99–1.03)	0.51
Diastolic	1.01 (0.98–1.05)	0.54
Repeat biopsy after initial nondiagnostic results	0.55 (0.07–4.15)	0.56
Current smoker	0.57 (0.13–2.45)	0.45
Ca diagnosed	0.60 (0.21–1.68)	0.33
Nephrometry score	1.12 (0.93–1.35)	0.22
No. radiologist 1st cases:		
25	0.26 (0.06–1.10)	0.07
50	0.67 (0.29–1.56)	0.35
Multivariate		
Cystic lesion (vs solid)	5.32 (3.34–8.51)	<0.001
Enhancing*	0.33 (0.17–0.66)	0.002
Skin-tumor distance/cm	1.10 (1.00–1.20)	0.05
Tumor diameter	0.91 (0.84–0.98)	0.02
Radiologist prior experience†	0.99 (0.98–1.00)	0.33

* Defined as greater than 20 HU and greater than 15% on magnetic resonance imaging.
† No. renal mass biopsies performed.

Institutional and Individual Radiologist Renal Mass Biopsy Experience

The average number of biopsies performed per year increased from 5 to 46 to 134 when comparing 2000 to 2006 with 2007 to 2010 and 2007 to 2010 with 2011 to 2017, respectively. No difference in the complication rate was identified among the 3 periods (2.8% vs 0.5% vs 2.4%, p = 0.21).

A total of 12 radiologists performed at least 50 renal mass biopsies in this series with a complication rate ranging from 0% to 3.6% (table 2). Risk was not increased during the first 25 or 50 cases of a radiologist (p = 0.07 and 0.35, respectively). The presence of a trainee also did not increase the complication rate (p = 0.10).

Nondiagnostic Biopsy Analysis

Overall biopsy findings were nondiagnostic in 145 cases (14.6%) with the rate ranging from 10.3% to 23.9% among individual radiologists. The nondiagnostic rate was higher for cystic than solid masses (40.8% vs 10.6%, p <0.001). Nondiagnostic rates for biopsies from 2000 to 2006 were similar to those from 2007 to 2010 and from 2011 to 2017 (18.2% vs 16.4% vs 14.1%, p = 0.60). For initial biopsies of renal masses less than 4 cm the nondiagnostic rate was 17.0%, including 21.4% for masses 1 cm or less, 20.8% for 1.1 to 2.0 cm and 15.5% for 2.1 to 3.9 cm. In patients with an initial nondiagnostic biopsy the repeat biopsy nondiagnostic rate was 19.2% compared to 14.2% for an initial biopsy (p = 0.23). In patients with an initial nondiagnostic biopsy there was no difference in the risk of a subsequent cancer diagnosis when comparing the initial biopsy finding of normal parenchyma and/or inadequate tissue vs necrosis and/or fibrosis (p = 0.76). Nondiagnostic findings were not associated with the first 25 or 50 cases of a radiologist (p = 0.57 and 0.91, respectively).

Multivariate analysis revealed that predictors of nondiagnostic findings included cystic features (OR 5.32, p <0.001), contrast enhancement (OR 0.33, p = 0.002), renal mass largest diameter (OR 0.91, p = 0.02) and skin-to-tumor distance (OR 1.1, p = 0.05, table 3). Radiologist experience indicated

by the overall number of biopsies performed did not predict the risk of nondiagnostic findings ($p = 0.33$).

DISCUSSION

With the increasing use of biopsy to characterize renal tumors[8] it is important to understand the risks of procedural complications and nondiagnostic findings. This large series of percutaneous core renal mass biopsies demonstrated no mortality with low overall and major complication rates (2.2% and 0.4%, respectively). The risk of complications was not associated with continued aspirin use, a mildly elevated INR (1.2 to 2.0) or lower serum platelets. Complications were not increased when more biopsy cores were obtained or a trainee was present. Biopsies were nondiagnostic in 10% of solid tumors and 40% of cystic tumors. Other independent predictors of nondiagnostic findings were decreased contrast enhancement (less than 20 HU), an increased skin-to-tumor distance and a decreased mass diameter. Prior experience with renal mass biopsy did not predict the risk of procedural complications or nondiagnostic findings.

