Kidney biopsy

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Abstract

The causes of acute and chronic decline in kidney function are vast. Understanding the underlying diagnosis is essential to slow the progression of the kidney disease or achieve recovery. Detailed clinical assessment and simple investigations can help identify the nature of kidney injury (pre-renal, intrinsic, post-renal). Used appropriately, kidney biopsy has the potential to generate valuable information to aid diagnosis, guide prognosis and management, and identify relapse of intrinsic kidney disease. However, kidney biopsy is an invasive procedure with significant, albeit small, complications because of the risk of bleeding. The decision to proceed should be led by the nephrology team and requires a careful risk–benefit assessment and close discussion with the patient.

Keywords Haematuria; kidney biopsy; proteinuria; renal insufficiency; uraemia

Key points

- Only a minority of patients require investigation with a kidney biopsy; when kidney biopsy is used appropriately, the findings can be invaluable to diagnosis and management
- Complications arise secondary to bleeding; kidney biopsy should be completed under the guidance of nephrology teams and in centres with interventional radiology support
- Treatment should not be delayed for a kidney biopsy if the diagnosis is clear from other investigations

Introduction

Despite advances in biochemical and imaging techniques, kidney biopsy remains an essential investigation for the diagnosis of intrinsic kidney disease. In addition to diagnosis, a biopsy can provide crucial information about prognosis and disease activity that helps to guide management. However, the value of a clinical result relies greatly on the indication as well as the procedure itself. This article summarizes common indications for ultrasound-guided percutaneous kidney biopsy in acute and chronic presentations of kidney disease, and practical information about the technique for non-specialists.

Indications for kidney biopsy

A decline in kidney function should prompt the investigations outlined in Table 1. An immunological screen is important in patients with acute kidney injury (AKI) and an active urinary sediment (i.e. blood and protein on urine dipstick). Not all patients with a decline in kidney function require a kidney biopsy (the minority in fact), but patients presenting with nephrotic syndrome often require one, as do individuals who present with AKI or chronic kidney disease (CKD) where the diagnosis is not clear.

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Urinalysis by urine dipstick is among the most important investigations in the work-up of a decline in kidney function. Blood and/or protein on urine dipstick often indicates intrinsic kidney disease and warrants an evaluation with kidney biopsy in certain circumstances. Below, we discuss presentations with haematuria/proteinuria that may necessitate further investigation with a kidney biopsy, and those that may not.

Haematuria

Haematuria may be classified as 'visible' or 'non-visible'. Both can be caused by nephrological (e.g. glomerulonephritis) or urological (e.g. malignancy, infection, calculi) pathology. Urological causes should not be investigated with a kidney biopsy. Figure 1 summarizes an evaluation and referral process for both visible and non-visible haematuria.[1]

Visible haematuria

A single episode of visible haematuria requires investigation, and transient causes should be excluded by rechecking a urine dipstick after an acute episode has resolved. Anticoagulant and antiplatelet therapy worsen haematuria but will not be the precipitant.

Pink-stained urine or frank blood indicates bleeding along the urinary tract – a urological aetiology. Visible haematuria that is dark ('cola-coloured') suggests a nephrological cause because of haemoglobin being converted to methaemoglobin in the acidic environment. Symptomatology is essential: for instance, flank pain suggests ureteric colic, while intercurrent upper respiratory tract infection followed by cola-coloured urine is suggestive of post-infectious glomerulonephritis or immunoglobulin (Ig) A nephropathy.

Isolated non-visible haematuria with normal renal function

Kidney biopsy to investigate non-visible haematuria on its own with normal renal function and normal blood pressure is unlikely to change management. Thin basement membrane nephropathy and IgA nephropathy are frequent causes. However, annual monitoring in primary care (blood pressure, urinalysis, serum creatinine concentration) are indicated in persistent isolated non-visible haematuria because there is a significant, albeit small, chance of developing CKD and progressing to end-stage kidney disease (ESKD).[2]

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Summary of the essential investigations to evaluate a decline in kidney function

