

Complications of Ultrasound-Guided Percutaneous Renal Biopsy at the National Kidney and Transplant Institute: A Radiologic Perspective

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Abstract

Objectives: This study aims to determine the incidence of complications associated with ultrasound-guided percutaneous native renal biopsies. It also aims to determine the association between the occurrence of complications and the following factors, if present: age, sex, serum creatinine, platelet count, hemoglobin, hematocrit, prothrombin time, partial thromboplastin time, international normalized ratio (INR), history of hypertension or diabetes, pre-biopsy blood pressure, renal length, biopsy laterality, and number of needle passes.

Methods: This was a retrospective multivariate analysis research done in a tertiary medical specialty center involving all patients aged 19 years and older who underwent ultrasound-guided percutaneous native kidney biopsy from July 2012 to June 2015. Data were gathered through a review of charts and electronic radiology and laboratory databases.

Results: A total of 984 patients were included. Overall incidence of complications detected by routine post-biopsy ultrasound was 51.7%, with only 1.0% classified as major. Factors shown to have statistically significant association with the development of complications were female sex, higher systolic and diastolic blood pressure, longer partial thromboplastin time, and shorter renal length by ultrasound.

Conclusion: Although there are no absolute contraindications to performing the procedure, and the decision to perform it rests on the clinician's judgment of whether the risks outweigh the benefits and on the patient's consent, following a nationwide protocol would help the clinician comprehensively assess whether the patient is a good candidate for the procedure, educate him or her on the potential complications, and address modifiable risk factors.

Key words: ultrasound, renal biopsy, NKTl, percutaneous

Introduction

Renal biopsy is an integral part in the diagnosis of renal diseases. As most of these diseases present with non-specific symptoms, it is necessary to confirm the physician's clinical impression with a definitive histopathologic examination before the most appropriate management can be instituted. A study by Richards et al showed that histopathologic diagnoses obtained by percutaneous renal biopsy altered management in 42% of cases.¹ However, there are a number of complications associated with this procedure, most common of which are hematoma formation and gross hematuria. With the introduction of ultrasound guidance, development of automated spring-loaded biopsy needles, and increasing skill and experience of nephrologists and radiologists regarding this procedure, the incidence of complications related to renal biopsy has decreased over the years. Currently, there is a paucity of local data on the incidence of renal biopsy-associated

complications and the possible risk factors affecting their occurrence. An unpublished retrospective study conducted in 2010 on a sample population of 172 out of 302 patients who underwent ultrasound-guided percutaneous native renal biopsy at the National Kidney and Transplant Institute showed that young age (11-20 years) and female gender were the only factors associated with increased incidence of post-biopsy hematoma (Tangonan, V. A descriptive study on the factors affecting postbiopsy hematoma in patients who underwent ultrasound guided renal biopsy of native kidney in National Kidney and Transplant Institute, *unpublished*, 2010). However, this study was limited by the small sample size and possibly incomplete documentation of complications during the study period. Previous researches done abroad showed complication rates within the range of 2.2% to 34.1%.^{2,3} Serum creatinine, female gender, younger age, increased baseline partial thromboplastin time and prolonged bleeding time were among the factors that were shown to increase the risk for complications.^{4,5}

This study aims to determine the incidence of complications associated with ultrasound-guided percutaneous native renal biopsies.

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It also aims to determine the association between the occurrence of complications and the following factors, if present: age, sex, serum creatinine, platelet count, hemoglobin, hematocrit, prothrombin time, partial thromboplastin time, international normalized ratio (INR), percent activity, history of hypertension or diabetes, pre-biopsy blood pressure, renal length, laterality, and number of passes.

Methodology

This is a retrospective analysis of all percutaneous ultrasound-guided renal biopsies done on native kidneys of adult patients (19 years and older) at the National Kidney and Transplant Institute from July 2012 to June 2015 (three years). Biopsies performed on pediatric patients and renal grafts are not included.

Biopsy technique

Biopsies were performed by a nephrology consultant or fellow under real-time ultrasound guidance by a radiology consultant, resident or fellow. An automated, spring-loaded, 18-gauge Bard Max-Core disposable core biopsy needle system was utilized in all procedures. Post-biopsy sonographic examination was routinely done the following morning for admitted patients, four hours after the procedure for out-patients, or earlier if clinically indicated. Repeat ultrasound examination or further examination with other imaging modalities was conducted as needed.

