

## The Native Kidney Biopsy: Update and Evidence for Best Practice

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### Abstract

The kidney biopsy is the gold standard in the diagnosis and management of many diseases. Since its introduction in the 1950s, advancements have been made in biopsy technique to improve diagnostic yield while minimizing complications. Here, we review kidney biopsy indications, techniques, and complications in the modern era. We also discuss patient populations in whom special consideration must be given when considering a kidney biopsy and the important role that the kidney biopsy plays in nephrology training. These data are presented to develop best practice strategies for this essential procedure.

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### Introduction

As an invasive diagnostic test, a kidney biopsy is recommended if the following criteria are met:

- (1) A kidney biopsy is required to make a diagnosis or provide information that guides treatment.
- (2) The natural history of suspected diseases is associated with significant morbidity and/or mortality.
- (3) The natural history of these diseases can be improved with therapy (*i.e.*, if the natural history of these disorders could not be altered, then a biopsy would not be performed).
- (4) The treatments for these diseases differ between diagnoses that are made by kidney biopsy (*i.e.*, one therapy does not exist for all renal diseases for which a biopsy is performed).
- (5) The treatments' adverse event profiles are acceptable to your patient in his/her current state of health.
- (6) The risk of the procedure is acceptable to your patient in his/her current state of health.

These criteria have been increasingly met for the kidney biopsy since its initial description by Iversen and Brun in 1951, the introduction of immunofluorescence and electron microscopy, the linking of histologic findings with clinical outcomes, and the introduction of treatment regimens that could alter the disease course with acceptable side effect profiles (1). A kidney biopsy is oftentimes not recommended in patients with isolated microscopic hematuria or low-grade proteinuria (<0.5–1.0 g/d) unless another indication, such as reduced kidney function, is present. The kidney biopsy can be invaluable in assessing the extent of disease activity (*e.g.*, inflammatory cell proliferation, crescent formation, and necrosis) and chronicity (*e.g.*, sclerosis and fibrosis), which may help guide prognosis and therapy, as well as establishing renal

involvement of systemic diseases, such as autoimmune and paraprotein disorders (2).

Physicians must consider the risks of a kidney biopsy in the context of the perceived benefit that an individual patient may derive from having a histologic diagnosis. Anatomic characteristics, such as cysts in the lower renal pole, atrophic kidneys with thin cortices, or horseshoe kidney, may contraindicate a biopsy in some patients, but alternative biopsy techniques (see below) can be considered when systemic diseases with high morbidity and mortality are suspected. Equally important is nephrologists' input as to which patients would not benefit from a biopsy. Potential contraindications for kidney biopsy in individual patients are listed in Table 1.

### Biopsy Technique and Operator

#### The Percutaneous Renal Biopsy

The percutaneous renal biopsy (PRB) is the current standard of care, and most large case series describe ultrasound-guided PRBs performed by nephrologists or radiologists (3). PRBs are most commonly performed under local anesthesia with disposable, automatic, spring-loaded devices using 14-, 16-, or 18-gauge needles (outer diameter of 2.11, 1.65, and 1.27 mm, respectively). Some but not all comparative studies have shown that automated needles provide superior yield (more glomeruli) (4) and lower major complication rates (5) than older, hand-driven (Trucut) systems. Although some operators use trocars to help guide the biopsy needle, most biopsy series do not describe using this technique.

Adequate tissue (the criteria for which differs between diagnoses [2]) is obtained in 95%–99% of PRBs, with a typical yield of about 10–20 glomeruli when using 14- and 16-gauge needles (4). The diagnostic yield does not seem to differ significantly when comparing 14- and 16-gauge needles, but some (although not all) studies indicate lower yield with smaller (18-gauge) needles (6–12). Other factors,