Essential initial investigations to evaluate renal function

Blood tests	Renal profile with eGFR
	Full blood count
	Bone profile
Bedside	Blood pressure
	Post-void bladder scan
Urine	Urine dipstick for blood, protein, nitrites and leucocytes
	Urine culture and sensitivity
	Urine protein:creatinine ratio
	Urine albumin:creatinine ratio
Imaging	Ultrasound scan: kidney, ureters, bladder (to assess kidney size and the presence of masses, cysts or hydronephrosis)
Immunology	Immunoglobulins and electrophoresis, ANCA, C3 and C4, ANA, dsDNA antibody, anti-GBM antibody, ASOT

ANA, antinuclear antibodies; ANCA, anti-neutrophil cytoplasm antibodies; anti-GBM antibody, anti-glomerular basement membrane antibody; ASOT, antistreptolysin O titre; eGFR, estimated glomerular filtration rate; C3, C4, complement component 3 and 4; dsDNA antibody, anti-double stranded DNA antibodies.

Table 1

Kidney biopsy has a role in the diagnosis of inherited conditions. Thin basement membrane nephropathy usually has a good prognosis with only a minority progressing to ESKD[2]; clear diagnosis can provide reassurance and avoid unnecessary further investigation. Alport syndrome has a lower prevalence but greater risk of progression to ESKD, especially in male individuals, and has extra-renal manifestations such as hearing impairment.[2] Early diagnosis and family screening to identity affected families is essential.

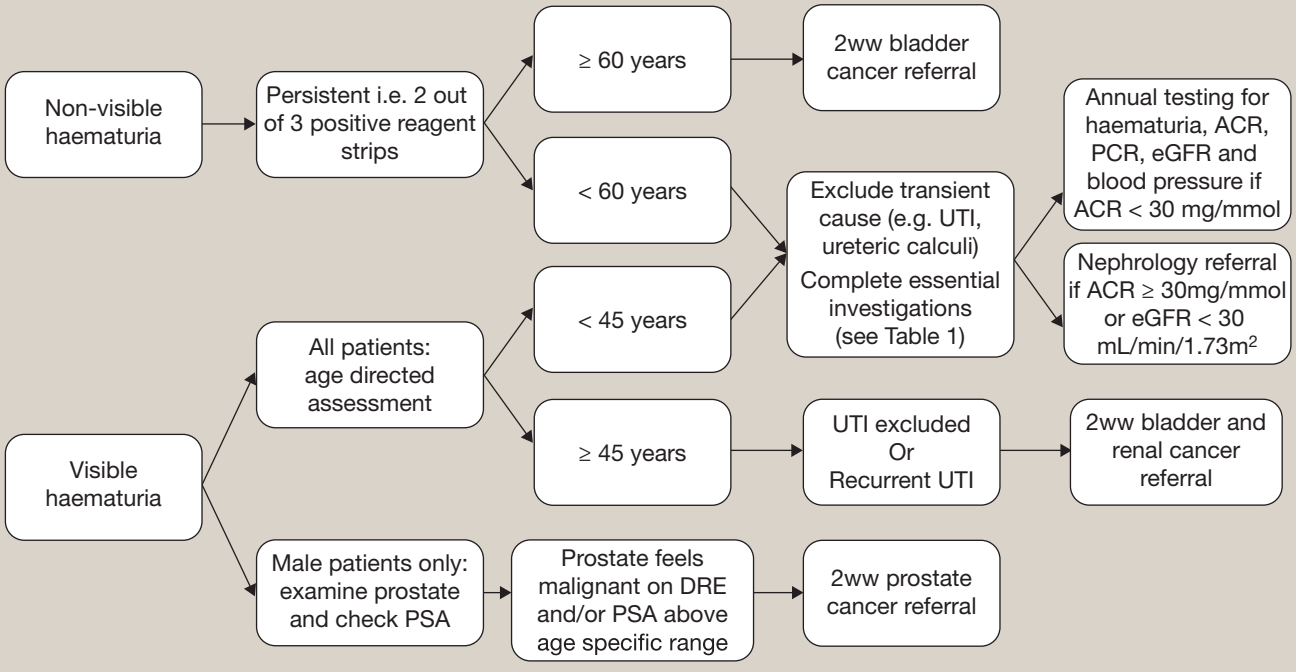
Non-visible haematuria with markers of abnormal renal function