Data gathering

A list of all ultrasound-guided percutaneous renal biopsy procedures satisfying the inclusion criteria during the study period was obtained through the Radiology Information System. Renal length by ultrasound, taken at most 30 days from the procedure, laterality of the biopsied kidney, and number of bites were retrieved from the same system.

Serum creatinine, platelet count, hemoglobin, hematocrit, prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR), taken within 30 days before the procedure, were recorded from the electronic laboratory database. Patients' charts were reviewed at the Medical Records Section, noting demographics, history of hypertension or diabetes, and pre-biopsy systolic and diastolic blood pressure. Development of hematoma, arteriovenous fistula (AVF) or pseudoaneurysm as detected on routine post-biopsy ultrasound examination was documented. In patients who showed sonographic evidence of the aforementioned complications, interventions consequently undertaken (PRBC transfusion, renal embolization, and/or nephrectomy) were noted. Observation period was limited to the duration

of hospital admission, or re-admission within a month after the biopsy. Patients' names and hospital numbers were encoded into an electronic abstraction sheet, where they were assigned number codes. De-identified number codes were utilized for data analysis.

Data Analysis

Multivariate analysis was done to determine association between the various variables noted and development of complications. Pearson Chi-Square Test and adjusted Fisher's Exact Test were used for categorical data, and Mann-Whitney U Test was used for continuous data.

Analysis was done using SPSS program. P-values <0.05 were considered significant.

Receiver operating characteristic (ROC) curves were plotted for parameters found to be significantly associated with development of major complications. For parameters with acceptable areas under the ROC curve, threshold values were approximated by balancing sensitivity and specificity.

Definition of Terms

- 1. *Complication*** – development of sonographically evident hematoma, arteriovenous fistula (AVF), or pseudoaneurysm following ultrasound-guided percutaneous native renal biopsy
- 2. *Major complication*** – any complication requiring intervention such as embolization, partial or total nephrectomy, or blood transfusion
- 3. *Minor complication*** – any complication that improved or resolved without any of the aforementioned interventions

Results

A total of 984 records were retrieved. Patient demographics are listed in Table I. Histopathologic diagnoses are enumerated in Table II. Two patients' histopathologic reports were not available at the laboratory database.

Incidence of complications

Sonographically evident complications developed in 509 out of 984 patients (51.7%), but only 10 of these (1.0%) were classified as major based on the necessity for subsequent intervention (PRBC transfusion, embolization and/or nephrectomy). Complications recorded were hematoma (500 patients, 50.8%), AVF (60 patients, 6.1%), and pseudoaneurysm formation (4 patients, 0.4 %).

Table I. Demographics of adult patients who underwent ultrasound-guided percutaneous renal biopsy at the National Kidney and Transplant Institute from July 2012 to June 2015

Characteristic	Measure
Number of patients, N	984
Age, years	38.31 ± 13.63
Sex, male:female	431:553
Systolic blood pressure, mmHg	118.23 ± 13.75
Diastolic blood pressure, mmHg	77.83 ± 9.20
Hemoglobin, g/dL	12.43 ± 2.36
Hematocrit, %	36.33 ± 9.59
Platelet, x 103/uL	300.17 ± 131.85
Prothrombin time, sec	11.34 ± 1.35
Partial thromboplastin time, sec	34.82 ± 15.56
International normalized ratio	0.97 ± 0.11
Serum creatinine, umol/L	141.44 (88.40 – 239.87)

Measures are expressed as mean ± standard deviation, median (interquartile range), or absolute frequency

Among those with hematoma formation, 223 (22.7%) had approximate hematoma volumes of at least 10 ml, and 277 (28.2%) had approximate hematoma volumes less than 10 ml. Sixty patients (6.1%) developed AVF. There were only four cases (0.4%) of post-biopsy pseudoaneurysm, but two of these were classified as major complications.

Hematomas were detected in all 10 patients deemed to have major complications. One patient had concurrent AVF and pseudoaneurysm formation, two had concurrent AVF formation, and one had concurrent pseudoaneurysm formation.

All 10 patients with major complications had to undergo PRBC transfusion, making this the most common intervention performed in the study.