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Table 1. Relative contraindications to percutaneous renal biopsy
<b>Condition</b>
Small kidneys or ESRD
Inability to provide informed consent
Multiple bilateral cysts
Uncorrectable bleeding diathesis, recent antiplatelet or anticoagulant therapy, or severe thrombocytopenia
Uncontrolled severe hypertension, which cannot be controlled with antihypertensive medications
Hydronephrosis
Urinary tract infection, pyelonephritis, or perirenal abscess/infection
Horseshoe kidney
Uncooperative patient or inability to follow instructions during biopsy

such as patient characteristics (*e.g.*, kidney size) and operator experience, may also affect diagnostic yield. The use of 14-gauge needles has been associated with higher transfusion (2.1%) rates compared with 16- (0.4%) and 18-gauge (0.6%) needles ( $P=0.05$ ) (13). Given these data, we use automated 16-gauge needles, and we immediately evaluate the adequacy of biopsy sampling with a light or dissecting microscope, which allows for appropriate division for light, immunofluorescence, and electron microscopic studies (Figure 1) (14,15).

Computed tomography (CT) may be used as a primary imaging modality or may be preferred in obese patients, those with complicated anatomies (*e.g.*, cysts or horseshoe kidney), and those for whom kidney visualization with ultrasound is difficult (16,17). Fluoroscopy-guided PRB with or without retrograde contrast injection through a urethral catheter has also been used for localization (18–20). Newer imaging techniques, such as CT fluoroscopy and fusion ultrasonography, may be useful in the future

in certain patients undergoing PRB (21). These options must be considered with the risk of radiation/contrast exposure and cost in mind.

Other Biopsy Techniques

Transjugular kidney biopsies (TJKBs) were initially described in the early 1990s, with many subsequent case series describing this technique in patients with contraindications to PRB or who required simultaneous liver/kidney biopsies (22). One series found no difference in diagnostic yield or major complications in patients undergoing PRB ( $n=400$ ) or TJKB ( $n=400$ ; 303 of whom had bleeding disorders) (23). However, contrast-induced nephropathy is a TJKB complication that is not encountered with PRBs, occurring in 7.8% of patients in one study (24), and some studies report high rates of capsular perforation that may require coil embolization (25).

A laparoscopic (through a retro- or transperitoneal approach) or open kidney biopsy may be the best option in selected circumstances, such as morbid obesity, solitary kidney, coagulopathy, failed PRB, polycystic kidney disease with rapidly progressive GN, high location of the kidney, and/or poor visualization with imaging (26–29). These approaches have the theoretical advantage of direct visualization and application of hemostatic materials (such as absorbable gelatin and oxidized cellulose) to the biopsy sites, but no studies have been performed to show improved complication rates.

Biopsy Operator

One retrospective study found no difference in diagnostic yield or complications (hematoma, need for transfusion, gross hematuria, pain, or infection) between ultrasound-marked, blind PRBs performed by nephrologists ( $n=271$ ) and real-time/ultrasound-guided PRBs performed by nephrologists ( $n=170$ ) or radiologists ( $n=217$ ) (30). It should go without saying that a kidney biopsy should only be done by someone skillful in performing the

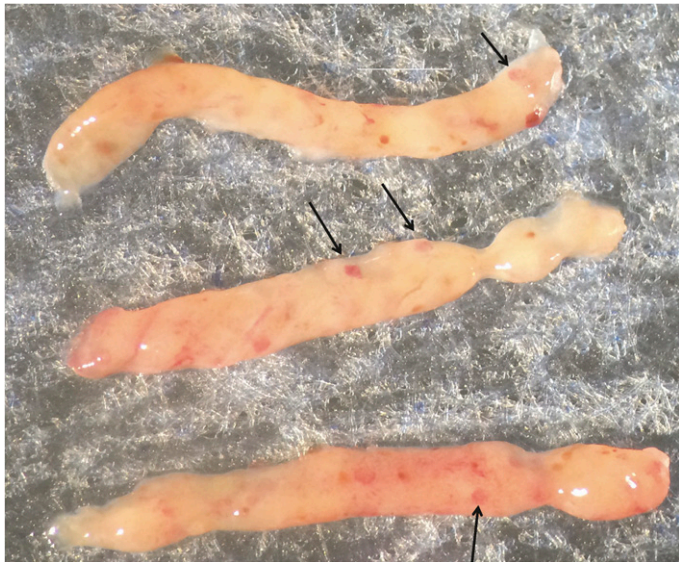


Figure 1. | Renal biopsy specimens as seen with a dissecting microscope. Black arrows point to glomeruli (wet prep, ×10).

procedure and when the tissue can be processed and interpreted by those with the skills necessary to do so (14).