Non-visible haematuria with increasing serum creatinine, reduced urine output, hypertension or proteinuria often reflects glomerular inflammation; kidney biopsy often helps with diagnosis. However, biopsy can be deferred or not completed if the patient is high risk, or to avoid treatment delays if the diagnosis is clear; for example, in antiglomerular basement membrane disease, the presence of circulating antibodies, rapidly progressive AKI and haematuria confirms the diagnosis.

Proteinuria

The presence of proteinuria should be confirmed on an early morning urine sample to rule out benign phenomena such as orthostatic (i.e. postural) proteinuria and avoid unnecessary investigation. Proteinuria should be quantified using both the

Haematuria assessment pathway



2ww, 2-week-wait; ACR, albumin:creatinine ratio; DRE, digital rectal (prostate) examination; eGFR, estimated glomerular filtration rate; PCR, protein:creatinine ratio; PSA, prostate-specific antigen; UTI, urinary tract infection.

Figure 1 Adapted from the national institute for health and care excellence (NICE) urological cancers clinical knowledge summary and NICE chronic kidney disease guidelines.[1,6]

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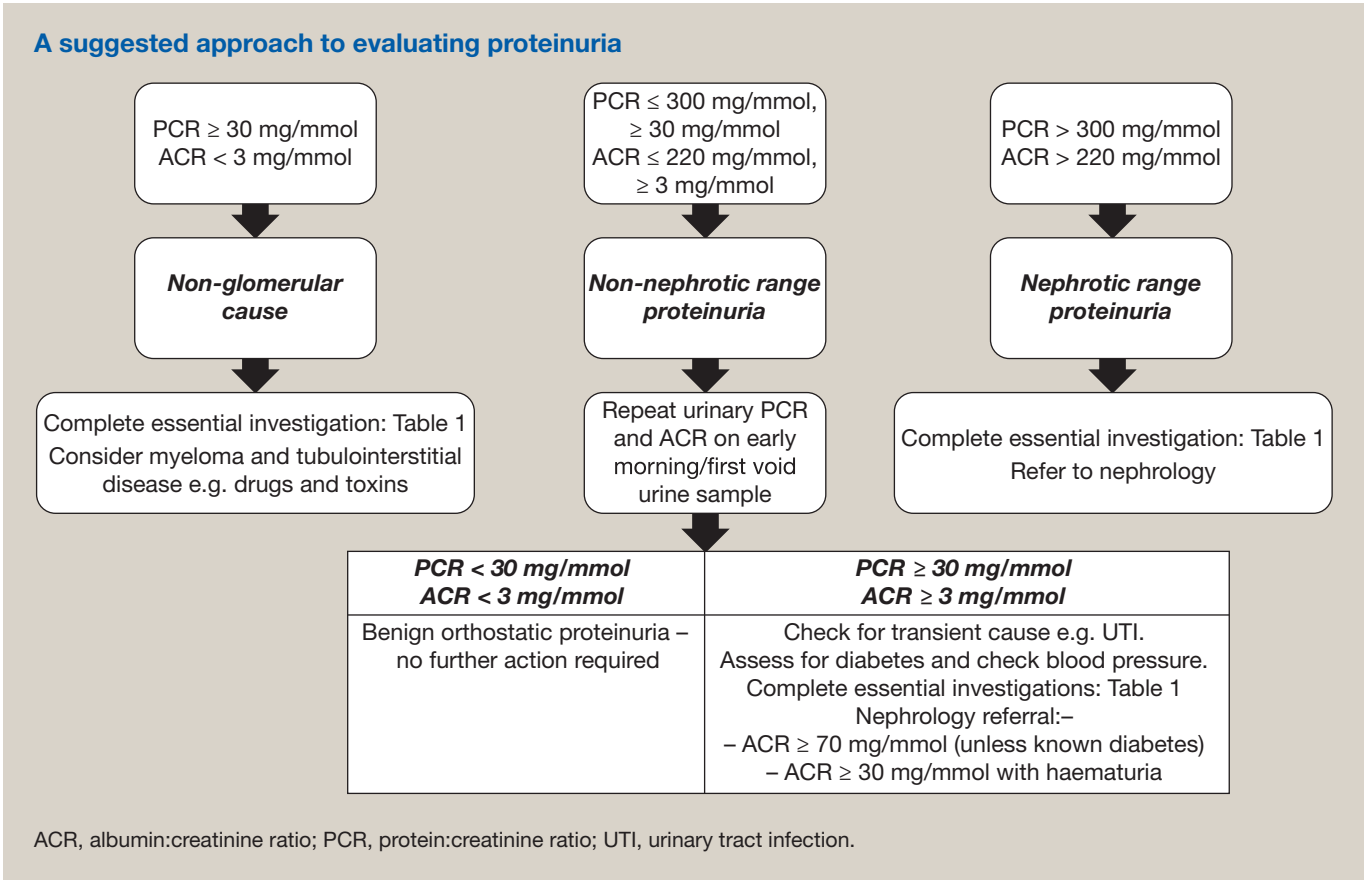