Collectively these findings suggest that biopsy provides diagnostic information with minimal morbidity for most solid tumors. In patients considering biopsy these data may be used for counseling about the individual risk of morbidity or nondiagnostic findings.

The overall complication rate of renal mass biopsy in this study was comparable to that in smaller series and systematic reviews.[2,3,10] In 2016 Marconi et al found that hematomas required transfusion in 0.7% of reported biopsies, self-limited hematuria in 3.2% and severe pain in 3%.[10] Rarely reported complications were gross hematuria, pseudoaneurysm requiring embolization, septic shock and pneumothorax. The most common complications in our study were symptomatic hematoma (0.5% of cases), self-limited gross hematuria (0.7%), severe pain (0.3%) and urinary tract infection (0.3%). It is important to note that we found no case of tumor seeding, consistent with consensus opinions that seeding is an exceedingly rare complication.[5,6,11]

Institutional and individual experience did not impact the overall low complication rate. An increased number of cores obtained during biopsy may improve diagnostic accuracy[7,12] but the effect of increased sampling on biopsy complications has not been widely reported.[7] In this series 3 or more cores were obtained in 500 patients (43.3%) during biopsy without an increased complication risk.

At our institution core biopsy of solid organs is allowed in patients with an INR of 2.0 or less measured within 6 months of the procedure if not on warfarin, or on the day if on warfarin, a platelet count greater than 25,000 per μl blood measured within 6 months of the procedure and continuation of aspirin therapy.[13] Mild coagulopathy, ie an INR less than 2.0, does not necessarily represent a bleeding diathesis and should not be a contraindication to biopsy. Likewise spontaneous bleeding is rare in patients with a platelet count higher than 10,000 to 20,000/μl blood.[14] In this cohort 15% of patients underwent biopsy with a low platelet count (above 25,000/μl blood) without an increase in adverse events.

In addition, daily aspirin is commonly recommended for primary prevention of cardiovascular disease and colorectal cancer[15] or to reduce the risk of myocardial infarction in coronary stent cases.[16] In this series 38% of patients remained on aspirin during biopsy without increasing the complication rate.

Nondiagnostic findings occur when a biopsy probe fails to sample adequate viable tissue from a renal mass, including the pathological findings of insufficient tissue, fibrosis, necrosis or normal renal parenchyma. This inclusive definition is useful because the purpose of biopsy is to evaluate for malignancy in a renal mass. The inability to make a definitive pathological diagnosis is a limitation regardless of whether nondiagnostic findings resulted from targeting and/or technical failures, or necrosis and/or fibrosis in renal tumors. It is important to note that a subsequent cancer diagnosis was not more likely with initial biopsy findings of necrosis and/or fibrosis compared to benign parenchyma and/or inadequate tissue, suggesting a complex explanation for many nondiagnostic biopsies.

Contemporary large institutional series have described a nondiagnostic rate ranging from 10% to 21% (supplementary table, https://www.jurology.com).[3,5,6,17–19] Variation in published rates may occur with nondiagnostic definitions. For example, renal mass biopsies containing only benign renal parenchyma are not always considered nondiagnostic. Similarly nondiagnostic rates are lower in series of only solid masses.

Interestingly nondiagnostic rates were not associated with increased institutional or individual experience in this study. Consistent with prior reports, independent predictors of nondiagnostic biopsy results included the lack of radiological enhancement greater than 20 HU, a smaller mass diameter, the presence of cystic features and an increased skin-to-tumor distance.[6] Importantly repeat biopsy in patients with initial nondiagnostic results has a similar nondiagnostic rate.