### Biopsy Protocol and Specimen Processing

It is common practice before kidney biopsies to obtain a complete blood count, international normalized ratio/prothrombin time, activated partial thromboplastin time, serum creatinine, and a type and screen. Medications should be reviewed for agents that may increase bleeding risk (anticoagulants, antiplatelet agents, and nonsteroidal anti-inflammatory drugs), and an appropriate informed consent should be obtained. Adequate intravenous access is necessary. Anxious, uncooperative, and/or pediatric patients may require anxiolytics or general anesthesia to safely perform the procedure.

After ultrasound localization of the kidneys, the overlying skin is prepped and draped in a sterile fashion, and a local anesthetic (we use 1% buffered lidocaine) is infiltrated to the depth of the kidney. We perform real-time, ultrasound-guided PRBs using an automated, spring-loaded, 16-gauge biopsy needle as described previously (3). Post-PRB, we prescribe bed rest for 6 hours, and we monitor vital signs every 15 minutes for 2 hours, every 30 minutes for 4 hours, and then, hourly for the remainder of the observation period. A complete blood count is checked 6–8 hours after PRB, and a urine specimen is evaluated for gross hematuria and to confirm voiding before discharge.

Nephrologists and biopsy operators should also be competent at biopsy specimen division and processing (14,15). This is particularly important in centers that send their biopsies to outside pathology laboratories, because specimens for light, immunofluorescence, and electron microscopies require different processing and fixation methods. Nephrologists' input on the basis of the biopsy indication can ensure proper specimen division for optimum diagnostic and prognostic yield.

### Complications of the PRB

Complication rates after native kidney biopsy are derived mostly from retrospective and prospective case series at individual centers. The strengths of these studies include the large patient numbers (500–2000) and uniform intra-institution operators, expertise, and technique. Their limitations include interstudy heterogeneity in technique (blind/ultrasound guided), needle gauge and type (Trucut/Vim-Silverman/automated), operator (nephrologist/radiologist), and definitions of complications. In addition to reporting bias, these differences can confound the interpretation of the literature as a whole and may not reflect real-life practice.

#### Bleeding

Bleeding is the most common, clinically relevant complication after a kidney biopsy. Studies from the 1970s and 1980s showed CT evidence of bleeding in 57%–91% of patients (versus 70% on ultrasound) using older scanners, biopsy techniques, and needles (31–33). A decrease in hemoglobin level after PRB is very common, but generalized bleeding rates after PRB are difficult to state given the heterogeneity in how bleeding is defined and diagnosed between studies. We consider a major bleeding complication

as one that results in an alteration of clinical practice, leading to significant pain, extended hospital stay, urinary obstruction, requirement for blood transfusion, intervention, surgery, or death. Operators should also be aware that postural changes may contribute to variations in hemoglobin levels commonly observed after PRB (34).

Corapi *et al.* (13) conducted a systematic review and meta-analysis of all adult PRB studies from 1980 to 2011 (34 studies with 9474 biopsies meeting inclusion criteria) and found the rates of complications as listed in Table 2. Higher complication rates were observed when a 14-gauge needle (versus a 16- or 18-gauge needle) was used and for studies in which patients had a mean serum creatinine >2.0 mg/dl (2.1% versus 0.4%;  $P=0.02$ ), patients were >50% women (1.9% versus 0.6%;  $P=0.03$ ), >10% kidney biopsies were done for AKI (1.1% versus 0.04%;  $P<0.001$ ), and patients had a baseline hemoglobin <12 g/dl (2.6% versus 0.5%;  $P=0.001$ ). Trends toward increased bleeding risk were observed in studies where mean age was >40 years old (1.0% versus 0.2%;  $P=0.20$ ) and systolic BP (SBP) was >130 mmHg (1.4% versus 0.1%;  $P=0.09$ ).

