Renal biopsy

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Abstract

Renal biopsy is an important diagnostic tool in nephrology and transplantation. Improvement in the technique over recent years has led to successful tissue yield with reduced risk of bleeding, making percutaneous renal biopsy a safe procedure with better outcomes. Adequate tissue is obtained in >99% of cases. The main complication is bleeding, with a life-threatening complication rate of 0.1%. Nevertheless, it is vital to justify the need for a renal biopsy as it is not without risk, and this decision should be consultant-led.

Keywords Adequacy; bleeding; MRCP; percutaneous renal biopsy; safety

Key points

- Renal biopsy is important in the diagnosis of renal disease
- The main complications are related to bleeding
- Renal biopsy should be avoided or deferred when the risk of bleeding is too high

Introduction

The technique of percutaneous renal biopsy (PRB) has developed progressively since its introduction in the early 1940s. The current use of real-time ultrasound-guided puncture with modern biopsy needles and better quality imaging has led to better diagnostic yield with fewer complications.

The value of renal biopsy

PRB is an important tool for the assessment of disease activity and chronicity. The presence of scarring and fibrosis enables the pathologist to estimate renal prognosis. This guides the treatment and management of a disease, and also allows the treating physician to avoid unnecessary therapies such as heavy immunosuppression. Identifying a pathological process during transplantation work-up can provide information on the likelihood of post-transplant disease recurrence. The indications for the procedure are shown in Table 1 and the contraindications in Table 2.

Nephrotic syndrome

In the absence of a systemic disease or evidence of drug-related injury, the glomerular pathology underlying this condition in an adult can only be made confidently with a PRB. However, in children presenting with nephrotic syndrome, minimal change disease (by far the most common cause of nephrotic syndrome in children) can be assumed unless there are atypical features, such as resistance to corticosteroid treatment, positive nephritic screen, visible haematuria, abnormal renal function and a positive family history of renal disease. PRB is more of a challenge in children and is often performed under sedation or even general anaesthesia.

Acute kidney injury

PRB is warranted in acute kidney injury if there is no sign of significant renal recovery despite all reversible causes having been addressed. An early biopsy can be indicated if there is active urinary sediment or the possibility of drug-related injury (e.g. interstitial nephritis).

Systemic disease and infections

Systemic conditions that can present with renal manifestations include diabetes mellitus, amyloidosis, myeloma, autoimmune diseases, and infections such as tuberculosis, HIV and hepatitis B and C. In patients with these systemic infections, histopathological findings can provide a valuable guide to the most effective treatment regimen. In anti-glomerular basement membrane disease or vasculitis, PRB not only confirms the diagnosis, but also identifies the extent of acute inflammation and any chronic changes; this is important information for deciding when to initiate treatment and how long to continue it for, particularly when the treatments themselves have an associated morbidity and mortality.

Renal transplant

Renal allograft biopsy is performed mainly to diagnose rejection and guide its treatment, but also to look for *de novo* and recurrent disease, drug toxicity and viral nephropathy. Many centres

Indications for renal biopsy in native and transplant kidney

Native kidney	Transplant kidney
Proteinuria >100 mg/dl	Persistent/unexplained rise in serum creatinine
Renal manifestations of systemic disease	If serum creatinine has not returned to baseline after treatment for acute rejection
Unexplained chronic kidney disease	7–10 days after renal transplantation if there is delayed graft function
Microscopic haematuria (relative indication)	If expected renal function has not been achieved 1–2 months after transplantation
Acute kidney injury	New onset proteinuria/proteinuria >3 g/dl

Table 1

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Contraindications to PRB in both native and transplant kidney

Absolute contraindications	Relative contraindications
Polycystic/multicystic kidneys	Single kidney excluding transplant kidney
Anatomical abnormalities (e.g. hydronephrosis)	Pregnancy
Known bleeding diathesis uncorrected	Thin cortices bilaterally
Uncontrolled hypertension (blood pressure >160/90 mmHg)	Small kidneys bilaterally
Uncooperative patient	Sepsis
	Antiplatelet agent/anticoagulant treatment
	Patient unable to consent (e.g. patient on intensive care unit)

Table 2

perform implantation and 'protocol' biopsies as part of routine monitoring of graft function.