In addition to PRBC transfusion, one of these patients, a 25-year-old female, underwent selective renal artery embolization for persistent pseudoaneurysm and enlarging hematoma (maximum approximate volume of 83 ml). Her pre-biopsy laboratory values were as follows: low hemoglobin count (8.9 g/dL), low hematocrit (25.3%), low platelet count (106 x 103/uL), normal PT, PTT, INR, and percent activity (11.1 seconds, 31.2 seconds, 0.92, and 90%, respectively), and elevated serum creatinine (503.88 umol/L). Her renal length measured by ultrasound was within normal limits at 10.2 cm. She had a history of hypertension and diabetes. Her pre-biopsy blood pressure was 160/100. Renal biopsy was performed with three passes on the left kidney. A total of 59 glomeruli were obtained, and histopathologic findings were compatible with pauci-immune crescentic glomerulonephritis, with 3.0% cellular crescents and 32% global glomerulosclerosis. Thrombotic microangiopathy

Table II. Frequencies of histopathologic diagnoses

Diagnosis	N (%)
IgA nephropathy	372 (37.88%)
IgM nephropathy	2 (0.20%)
C3 glomerulonephritis	1 (0.10%)
Complement-mediated glomerulonephritis	1 (0.10%)
Immune complex-mediated glomerulonephritis	37 (3.77%)
Lupus nephritis	81 (8.25%)
Crescentic glomerulonephritis	7 (0.71%)
Other glomerulonephritis	54 (5.50%)
Focal segmental glomerulosclerosis	88 (8.96%)
Diffuse glomerulosclerosis	4 (0.41%)
Nodular glomerulosclerosis	1 (0.10%)
Hypertensive nephrosclerosis	5 (0.51%)
Diabetic nephropathy	32 (3.26%)
Amyloidosis	8 (0.81%)
Membranous glomerulopathy	32 (3.26%)
Thin basement membrane disease	39 (3.97%)
Minimal change disease	46 (4.68%)
Minor glomerular abnormalities	69 (7.03%)

with necrotizing angitis, hyperplastic arteriolitis and thrombosis, acute tubular injury, mild interstitial fibrosis and tubular atrophy were also noted. Post-biopsy ultrasound showed hematoma and pseudoaneurysm formation. On conventional renal angiography, three separate bleeding tracts were noted to lead to the pseudoaneurysm, and these were all successfully embolized using a total of six coils.

Another patient, a 42-year-old male, underwent emergency nephrectomy due to ruptured pseudoaneurysm. His pre-biopsy laboratory values were as follows: slightly low hemoglobin and hematocrit counts (12.4 g/dL and 34.5%, respectively), normal platelet count (260 x 103/uL), PT (12 seconds), PTT (35.5 seconds), INR (1.15), and percent activity (81%), and elevated serum creatinine (397.8 umol/L). His renal length measured by ultrasound was in the lower limit of normal at 9.1 cm. His pre-biopsy blood pressure was normal at 130/80. He had a history of hypertension and diabetes. Renal biopsy was performed with three passes on the right kidney due to presence of cysts and lithiasis on the left. A total of 42 glomeruli were obtained, with histopathologic diagnosis of focal segmental glomerulosclerosis, moderate interstitial fibrosis and tubular atrophy, marked arteriosclerosis and hyaline arteriolosclerosis. On post-biopsy ultrasound performed the day after the procedure, he was found to have approximately 30 to 40 ml of subcapsular hematoma, and a pseudoaneurysm. He was transfused with packed RBC

Table III. Distribution of variables in patients with and without post-biopsy complications

Variable	Value in patients with complications	Value in patients without complications	P-value
Age, years	37.39 ± 12.97	39.29 ± 14.26	0.052
Sex, male:female	207:303	224:250	0.040
Systolic blood pressure, mmHg	119.2 ± 14.29	117.15 ± 13.06	0.021
Diastolic blood pressure, mmHg	78.58 ± 9.14	77.02 ± 9.19	0.005
Hemoglobin, g/dL	12.31 ± 2.39	12.55 ± 2.31	0.178
Hematocrit, %	36.29 ± 11.71	36.38 ± 6.50	0.336
Platelet, x 103/uL	291.00 ± 97.25	310.33 ± 161.31	0.064
Prothrombin time, sec	11.36 ± 1.49	11.32 ± 1.18	0.496
Partial thromboplastin time, sec	34.99 ± 14.87	34.64 ± 16.31	0.048
International normalized ratio	0.98 ± 0.10	0.97 ± 0.12	0.263
Serum creatinine, umol/L	1141.4 (88.4 – 249.4)	132.6 (79.6 – 221.0)	0.194
History of hypertension, N (%)	229 (49.6%)	233 (50.4%)	0.092
History of diabetes, N (%)	41 (45.6%)	49 (54.4%)	0.180
Renal length by ultrasound, cm	10.26 ± 1.08	10.55 ± 1.17	0.000
Biopsy laterality, right:left	13:489	14:452	0.702
Number of bites	2.44 ± 0.57	2.39 ± 0.60	0.080