Although the overall incidence of requiring a blood transfusion in this meta-analysis was 0.9% (95% confidence interval, 0.4% to 1.5%), transfusion rates as high as 5%–9% have been described in large single-center case series from major academic centers (7,12,35–37). This may be because of some PRBs being performed by nephrology trainees and more high-risk patients undergoing PRBs at large academic centers. Lower complication rates have also been observed in series that exclude high-risk patients (38).

#### Other Complications

Infection after kidney biopsy has been described in some case series (39), but if sterile technique is used and unless bowel perforation occurs, it is an extremely rare complication of PRB.

**Table 2. Risk of complications after percutaneous renal biopsy**

Complication	Incidence
<b>Minor (%)</b>	
Gross hematuria (95% CI)	3.5 (0.3 to 14.5) <sup>a</sup>
Hematoma on CT scan	57–91 <sup>b</sup>
<b>Major (%)</b>	
PRBC transfusion (95% CI) <sup>c</sup>	0.9 (0.4 to 1.5) <sup>a</sup>
Intervention (95% CI)	0.6 (0.4 to 0.8) <sup>a</sup>
Nephrectomy	0.01 <sup>a</sup>
Bladder obstruction	0.3 <sup>a</sup>
Death	0.02 <sup>a</sup>

95% CI, 95% confidence interval; CT, computed tomography; PRBC, packed red blood cell.

<sup>a</sup>Information from ref. 13.

<sup>b</sup>Information from refs. 31–33 and 81. Studies were conducted in the 1980s and 1990s using the CT scanners of that time; incidence may increase using CT scanners with higher sensitivities.

<sup>c</sup>Other large series from academic centers observed transfusion rates as high as 5%–9% (7,12,35–37).



Although the development of Page kidney after allograft kidney biopsy has been described (0.8% of patients in a recent case series [40]), no patients with Page kidney after native kidney biopsy have been reported (41). The puncture of other organs is a rare complication of the PRB. In patients where other organs (such as bowel) are in close proximity to the kidney, CT imaging and/or another biopsy approach (TJKB, laparoscopic, or open) may be required to safely perform the procedure.

### Timing of Complications

Analyzing the timing of complications is important in determining the optimal post-PRB observation period. The data on the timing of complications after PRB are composed of prospective and retrospective case series with intra- and interstudy heterogeneity in operator, needles used, and definitions of complications. Whittier and Korbet (42) found that 67% of major complications (need for transfusion or invasive procedure, acute renal obstruction or failure, septicemia, or death) occurred during the first 8 hours of observation, with 91% detected by 24 hours and 9% detected after 24 hours. In a smaller retrospective series, Simard-Meilleur *et al.* (36) found that 100% of complications in outpatients undergoing PRB occurred within 8 hours versus 72% of complications in inpatients and that 10% of inpatients had complications >24 hours after PRB. The most recent large biopsy series found that 91% of major complications occurred within 12 hours of PRB, with 7.4% occurring between 12 and 24 hours and 1.85% occurring after 24 hours (43). On the basis of these data, our practice is to discharge uncomplicated outpatients who live close to the medical center 8–12 hours after PRB but recommend an extended (24-hour) observation period for high-risk patients or those who live far from the hospital.