Isolated haematuria

In the absence of structural abnormalities in the genitourinary tract, persistent microscopic haematuria can be an indication for PRB, especially if the family history suggests genetically inherited renal disease, or haematuria is found during donor work-up for transplantation. However, in the absence of significant proteinuria, many clinicians argue that the likelihood of finding a lesion needing treatment is low and the risks outweigh any potential benefits.

Non-nephrotic range proteinuria

In patients with proteinuria <3.5 g/24 hours, PRB can identify a disease process, provide prognostic information and guide therapy.

Unexplained chronic kidney disease

With normal imaging findings, negative immunology and serology, and no evidence of protein or blood on a urine dipstick, a biopsy can still be indicated if the cause of chronic kidney disease is unclear. Chronic tubulo-interstitial disease, such as that seen in sarcoidosis or tuberculosis nephritis, can be identified.

Percutaneous renal biopsy as a procedure

Pre-biopsy preparation checklist

- The kidneys should be of normal size with no structural defects that could complicate the procedure.
- Blood pressure should be <160/90 mmHg.
- The urine should be sterile.
- Haemoglobin should be >80.0 g/dl, platelet count >80 × 10^9/litre, international normalized ratio <1.2, and partial thromboplastin time and activated partial thromboplastin time <1.2 (prolonged times require further investigation with a mixing study). The safety of PRB in patients with deranged coagulation function is controversial. An abnormal coagulation test does not appear to predict increased bleeding risk, especially if there is no history of previous bleeding.
- Aspirin and antiplatelet agents should be stopped 5–7 days before the procedure.
  - Patients taking a coumarin anticoagulant should have a risk–benefit assessment. If anticoagulant cover is essential, warfarin should be converted to low-molecular-weight heparin, which should be omitted for 24 hours before the procedure. In certain cases, intravenous heparin is also required, with only a small gap in therapy at the time of procedure. Heparin, warfarin etc can be restarted once there is clear evidence that there is no active bleeding. Haematology advice should be sought when patients are taking novel anticoagulants as standard laboratory tests can be falsely reassuring.
  - Patients taking antiplatelet agents who require urgent biopsy can be given a platelet transfusion to minimize the risk of platelet dysfunction, although there are no clear guidelines on this. A recent study suggested that stopping antiplatelet agents >3 days before PRB had no effect on the rate of major complications, but continuing aspirin at high dose for <3 days before the biopsy carried a 6-fold relative risk of major bleeding.[1]
- Administration of desmopressin acetate (DDAVP) 30 minutes before the procedure has been based on historical practice rather than clear evidence of benefit. It was routinely administered in patients with significant renal impairment: blood urea nitrogen >56 mg/dl (serum urea >20 mmol/litre) or serum creatinine >3 mg/dl (250 micromol/litre). However, many units no longer pursue this approach.

The procedure

The kidney is identified using ultrasound and a suitable site for biopsy identified (Figure 1). The skin is sterilized and local anaesthetic instilled into the skin and down to the kidney under direct ultrasound guidance. A 2–3 mm cut is made in the skin and the biopsy needle is guided towards the kidney (Figure 2). While the patient holds their breath in inspiration (unnecessary during transplant kidney biopsy), the needle is inserted into the kidney and the sample taken from the lower/outer pole (in transplant biopsy, the upper/outer pole). Two cores are usually taken to ensure a diagnostic sample. The patient then lies supine for 4–6 hours depending on local protocols, and is discharged later the same day.

The tissue sample is sent for light microscopy. Immunofluorescence and electron microscopy are performed after discussion between the nephrologists and pathologists.