To our knowledge the optimal utilization of biopsy for renal mass evaluation is unknown.[20] After discussing the risks, benefits and alternatives we offer renal mass biopsy if the results would

potentially alter treatment decision making, as suggested in the AUA guidelines.[1]

In recent years multiple factors have contributed to the increased utilization of biopsy nationwide[21] and at our institution. 1) Pretreatment renal mass biopsy is more commonly offered because of the recognition that biopsy has low morbidity with high accuracy to diagnose cancers vs benign/indolent tumors.[22] In many patients biopsy enables better informed consent by providing more information which may guide treatment decisions. For example, older patients with a small renal mass often elect surveillance when diagnosed with oncocytic tumors on biopsy.[23]

2) The use of thermal ablation as renal mass treatment has increased.[24] We recommend biopsy before ablation to establish a pathological diagnosis and allow for a discussion of all treatment options.[25]

3) Finally, active surveillance has become better accepted in select patients with a small renal mass.[1,26–28] Although it is not helpful in all patients undergoing surveillance, up-front biopsy may identify some high grade cancers that should be treated surgically. Conversely biopsy identification of benign tumors prior to surveillance enables less aggressive imaging protocols to be used in the patients at lowest risk.

In 2 recent systematic reviews the methodology of reporting biopsy complications was noted to be extremely variable.[2,10] In the current study we attempted to minimize reporting variability using the Clavien-Dindo classification. Given the retrospective nature of this study, underreporting complications after biopsy is a potential limitation. However, patients were routinely telephoned by nursing staff 48 hours after biopsy specifically to evaluate for complications.

Furthermore, the goal of this study was to identify clinically relevant complications which could delay treatment. Individual experience was not associated with fewer complications or nondiagnostic results even during the first 25 or 50 procedures performed by individual radiologists. Selection bias may have impacted this analysis if more experienced radiologists were selected for biopsies which were perceived as more difficult. It is also important to acknowledge that institutional experience may result in better outcomes overall, which cannot be measured at a single institution.

Finally, the rarity of complications following biopsy may have limited the analysis of prognostic factors. However, to our knowledge we report the largest single institution series of renal mass biopsies. The low risk of complications is representative of our experience.

CONCLUSIONS

Renal mass core biopsy has low overall and major complication rates. No increase in the complication rate was identified when more cores were obtained during biopsy, or when patients had a low platelet count, a mildly elevated INR or remained on aspirin. Independent predictors of nondiagnostic findings included poor radiological enhancement, mass size, the presence of cystic features and a longer skin-to-tumor distance. Repeat biopsy after an initial nondiagnostic attempt has a nondiagnostic rate similar to that of the initial biopsy.

REFERENCES

1. Campbell S, Uzzo RG, Allaf ME et al: Renal mass and localized renal cancer: AUA guideline. J Urol 2017; **198:** 520.
2. Patel HD, Johnson MH, Pierorazio PM et al: Diagnostic accuracy and risks of biopsy in the diagnosis of a renal mass suspicious for localized renal cell carcinoma: systematic review of the literature. J Urol 2016; **195:** 1340.
3. 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.
4. Culkin DJ, Exaire EJ, Green D et al: Anticoagulation and antiplatelet therapy in urological practice: ICUD/AUA review paper. J Urol 2014; **192:** 1026.
5. Leveridge MJ, Finelli A, Kachura JR et al: Outcomes of small renal mass needle core biopsy, nondiagnostic percutaneous biopsy, and the role of repeat biopsy. Eur Urol 2011; **60:** 578.
6. Prince J, Bultman E, Hinshaw L et al: Patient and tumor characteristics can predict nondiagnostic renal mass biopsy findings. J Urol 2015; **193:** 1899.
7. Abel EJ, Heckman JE, Hinshaw L et al: Multiquadrant biopsy technique improves diagnostic ability in large heterogeneous renal masses. J Urol 2015; **194:** 886.
8. Leppert JT, Hanley J, Wagner TH et al: Utilization of renal mass biopsy in patients with renal cell carcinoma. Urology 2014; **83:** 774.
9. Dindo D, Demartines N, Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; **240:** 205.
10. Marconi L, Dabestani S and Lam TB et al: Systematic review and meta-analysis of diagnostic accuracy of percutaneous renal tumour biopsy. Eur Urol 2016; **69:** 660.
11. Haifler M and Kutikov A: Update on renal mass biopsy. Curr Urol Rep 2017; **18:** 28.
12. Hobbs DJ, Zhou M, Campbell SC et al: The impact of location and number of cores on the diagnostic accuracy of renal mass biopsy: an ex vivo study. World J Urol 2013; **31:** 1159.
13. O'Connor SD, Taylor AJ, Williams EC et al: Coagulation concepts update. AJR Am J Roentgenol 2009; **193:** 1656.
14. DeAngelis GA, Khot R, Haskal ZJ et al: Bleeding risk and management in interventional procedures in chronic liver disease. J Vasc Interv Radiol 2016; **27:** 1665.
15. Bibbins-Domingo K and U.S. Preventive Services Task Force: Aspirin use for the primary prevention of cardiovascular disease and colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2016; **164:** 836.