### Postbiopsy Imaging

Although post-PRB ultrasonography or CT is routinely performed in some centers, its utility in predicting relevant clinical complications or altering management has not been shown. Waldo *et al.* (44) analyzed 162 patients with native, ultrasound-guided PRBs (automated needle) who had an ultrasound 1 hour postprocedure. Minor complications occurred in 8% of patients, and major complications occurred in 8% of patients (transfusion,  $n=12$ ; radiologic intervention,  $n=2$ ); 69% of patients with minor complications and 87% of patients with major complications had a detectable hematoma. The size of the hematoma did not predict complication, although there was a trend toward association with a hematoma size >3 cm (55% versus 26%;  $P=0.06$ ). The positive predictive value of a hematoma for developing a complication was 43%, whereas the negative predictive value was 95%.

In another case series, Ishikawa *et al.* (45) retrospectively analyzed 317 PRBs at one center with an ultrasound performed 10 minutes after biopsy; 86% of patients had a detectable hematoma (13% had hematoma >2 cm). Although the presence of a >2-cm hematoma was associated with a greater absolute decrease in hemoglobin (6.9% versus 2.9% for <2 cm and 2.0% for no hematoma) and a hemoglobin decrease >10%, it was not associated higher rates of transfusion or intervention. These data and others (46) show

that the presence of hematoma on postbiopsy imaging does not predict clinically relevant complications, but the absence of hematoma has a high negative predictive value for complications and may be used to determine which patients can be discharged with a shorter observation period. Otherwise, we suggest that postbiopsy imaging be performed only when clinically indicated.

## Considerations and Management of Bleeding Risk after PRB

### Antiplatelet Agents

Although it is routine to stop antiplatelet agents before an elective procedure, only two studies have explored the association between antiplatelet agents and PRB complications. Mackinnon *et al.* (47) retrospectively compared complication rates after native PRB (ultrasound-guided, 16-gauge automated needles; median of two to three passes) between centers where antiplatelet agents were stopped 5 days before biopsy ( $n=75$ ) or continued ( $n=60$ ). Patients were not biopsied if they had a BP>160/90 mmHg, international normalized ratio >1.4, or platelet count <100×10<sup>9</sup>/L. Although continuation of antiplatelet agents was associated with a greater absolute decrease in hemoglobin and percentage of patients with a >1-g/dl drop, no difference in major complications (requirement for transfusion or radiologic or surgical intervention) was observed between patients undergoing elective (1.3% versus 0%;  $P=0.56$ ) or urgent (5.2% versus 3.4%;  $P=0.17$ ) PRB.

A second study by Atwell *et al.* (48) described a single-center experience of 15,181 percutaneous biopsies of multiple organs, including 5832 native and allograft kidney biopsies, between 2002 and 2008 and found no difference in bleeding between patients who did or did not take aspirin within 10 days of biopsy (1% versus 0.6%;  $P=0.53$ ). In the meta-analysis by Corapi *et al.* (13), the rate of transfusion did not differ between patients in whom antiplatelet agents were held for ≥7 days (nine studies; 2116 biopsies) and patients in whom antiplatelet agents were not held for ≤7 days (seven studies;  $n=4009$ ; 0.5% versus 0.7%,  $P=0.7$ ). However, given the limited data exploring this question and that most kidney biopsies are elective procedures, we hold antiplatelet agents for 7 days before the procedure when possible.

### Peribiopsy Anticoagulation

Patients who require chronic anticoagulation with warfarin or low molecular weight heparin pose logistic problems but can often safely undergo a PRB with a brief period off anticoagulation or use of a heparin bridge in the peribiopsy period. Because there are no studies exploring this issue specifically in PRBs, we adhere to evidence-based guidelines on the perioperative management of antithrombotic therapy (Table 3) (49). There are no data on the effect of newer anticoagulants on PRB complication rates.