Post-biopsy care and management

After the procedure has been completed, the patient is rolled over to lie flat on their back for 4–6 hours of strict bed rest. During this period, any voided urine is observed for visible haematuria. The development of flank or abdominal pain, visible haematuria or deranged vital observations should prompt urgent clinical assessment.

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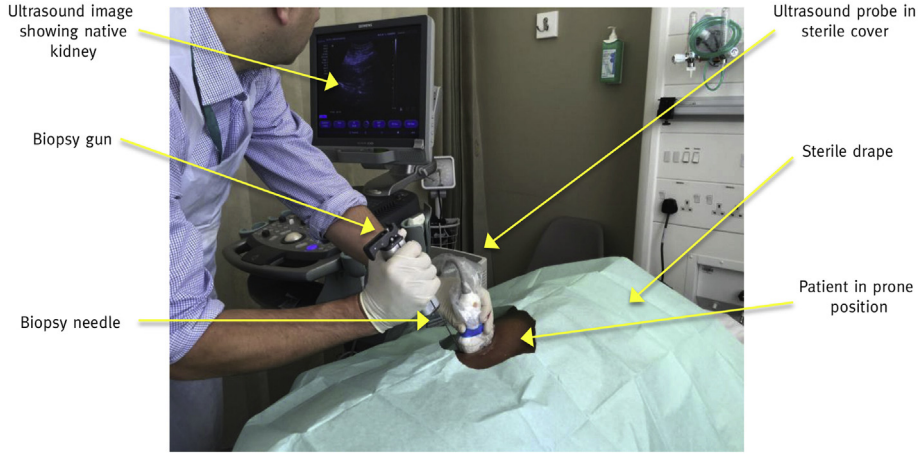

Figure 1 An image of a native renal biopsy being performed. The patient is instructed to lie in a prone position.

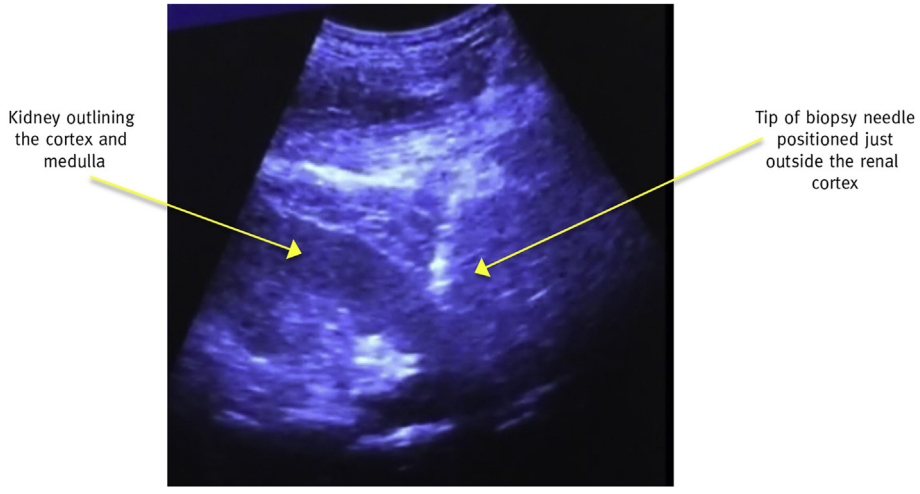

Figure 2 Ultrasound-guided image of a native kidney during a renal biopsy with the needle lying just outside the renal cortex before the sample is taken.

PRB was previously an inpatient procedure with overnight stay, but cost has led to a wider use of day-case procedures. However, a recent study found that more than one-third of minor and major complications occurred >8 hours after the procedure, and recommended an observation period of at least 24 hours.[2] No studies have shown the optimal observation time required for assessment of risk after the procedure. Most units stratify patients for day-case PRB according to individual risk, taking into account frailty, lack of home support and travelling distance from the centre.