16. Piccolo R and Windecker S: Low-dose aspirin to reduce the risk for myocardial infarction among patients with coronary stents undergoing noncardiac surgery. Ann Intern Med 2018; **168:** 289.

17. Menogue SR, O'Brien BA, Brown AL et al: Percutaneous core biopsy of small renal mass lesions: a diagnostic tool to better stratify patients for surgical intervention. BJU Int 2013; **111:** E146.

18. Richard PO, Lavallee LT, Pouliot F et al: Is routine renal tumor biopsy associated with lower rates of benign histology following nephrectomy for small renal masses? J Urol 2018; **200:** 731.

19. Jeon HG, Seo SI, Jeong BC et al: Percutaneous kidney biopsy for a small renal mass: a critical appraisal of results. J Urol 2016; **195:** 568.

20. Blute ML Jr, Drewry A and Abel EJ: Percutaneous biopsy for risk stratification of renal masses. Ther Adv Urol 2015; **7:** 265.

21. Maurice MJ, Zhu H, Kiechle JE et al: Increasing biopsy utilization for renal cell carcinoma is closely associated with treatment. Urology 2015; **86:** 906.

22. Blute ML Jr and Abel EJ: The evolving role of renal mass biopsy. Ann Transl Med 2016; **4:** 83.

23. Miller BL, Mankowski Gettle L, Van Roo JR et al: Comparative analysis of surgery, thermal ablation, and active surveillance for renal oncocytic neoplasms. Urology 2018; **112:** 92.

24. Shah PH, Alom MA, Leibovich BC et al: The temporal association of robotic surgical diffusion with overtreatment of the small renal mass. J Urol 2018; **200:** 981.

25. Wells SA, Wong VK, Wittmann TA et al: Renal mass biopsy and thermal ablation: should biopsy be performed before or during the ablation procedure? Abdom Radiol (NY) 2017; **42:** 1773.

26. Alam R, Patel HD, Osumah T et al: Comparative effectiveness of management options for patients with small renal masses: a prospective cohort study. BJU Int 2018; **123:** 42.

27. Pierorazio PM, Johnson MH, Ball MW et al: Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. Eur Urol 2015; **68:** 408.

28. Finelli A, Ismaila N, Bro B et al: Management of small renal masses: American society of clinical oncology clinical practice guideline. J Clin Oncol 2017; **35:** 668.

EDITORIAL COMMENTS

In recent years there has been a resurgence in renal mass biopsies, particularly with the increasing use of active surveillance of small renal masses. The authors present their robust institutional experience with 1,155 renal mass biopsies. The complication and nondiagnostic rates are consistent with those in several prior reports (reference 10 in article). However, a novel aspect of their work highlights the safety of renal mass biopsy despite mild coagulopathy. Nonetheless, renal mass biopsy is not without serious risks as some patients required arterial embolization, abscess drainage or intensive care unit admission. Thus, as for any invasive procedure patient selection and the value of information gained from intervening must be strongly considered before proceeding (reference 1 in article).

While the authors report a 15% nondiagnostic rate, we suspect that having a dedicated pathologist review frozen sections at the time of renal mass biopsy to confirm tissue presence and adequacy (which is our practice) may help reduce the nondiagnostic rate or the need for repeat renal mass biopsy. Furthermore, we have found a growing role for sophisticated imaging protocols in reducing the need for invasive renal mass biopsies at our institution based on the strong correlation of multiparametric magnetic resonance imaging with small renal mass histology.[1] We anticipate that widespread adoption of such techniques may mitigate the morbidity and nondiagnostic rates associated with renal mass biopsies.