### Desmopressin

Manno *et al.* (50) explored the use of desmopressin acetate (0.3 µg/kg 1 hour before the procedure) in native, ultrasound-guided kidney biopsies in a placebo-controlled, double-blind, randomized, controlled trial in 162 patients with preserved renal function (creatinine <1.5 mg/dl

**Table 3. Perioperative management of antithrombotic therapy**

Agent	Patient Population	Recommendation (Recommendation Grade)
Aspirin	High risk for CV event Low risk for CV event	Continue aspirin (2C) Stop 7–10 d before procedure (2C)
Vitamin K antagonists ( <i>e.g.</i> , warfarin)	High risk for thromboembolism Low risk for thromboembolism	Use bridging anticoagulation (2C) Stop 5 d before procedure (1C); resume 12–24 h after procedure (2C)
Intravenous UFH as bridging anticoagulation LMWH as bridging anticoagulation	High risk for thromboembolism High risk for thromboembolism	Stop 4–6 h before procedure (2C) Last therapeutic dose 24 h before procedure; for procedures at high risk of bleeding, resume 48–72 h after procedure (2C)

CV, cardiovascular; 2C, weak recommendation on the basis of low-quality evidence; 1C, strong recommendation on the basis of low-quality evidence; UFH, unfractionated heparin; LMWH, low molecular weight heparin. Modified from ref. 49, with permission.

and/or eGFR >60 ml/min per 1.73 m<sup>2</sup>) and normal coagulation parameters. Desmopressin use was associated with fewer (13.7% versus 31%) and smaller ultrasound-detected hematomas after biopsy but did not result in fewer transfusions or interventions, and no serious adverse events were observed. Additionally, a retrospective, single-center analysis found that patients with prolonged bleeding time tests continued to be at increased risk for PRB complications, despite preprocedure correction with desmopressin (51). No study has explored the effect of desmopressin exclusively in patients with severe renal dysfunction, the patient population in which desmopressin is most often considered.

### Hypertension

The data on the effect of high BP on PRB complication rates are not consistent, and a selection bias exists, because hypertension (usually defined as >140/90 mmHg) is an exclusion criteria in much of the biopsy literature. The meta-analysis by Corapi *et al.* (13) found an increased risk of complications for patients whose SBP was >130 mmHg that was not statistically significant but may be clinically significant (1.4% versus 0.1%; *P*=0.09). Another series found a higher risk of bleeding in patients with prebiopsy SBP ≥160 versus <160 mmHg (10.71% versus 5.25%; *P*=0.03), diastolic BP ≥100 versus <100 mmHg (13.04% versus 5.38%; *P*=0.02), and mean arterial pressure ≥120 versus <120 mmHg (12.5% versus 5.1%; *P*<0.01) (52). However, this difference was not observed when patients with a history of hypertension were stratified by prebiopsy BP level, indicating that a history of hypertension was the independent risk factor. Given that most patients' BPs can be controlled with medications on the day of the biopsy, and that many patients getting biopsies have a history of hypertension, we attempt to control the BP to <160/100 mmHg and preferably, <140/90 mmHg.

### Coagulopathies and Thrombocytopenia

Most biopsy series exclude patients with coagulopathies and thrombocytopenia (usually <100×10<sup>9</sup>/L). One series found an increased risk of symptomatic hematoma in patients with platelet counts <140×10<sup>9</sup>/L (36).

### Other

Korbet *et al.* (35) found no difference in complication rates when stratified by the number of passes or cores taken, and another study found no difference in complications (pain requiring analgesics or bleeding risk) with 2 versus 7 hours of strict bed rest after kidney biopsy (53). No data exist to guide how long manual compression should be applied after kidney biopsy.

### Patient Populations with Special Considerations for Kidney Biopsy

#### Elderly/Very Elderly Patients

AKI (54–56) and CKD (57) are common in elderly (≥60–65 years of age) and very elderly (≥80 years of age) patients (Table 4). Elderly patients make up a small proportion (3%–13%) of kidney biopsy registries, possibly because of concerns about PRB risk as well as the perception that treatment (immunosuppression) –associated adverse events may outweigh clinical benefit in this population (54,56,58). However, these perceptions are not supported by the literature.