On discharge, patients are advised to avoid any heavy lifting or strenuous activity for a week.

Renal biopsy complications[3]

Bleeding is the most frequent complication of PRB. It is more common in women and older patients, and in patients with hypertension, raised serum creatinine, uraemia or a known bleeding diathesis; it also occurs when there has not been sufficient time to stop antiplatelets or anticoagulants.

Minor bleeding complications include macroscopic haematuria, clot retention and post-biopsy haematoma. Major bleeding includes the need for blood transfusion and intervention. A recent meta-analysis showed that the overall rate of bleeding was 3.5%, with 0.9% of patients requiring blood transfusion and 0.6% angiographic intervention. Life-threatening complications occur in <0.1%.[4] Transplant renal biopsy seems to carry a lower complication rate than native renal biopsy, but there are fewer data on renal transplant biopsies. Bleeding complications can usually be managed with bed rest and blood product support if required. Radiological intervention can be necessary in the event of uncontrolled bleeding despite optimal medical management and correction of factors that could promote bleeding.

Formation of arteriovenous fistula is a rare complication; if identified, it can be embolized.

Infections resulting from perinephric haematomas can usually be managed medically and rarely require nephrectomy.

Injury to other organs such as the spleen, liver, lung (causing haemo/pneumothorax) and bowel can occur, especially in renal transplant biopsies.

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Page kidney occurs when a resulting perinephric haematoma compresses the kidney, causing renin-mediated hypertension; pulmonary oedema can result.

Death as a result of bleeding usually occurs in patients with underlying cardiac disease that is unmasked by bleeding, leading to myocardial infarction.

Sample yield and adequacy

There is no consensus on the number of glomeruli, tubules or vessels required to provide an accurate diagnosis. In some conditions, such as membranous glomerulonephritis and amyloidosis, only one glomerulus is required for an accurate diagnosis; however, as a general rule, a native kidney biopsy should contain at least 20 glomeruli to help exclude any focal pathology. In transplant biopsies, according to the Banff criteria, at least 10 glomeruli with two arteries are required.

Alternative biopsy techniques

If PRB proves unsuccessful or there is any tendency towards a bleeding diathesis, a sample can be obtained using one of the following methods, provided appropriate local expertise is available:

- US-guided biopsy with an injection of Gelfoam®/thrombin into the biopsy tract using a co-axial needle
- CT-guided PRB – performed by radiologist with an approach similar to PRB (and useful in obese patients)
- transjugular renal biopsy – used in patients with a bleeding diathesis, hypertension or morbid obesity and those being ventilated. The procedure is technically complex and results in the retrieval of fewer glomeruli than PRB. Transjugular biopsy is reserved for high-risk patients if renal biopsy is crucial. As such, it still carries a high (30%) complication rate because of selection bias of the candidates
- open renal biopsy – a surgical approach involving general anaesthesia. It is a relatively safe technique but is used selectively owing to the risk of general anaesthesia and the recovery period involved
- laparoscopic renal biopsy – performed using a retroperitoneal or transperitoneal approach; this method combines the advantage of PRB with low morbidity.

Future of renal biopsy

Despite current research to identify novel biomarkers that could aid diagnosis, especially in high-risk patients, and the monitoring of disease activity, renal biopsy remains the gold standard in providing an accurate diagnosis and prognosis in patients with renal disease. In certain conditions, such as membranous glomerulonephritis or amyloidosis, it could be argued that the combination of nephrotic syndrome with suggestive other investigations – PLAR2 (antiphospholipase A2 receptor) antibodies or positive serum amyloid protein scanning – makes the diagnosis highly likely and biopsy could be of less diagnostic benefit as these tests are highly specific for the underlying disease. In the case of membranous glomerulonephriris for example when the presentation might be with pulmonary embolism requiring anticoagulation a positive PLAR2 in this context could avoid a risky biopsy. ◆

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