Table IV. Suggested threshold values based on receiver operating curves

Parameter	Suggested threshold value	Sensitivity	Specificity
Hemoglobin (g/dL)	10.55	80%	80%
Hematocrit (%)	30.55	80%	80%
Platelet count (x 103/uL)	245.50	70%	71%
Serum creatinine (umol/L)	296.50	80%	82%

and referred for surgical evaluation, but subsequently sent home for out-patient follow-up. A few days after discharge, the patient was re-admitted for severe flank pain. Ultrasound then showed significant increase in the volume of hematoma to approximately 1600 ml, likely from rupture of previously noted pseudoaneurysm. Emergency nephrectomy was done due to unstable vital signs.

Factors Associated with Occurrence of Complications

A number of variables were analyzed for possible association with the occurrence of complications, as shown in Table III.

Among the variables tested, female sex, higher systolic and diastolic blood pressure, longer partial thromboplastin time, and shorter renal length by ultrasound were found to have a statistically significant association with the development of complications (Table III).

Significant risk factors associated with development of major complications were lower hemoglobin, hematocrit and platelet counts (p values = 0.001, 0.001 and 0.001, respectively), higher serum creatinine level (p value = 0.001), higher systolic and diastolic blood pressures (p values = 0.000 and 0.019, respectively), and history of diabetes (p value = 0.024).

Of the factors associated with development of major complications, hemoglobin, hematocrit, platelet and serum creatinine levels were found to have acceptable areas under the receiver operating characteristic (ROC) curve (Figures 1 to 4). Suggested threshold values are shown in Table IV, with range of sensitivities and specificities outlined in the Appendix.

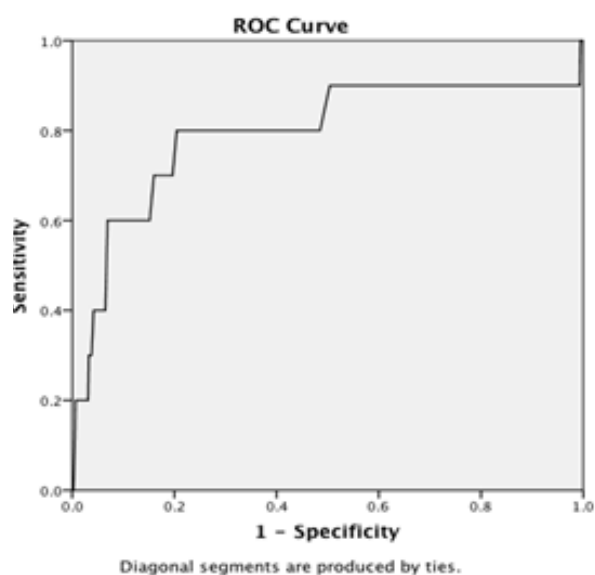


Figure 1. Receiver operating characteristic (ROC) curve of hemoglobin level as a predictor for developing major complication

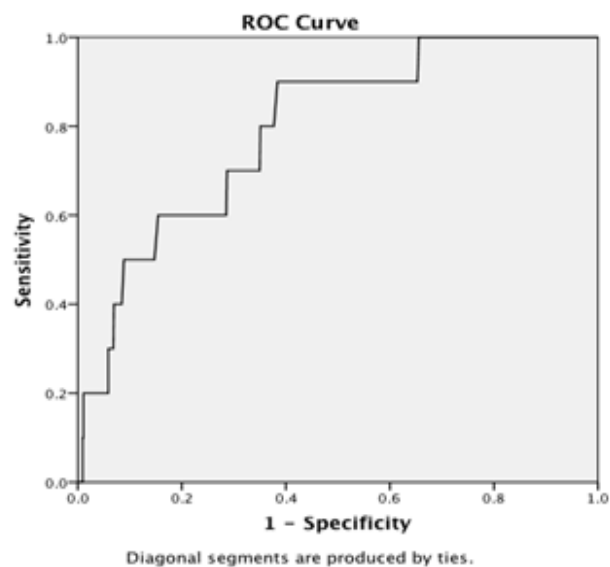


Figure 3. Receiver operating characteristic (ROC) curve of platelet level as a predictor for developing major complication