Figure 2

urinary protein:creatinine ratio (PCR) and albumin:creatinine ratio (ACR). Albuminuria (ACR ≥3 mg/mmol) has greater prognostic value and reflects glomerular injury in kidney disease, whereas the presence of proteinuria with minimal albuminuria is suggestive of myeloma. Albuminuria can be subdivided into microalbuminuria (ACR ≥3 to ≤30 mg/mmol) and macroalbuminuria (ACR >30 mg/mmol), guiding monitoring and secondary care referral.

Proteinuria in the presence of kidney disease secondary to systemic illness (e.g. diabetes mellitus and hypertension) typically does not warrant kidney biopsy. However, kidney biopsy in individuals with unexplained proteinuria provides valuable information. Furthermore, nephrotic-range proteinuria (PCR >300 mg/mmol or ACR >220 mg/mmol) with or without the other features of nephrotic syndrome (hypoalbuminaemia, oedema ± significant hypercholesterolaemia) often requires kidney biopsy to aid diagnosis. An overview of the evaluation of proteinuria is outlined in Figure 2.

Kidney biopsy procedure

Safety of the procedure

Complications of renal biopsy occur as a result of bleeding: haematoma formation (11%), blood transfusion (1.6%), pain (4.3%), macroscopic haematuria (3.5%) and death (0.06%).[3] Because of the risk of bleeding, patients should be carefully assessed for contraindications (Table 2). The procedure should only take place in centres with interventional radiology support.

Relative and absolute contraindications for renal biopsy

Contraindication
Relative
• Hypertension
• Coagulopathy
• Uraemia (consider acute renal replacement therapy and/or desmopressin before the procedure)
• Renal asymmetry
• CKD and bilaterally small kidneys on imaging
• Single kidney (excluding transplant biopsies)
• Renal masses (requires interventional radiology or surgical biopsy)
Absolute
• Active pyelonephritis
• Skin infection at the site of needle insertion
• Uncontrollable hypertension or coagulopathy
• Polycystic kidney disease
• Hydronephrosis/obstructed kidneys

Table 2

Preparing for the kidney biopsy

Proceeding with a kidney biopsy requires shared decision-making between the nephrologist and the patient, followed by

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informed written consent. Two weeks before the kidney biopsy, the following investigations are required:

- ultrasound scan of the kidneys, ureter and bladder
- urine culture
- full blood count
- clotting profile
- group and save.

The results must be reviewed before the biopsy. On the day of the procedure, clinical observations including blood pressure are required.