Nirmish Singla and Vitaly Margulis
Department of Urology
University of Texas Southwestern Medical Center
Dallas, Texas

REFERENCE

1. Kay FU, Canvasser NE, Xi Y et al: Diagnostic performance and interreader agreement of a standardized MR imaging approach in the prediction of small renal mass histology. Radiology 2018; **287:** 543.

In a large institutional series of percutaneous renal mass biopsies performed by fellowship trained radiologists the overall nondiagnostic rate was 14.6%, reaffirming the value of 14.1% in a recent systematic review (reference 2 in article). While there was variation among radiologists, the factors associated with the nondiagnostic rate included cystic features, a smaller tumor diameter and a greater skin-to-tumor distance. Radiologist experience was not associated. The complication rate was low with major complications in 0.4% of patients and hospital readmission in 1.0%.

Importantly, 38.1% of biopsies were performed in patients on aspirin, which did not increase the complication risk. Thrombocytopenia (25,000 to less than 160,000 platelets per μl) or an elevated INR (1.2 to 2.0) also did not appear to increase the risk of bleeding complications. These findings are

reassuring because bleeding complications are often the primary concern after renal mass biopsy with limited data available in these higher risk subsets.

What remains uncertain, however, is how much a diagnostic biopsy impacts subsequent management to balance with the potential risks of the procedure. A positive result of cancer on biopsy correlates almost 100% with surgical pathology findings but a benign result, including the suggestion of oncocytoma, correlates only 70%.[1] Going forward, it will be important to better evaluate the impact of biopsy pathology on management decisions.

Hiten D. Patel and Phillip M. Pierorazio
James Buchanan Brady Urological Institute and Department of Urology
Johns Hopkins Medical Institutions
Baltimore, Maryland

REFERENCE

1. Patel HD, Druskin SC, Rowe SP et al: Surgical histopathology for suspected oncocytoma on renal mass biopsy: a systematic review and meta-analysis. BJU Int 2017; **119:** 661.

REPLY BY AUTHORS

Percutaneous renal mass biopsy is a low morbidity procedure which reliably provides a pathological diagnosis of renal cell carcinoma. However, the usefulness of biopsy depends on careful interpretation and communication of results. Samples containing only normal parenchyma, necrosis or fibrosis do not provide actionable information. As with any solid tumor core biopsy (eg renal or prostate biopsy) patients should be informed beforehand about the potential for nondiagnostic results. Advanced pathological analysis or targeting masses using radiological fusion technologies may improve future diagnostic abilities.

In this era of personalized medicine small renal mass biopsy can improve shared decision making in many patients considering treatment vs active surveillance. It is important to consider the potential impact of treatment on life expectancy because half of the patients with kidney cancer are older than 65 years and many have serious comorbidities, including chronic kidney disease. When treatment decisions are not straightforward, biopsy provides value by improving the individual estimation of cancer related risks. Although biopsy has limited ability to distinguish oncocytoma from other eosinophilic neoplasms (reference 23 in article), the overall risk of progression of renal oncocytic tumors 4 cm or less is exceptionally small. Three recent series demonstrated the safety of observation of small oncocytic tumors with metastasis developing in no patient while on surveillance.[1,2]

Clinicians should use biopsy judiciously. It is critical to understand the limitations of any diagnostic test to estimate risk. In our current practice pretreatment biopsy is rarely helpful in younger and healthier patients, in whom surgery remains a standard treatment recommendation.

REFERENCES

1. Richard PO, Jewett MA, Bhatt JR et al: Active surveillance for renal neoplasms with oncocytic features is safe. J Urol 2016; **195:** 581.

2. Liu S, Lee S, Rashid P et al: Active surveillance is suitable for intermediate term follow-up of renal oncocytoma diagnosed by percutaneous core biopsy. BJU Int, suppl., 2016; **118:** 30.