One small prospective study compared complication rates after PRB between age groups and found a higher incidence of gross hematuria in patients 61–78 years old (*n*=26; 15%) versus those <60 years old (*n*=184; 0.03%) but no difference in hemodynamic compromise, perinephric hematoma, or need for vascular intervention (59). None of the large biopsy series or the meta-analysis by Corapi *et al.* (13) identified age as an independent risk factor for complications. Additionally, many diagnoses are made on PRB in the elderly who are potentially treatable and have implications for extrarenal organ involvement. Notably, one third of biopsies for AKI in this population reveal pauci-immune GN (60), and one retrospective case series found a lower rate of ESRD at 1 year and a lower rate of ESRD and mortality at 2 years in very elderly patients with biopsy-proven ANCA-associated vasculitis who were treated versus those who were not treated (61).

### Pregnancy

Indications for a kidney biopsy in pregnancy include unexplained renal failure, symptomatic nephrotic syndrome,

**Table 4. Patient populations with special considerations for kidney biopsy**

Patient Population	PRB Risk	Additional Considerations
Elderly ( $\geq 60$ –65 y of age)	No difference in major complications versus younger patients (13,59)	Treatment options may differ because of age-specific side effects
Pregnancy	Systematic review (63) found complication rate of 7% (2% major and 5% minor) during gestation versus 1% after pregnancy ( $P < 0.01$ ); all complications occurred during gestation weeks 23–28; insufficient evidence to determine association risk of fetal loss	Lateral decubitus positioning or sitting upright may be preferred because of the gravid uterus; treatment options may be limited; biopsy may distinguish preeclampsia from other disorders
Cirrhosis	Insufficient evidence to determine PRB risk (published safety data are on TJKB)	Immunosuppression options may be limited; coagulopathies are common
Amyloidosis and monoclonal gammopathies	Limited data do not show increased risk (68–71)	
Solitary kidney	Limited data do not show increased risk (66)	
Horseshoe kidney	No published data on risk	May be high risk because of anomalous vasculature and proximity to aorta
Mechanical ventilation	No published data on risk	
Ventricular assist device	No published data on risk	Acquired von Willebrand syndrome is common and may increase bleeding risk (82)
Patient on ventilation	Limited data do not show increased risk (83)	A ventilator pause can be used to stop kidney movement with respiration

PRB, percutaneous renal biopsy; TJKB, transjugular kidney biopsy.

to help guide management of patients with lupus nephritis (62), and to make/exclude the diagnosis of preeclampsia. Treatment options are limited given the teratogenicity of some agents commonly used in glomerular disease. There is also concern for increased complication rates in pregnant patients because of increased renal blood flow during gestation. Because a gravid uterus can affect a patient's ability to lie prone, alternate positioning (sitting upright or lying in the lateral decubitus position) for PRB may be preferred.

In a systematic review, Piccoli *et al.* (63) found that, of 197 PRBs performed during pregnancy that also reported complications, four major events occurred (2%; two of which were associated with preterm delivery, and one of which may have been associated with fetal death) at a median time of 25 weeks gestation (range =23–26 weeks). All major complications occurred during weeks 23–28 of pregnancy, whereas no complications occurred in early (up to 21 weeks) or late (28 weeks to term) phases. Minor complications (hematomas not requiring transfusion or macrohematuria with loin pain) occurred in 5% of intra-gestational PRBs. The total complication rate for PRB after pregnancy ( $n=268$ ) was 1.3% ( $P < 0.01$  versus during pregnancy). Importantly, this review found that PRB changed management in 66% of patients. This study is limited in that it is comprised of mostly retrospective case series and that only one half of the published literature on PRB in pregnancy reported complication rates. One controversial prospective study compared complication rates in 36 pregnant women who underwent PRB for hypertensive disease with 18 healthy pregnant women as controls, finding only

one major complication in a patient with severe preeclampsia (64).

### Hepatic Failure

In addition to the standard indications, a kidney biopsy may be indicated in a patient who is cirrhotic to make a diagnosis of hepatitis C-associated GN and cryoglobulinemic vasculitis or decide if a patient is a suitable liver/combined liver-kidney transplant candidate. However, patients who are cirrhotic are at increased risk for procedure-associated bleeding as well as immunosuppression-associated infections.