Mitigating post-biopsy bleeding risk

Individuals with uraemia have an increased risk of a bleed when undergoing a kidney biopsy. In these situations, acute haemodialysis and/or desmopressin can be considered. Desmopressin has been proposed to reduce bleeding risk by improving the platelet dysfunction that occurs with uraemia.[4]

Anticoagulation

Managing anticoagulation can be a challenge, as in certain presentations of kidney disease (e.g. nephrotic syndrome) patients require anticoagulation because of an increased risk of thrombosis. Local guidelines and specialist advice regarding anticoagulation and kidney biopsy should always be reviewed before the procedure. Warfarin has a long plasma half-life of 30–40 hours, however this is changeable among individuals. The plasma half-life of direct-acting oral anticoagulants (DOACs) vary depending on the specific agent but it is much shorter in comparison to warfarin (<16 hours for commonly prescribed agents). However, all DOACs rely on renal elimination and so the half-life is unpredictably extended in kidney disease. Therefore, for both warfarin and DOACs, they are stopped at least 72-hours before the procedure.

In higher risk cases (e.g. thromboembolism within 3 months) bridging therapy with low- weight heparin (half-life ≈4 hours; will be lengthened in kidney disease) or intravenous heparin (in clinical practice, the half-life is considered to be 60–90 minutes) can be warranted, stopping 12 hours before the procedure. Anticoagulation is typically recommenced 48–72 hours after the procedure if there have been no bleeding complications. Antiplatelet agents are usually withheld for 7 days before the procedure to allow for platelet recovery (platelet lifespan ≈7–10 days).

The procedure

Real-time ultrasound-guided percutaneous renal biopsy (native and transplant) is usually performed by a nephrologist (sometimes a radiologist). It is a sterile procedure.

Native kidney biopsy: the patient lies in the prone position. Ultrasonography is used to identify the lower pole of the kidney and local anaesthetic is administered. A small incision (≤3 mm) is made to enable the kidney biopsy needle, which is located in a spring-loaded automated biopsy device, to be introduced. The patient is instructed to breathe in and hold the breath, the biopsy needle is inserted through the incision, and the sample is taken from the lower pole (a 'pop' is heard as the biopsy device is released and the patient should feel pressure, not pain). This is repeated 2–3 times. Once the samples have been obtained, the patient is repositioned supine for at least 6 hours.

Transplant biopsy: the procedure is the same as for a native kidney biopsy except that:

- the patient remains supine throughout the procedure
- an inspiratory breath-hold is not required
- samples are often taken from the upper pole, although this is guided by the judgement of the operator on the safest pole and the presence of any overlying bowel that needs to be avoided.

Sample management

Two or three samples are usually obtained by core needle biopsy. Histological compartments – glomerular, interstitial, tubular and vascular – are analysed by a renal pathologist. This requires intricate processing to ensure full evaluation: light microscopy with multiple stains to demonstrate different structures (e.g. haematoxylin–eosin, periodic acid–Schiff), immunohistochemistry, immunofluorescence and electron microscopy. There is no consensus on the minimum number of glomeruli required to provide an adequate sample; this varies with the underlying diagnosis, associated clinical presentation and investigations.

After the procedure

Low-risk patients should be observed for 6–8 hours after the procedure to check for visible haematuria, alongside pain, blood pressure and heart rate monitoring. Clear documentation within the discharge letter is essential to help community colleagues and emergency services with identifying complications. Higher risk candidates should be admitted overnight. Visible haematuria after biopsy or any evidence of bleeding (haemodynamic compromise, increasing pain) requires admission for clinical assessment and full blood count measurement. A computed tomography angiogram is the next most appropriate step to identify active bleeding which might be amenable to endovascular intervention by radiology.

Special circumstances

Myeloma

Light-chain cast nephropathy is a 'myeloma-defining' event and can be confirmed on kidney biopsy. However, a presumptive diagnosis can be made from high serum free light chain concentrations (>1500 mg/litre) and AKI[5] – a kidney biopsy should not delay treatment in such cases.

Lupus nephritis

Kidney biopsy is the gold standard for diagnosing lupus nephritis and should be considered in any individual with serological evidence of lupus who has declining kidney function, proteinuria or active urinary sediment. The different histological subtypes of lupus nephritis guide immunosuppression treatment and prognosis; repeat biopsy can identify disease progression and guide withdrawal of immunosuppression. ◆

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