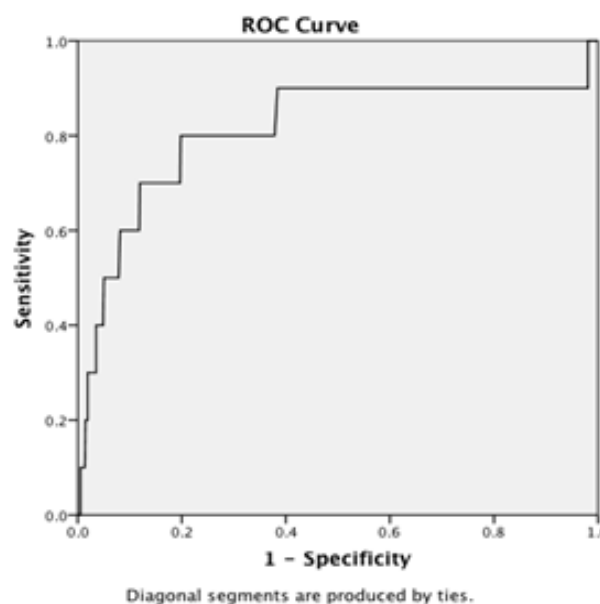


Figure 2. Receiver operating characteristic (ROC) curve of hematocrit level as a predictor for developing major complication

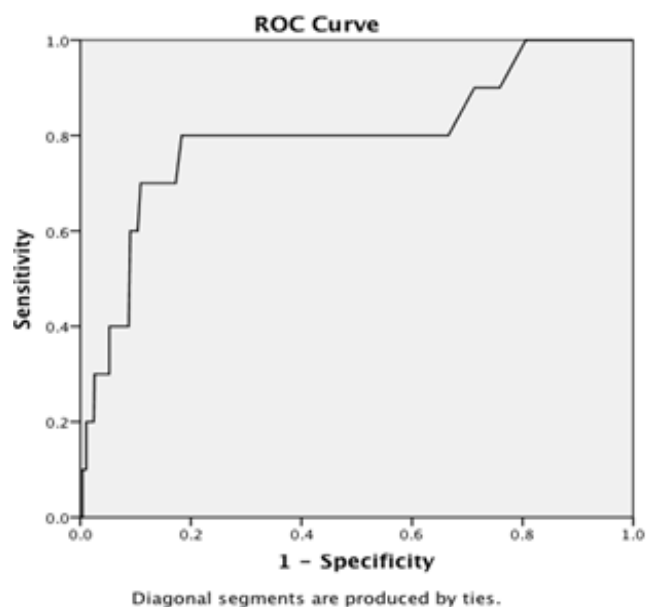


Figure 4. Receiver operating characteristic (ROC) curve of serum creatinine level as a predictor for developing major complication

Discussion

In this retrospective review of 984 patients who underwent ultrasound-guided percutaneous renal biopsy at the National Kidney and Transplant Institute, the incidence of renal biopsy complications was relatively high (51.7%) compared to international published data (5.3% to 34.1%).^{2,3,4,5} However, a great majority of these were minor complications, with only 1.0% requiring subsequent intervention. The most common complication detected in this study was hematoma (50.8%), consistent with previous researches.^{4,5} Pseudoaneurysm was the least common complication, seen in only four patients (0.004%), but it is noteworthy that two of these four patients had to undergo subsequent emergency nephrectomy and renal artery embolization, respectively.

Variables shown to be significantly associated with the development of major complications requiring subsequent intervention were higher systolic and diastolic blood pressures; lower hemoglobin, hematocrit and platelet counts; higher serum creatinine level; and history of diabetes. When minor complications were included in the analysis, female sex, longer partial thromboplastin time, and shorter renal length by ultrasound also emerged as significant risk factors, while hemoglobin, hematocrit, platelet, and serum creatinine counts, as well as history of diabetes, appeared negligible. Higher systolic and diastolic blood pressures were consistently associated with both major and minor complications.