There are no published case series on PRBs in patients with cirrhosis. A case series of 70 patients who were cirrhotic and underwent TJKB (because of thrombocytopenia and coagulopathy) reported the need for blood transfusion in 3 patients and reversible AKI in 1 patient (65). As noted above, TJKBs carry the risk of other complications, such as contrast-induced nephropathy and capsular perforation (23–25,65).

### Solitary Kidney and Horseshoe Kidney

Data on PRB complications with a solitary kidney are limited. One prospective registry included successful PRBs in eight of nine patients with solitary kidneys, with a minor complication (gross hematuria) occurring in only one patient (66). Although the complication rates of PRBs in solitary kidneys may not be higher, the consequence of a major complication can be more severe in these individuals. We agree that a solitary kidney biopsy should no longer be considered an absolute contraindication to PRB (67),

particularly in patients in whom a PRB can diagnosis a systemic and life-threatening disease, but PRBs should be performed by expert operators with an extended observation period.

Patients with a horseshoe kidney may be at increased risk of bleeding after PRB because of anomalous vasculature and proximity to the aorta. The data on biopsy of horseshoe kidney are limited to case reports. If a biopsy is recommended, use of color Doppler on ultrasound, alternative (CT) imaging, or other techniques (such as laparoscopic kidney biopsy) may be indicated.

### Monoclonal Gammopathies and Paraprotein Diseases

Patients with monoclonal gammopathies may require a kidney biopsy to document end organ damage from the offending paraprotein. Although it has been suggested that patients with monoclonal gammopathies and amyloidosis have a higher risk of complications from bleeding diathesis (68), there is no evidence that this translates to a higher clinical risk with PRBs. One series found a statistically increased risk of bleeding in patients who had renal amyloidosis (69), but the definition of bleeding was a hemoglobin decrease  $>1$  g/dl and did not include need for transfusion or intervention. A second series found no difference in overall (9.9% versus 10.6%) or major (4% versus 2.1%;  $P=0.40$ ) bleeding complications after PRB in patients with systemic amyloidosis versus controls (70). Another series found no increased risk of PRB complications for patients with monoclonal gammopathies versus controls (without monoclonal gammopathy; 4.1% versus 3.9%;  $P=0.88$ ) (71).

### The Role of Nephrologists in Kidney Biopsies

The Accreditation Council on Graduate Medical Education requires that nephrology fellows must be able to competently perform PRBs of both native and transplanted kidneys (72), and the American Board of Internal Medicine requires that competence in the performance of native and allograft PRBs be verified by the fellowship program director for initial certification in nephrology (73). Requirements for training and determination of competence are at the discretion of the individual training program and vary widely (74). In one survey of nephrologists who completed their fellowship training from 2004 to 2008, 15%–20% indicated that they did not feel competent performing native and transplant PRBs (75). Evidence-based standards for assessment and documentation of proficiency among nephrology fellows are needed (76), and use of simulation training may enhance competency (77,78).

It is a matter of ongoing debate as to whether nephrology fellowship programs should be required to provide sufficient training for graduates to independently and safely perform PRBs (79). Some of the reasons cited for eliminating this requirement include time constraints, malpractice insurance costs, nephrologists do not do biopsies in practice, and inability to provide sufficient supervised experience. In fact, many nephrologists continue to perform kidney biopsies, and with proper training, nephrologists can become experts at ultrasound marking for biopsy (80). Inability of training programs to provide sufficient supervised experience to achieve this requirement should not

be used as justification for removing (or ignoring) the requirement.

Given how integral it is in the diagnosis and treatment of patients with kidney disease, we believe that the PRB should remain an essential component of nephrology training and practice. Rather than giving up performance of a procedure long considered to be a critically important component of the scope of practice of nephrologists, we believe that standards for establishing and documenting that all fellows are competent to perform kidney biopsies independently and without direct supervision at the completion of fellowship are essential and urgently needed.

### Disclosures

None.

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