Based on the study data, threshold values for some of the factors associated with development of major complications are suggested in Table IV. Future prospective researches may seek to validate these values for possible inclusion in local renal biopsy guidelines.

Most of the identified risk factors associated with the occurrence of complications, namely higher systolic and diastolic blood pressures, lower hemoglobin, hematocrit and platelet counts, deranged bleeding parameters, and higher serum creatinine levels, were consistent with international published data.^{3,4,6} Lower pre-biopsy hemoglobin and hematocrit counts have not been previously linked to renal biopsy complications, but may have contributed to the need for post-biopsy PRBC transfusion, and were thus associated with the occurrence of major complications. Likewise, there has been no reported link between history of diabetes and occurrence of significant post-biopsy complications in available literature, but diabetes has been associated with bleeding in several other organ systems and conditions, such as in patients with atrial fibrillation⁷ and in cirrhotic patients with gastroesophageal varices.⁸

The relatively high complication rate in this study may be due in part to the utilization of routine post-

biopsy sonographic findings as the basis for determining the presence of complications, whether or not these were clinically significant. This was in contrast to previous researches, which defined complications differently. Manno et al³ made use of both radiologic and clinical parameters such as flank pain, hematuria, and hypotension as criteria for the presence of complications. Waldo et al,⁵ as well as Whittier and Korbet,⁴ considered only clinically relevant signs and symptoms such as gross hematuria, flank pain, hypotension or decrease in hemoglobin requiring transfusion. While making use of sonographic findings as the basis for determining presence of complications minimized subjectivity and bias, it may have inflated the number of reported complications, which included even clinically silent ultrasound findings.

Another possible reason for the higher complication rate could be the relative lack of clear practice guidelines in the institution with regards to renal biopsy contraindications as of the study period. Previous studies employed stricter institutional protocols on the selection and exclusion of patients for the procedure, with consideration of some of the established risk factors for post-biopsy complications. In the study by Manno et al,³ biopsy was performed only on kidneys more than 9.0 cm in length, and oral nifedipine was administered to all patients with pre-biopsy blood pressures higher than 140/90. In the study by Hergesell,² biopsies were performed only on normotensive patients with normal coagulation parameters, and medications such as aspirin or non-steroidal anti-inflammatory drugs were withheld for at least five days prior to biopsy. They routinely tested for bleeding time on the morning prior to biopsy, and corrected or addressed any abnormality before the procedure. They likewise deferred biopsies on kidneys with cortical widths less than 10 mm. Although similar measures were taken by the nephrologists and radiologists who performed the renal biopsies in this study, the lack of standardized local guidelines on the performance of this procedure during the study period allowed for a wider leeway and subjectivity in terms of clinical decision-making.

This stresses the importance of adopting nationwide guidelines in the process of selecting and educating patients for renal biopsy. Although there are no absolute contraindications to performing the procedure, and the decision to perform it rests on the clinician's judgment of whether the risks outweigh the benefits and on the patient's consent, following a nationwide protocol would help the clinician comprehensively assess whether the patient is a good candidate for the procedure, educate him or her on the potential complications, and address modifiable risk factors.

A limitation of this retrospective study is that it inevitably relies on existing records, which may or may not contain complete and accurate data. Variables of interest may

not have been properly documented in the charts or information systems, and depend on the subjective opinions and unintentional biases of the medical team at certain points in time. Retrospective chart reviews are vulnerable to various errors, which may affect the quality of abstracted data.⁹

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Conclusion

These preliminary results pave the way for larger prospective studies to be conducted, focusing on the risk factors here shown to be statistically associated with the development of post-biopsy complications. Future researches may seek to validate the suggested threshold values for each of the parameters that significantly affect biopsy outcome. Furthermore, a scoring system may be devised to estimate the risk of developing post-biopsy complications. Ultimately, it is hoped that this would lead to the wide acceptance and utilization of locally appropriate evidence-based policies, and help guide clinicians and patients alike in deciding whether the risk of performing the procedure outweighs the benefit of obtaining a definitive diagnosis.

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