The kidney biopsy

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INTRODUCTION

A percutaneous kidney biopsy may be obtained for a number of reasons, including establishment of the exact diagnosis, as an aid to determine the nature of recommended therapy or to help decide when treatment is futile, and to ascertain the degree of active (ie, potentially reversible) and chronic (ie, irreversible) changes. The degree of active or chronic changes helps determine prognosis and likelihood of response to treatment. In addition, kidney biopsy can be performed to help assess genetic diseases.

It is important to recognize that prognostication based upon kidney pathology alone may be affected by the sample size (particularly in lesions that are focal in nature, such as vasculitis and focal and segmental glomerulosclerosis [FSGS]) and may not be very accurate in biopsies with few glomeruli (ie, ≤5). The findings in a kidney biopsy always need to be interpreted in the context of the clinical and laboratory features. Chronic changes (interstitial fibrosis and tubular atrophy), for example, are a sign of the magnitude and duration of prior injury.

This topic will provide an overview of issues relating to percutaneous kidney biopsy of the **native** (nontransplant) kidney. Nonpercutaneous kidney biopsy techniques are also discussed.

APPROPRIATE USE OF KIDNEY BIOPSY

The indications for performing a kidney biopsy vary among nephrologists, determined in large part by the presenting signs and symptoms [1-5]. This is an important issue since the following discussion will include a number of settings in which kidney biopsy is **not indicated**, which will

avoid the potential risk of bleeding and other complications associated with the kidney biopsy. (See 'Complications' below.)

The overall rate of native kidney biopsy (in number of procedures per million population [pmp]) varies from over 250 pmp in Australia to 175 pmp in the United States [6]. The kidney biopsy rate is higher in adults than in children. These differences in kidney biopsy rate are not driven by differences in the spectrum of kidney pathology but rather by opinions regarding the value of the procedure in diagnosis, prognosis, and therapy.

The results of the kidney biopsy impact decisions about patient care in up to 60 percent of cases [3,7-10], depending upon the clinical setting. However, the utility of the biopsy may differ considerably based upon the indication. Performance of a kidney biopsy when there is likely to be no direct benefit to the patient should be regarded as research in nature and require specific forms of informed consent governed by institutional review boards.

Indications

Nephrotic syndrome — A kidney biopsy is performed in most adults and older children with apparently idiopathic nephrotic syndrome (ie, no apparent underlying disease). In this setting, it is likely that one of the three major causes of the idiopathic nephrotic syndrome is present: minimal change disease, focal segmental glomerulosclerosis (FSGS), or membranous nephropathy. The findings on kidney biopsy frequently influence therapy in older children and adults. In one report, for example, kidney biopsy for nephrotic syndrome in adults influenced the management decision in 86 percent of cases [3]. This is due in part to the presence of an unexpected diagnosis, such as primary (AL) amyloidosis, fibrillary or immunotactoid glomerulopathy, or membranous nephropathy with signs of underlying lupus that may occur in the absence of the typical serologic changes. (See "Overview of heavy proteinuria and the nephrotic syndrome", section on 'Etiology'.)

Kidney biopsy is also often indicated in patients with systemic lupus erythematosus who present with nephrotic syndrome because, even if there is a good chance the patient has lupus membranous nephropathy, a proliferative component may also be present.

In contrast to these indications, there are a variety of patients with the nephrotic syndrome in whom kidney biopsy is usually **not** performed at diagnosis. These include:

- Patients with diabetes mellitus for many years in whom the initial manifestation is moderately increased albuminuria (formerly called microalbuminuria) that slowly progresses to overt proteinuria over many years. However, nondiabetic kidney disease can occur, and there are a variety of clinical clues that suggest nondiabetic disease. This issue is

discussed in detail elsewhere. (See "Diabetic kidney disease: Manifestations, evaluation, and diagnosis", section on 'Confirmatory biopsy if diagnosis is doubtful'.)

- Patients with nephrotic syndrome that seems, from the history and presence of extrarenal involvement, to be due to primary (AL) or secondary (AA) amyloidosis, which can be diagnosed by less invasive tissue biopsy (such as abdominal fat pad biopsy) unless a kidney biopsy is determined to change management. (See "Clinical presentation, laboratory manifestations, and diagnosis of immunoglobulin light chain (AL) amyloidosis", section on 'Choosing a biopsy site'.)

- Children under the age of six years with the acute onset of nephrotic syndrome, since over 90 percent have minimal change disease. Other causes of nephrotic syndrome may occur in older children. (See "Etiology, clinical manifestations, and diagnosis of nephrotic syndrome in children", section on 'Epidemiology'.)

- Patients (children and adults) with relapse of steroid-sensitive nephrotic syndrome following the cessation of appropriate immunosuppressive therapy, such as frequently relapsing minimal change disease.

- Patients with nephrotic syndrome that may be related to a drug such as a nonsteroidal antiinflammatory drug, pamidronate, penicillamine, gold, or lithium. The time to recovery after cessation of the offending drug can be as long as several years, as seen with nephrotic syndrome due to penicillamine or gold. Kidney biopsy may be performed at diagnosis if the nephrotic syndrome is accompanied by moderate to severe acute kidney injury. (See "Etiology, clinical features, and diagnosis of minimal change disease in adults", section on 'Drugs' and "Membranous nephropathy: Epidemiology, pathogenesis, and etiology", section on 'Drugs' and "Clinical manifestations and diagnosis of acute interstitial nephritis", section on 'NSAID-induced AIN and nephrotic syndrome' and "Renal toxicity of lithium", section on 'Nephrotic syndrome'.)

- Patients with overt (already diagnosed) malignancy. The major associations are membranous nephropathy with solid tumors and less often a hematologic malignancy, such as chronic lymphocytic leukemia, and minimal change disease with lymphoma or leukemia. In these settings, the nephrotic syndrome often resolves with effective treatment of the malignancy. However, a kidney biopsy may be indicated during the treatment phase, as anticancer agents can cause nephrotoxicity, and knowledge of kidney toxicity may lead to a change in oncologic therapy [11]. (See "Membranous nephropathy: Epidemiology, pathogenesis, and etiology", section on 'Malignancy' and "Etiology, clinical features, and diagnosis of minimal change disease in adults", section on 'Neoplasms'.)

- Patients with massive obesity who have slowly increasing proteinuria over time that is often subnephrotic rather than the abrupt onset of nephrotic syndrome. These patients usually have secondary FSGS (called obesity-related glomerulopathy) or diabetic nephropathy. The proteinuria in patients with secondary FSGS often improves with weight loss. By contrast, we would perform a kidney biopsy in an obese patient with abrupt nephrotic syndrome. (See "Focal segmental glomerulosclerosis: Pathogenesis", section on 'Severe obesity'.)

- Patients with nephrotic syndrome who test positive for serum anti-phospholipase A2 receptor (PLA2R) antibodies. These patients can be generally be diagnosed with primary membranous nephropathy without the need for kidney biopsy. However, a kidney biopsy should be performed in such patients who present with other markers of secondary disease (eg, hepatitis B antigen, antinuclear antibodies [ANAs]) to differentiate primary versus secondary disease or in those with an active urinary sediment or rapidly worsening kidney function to exclude superimposed crescentic glomerulonephritis and to assess the degree of chronic damage. (See "Membranous nephropathy: Clinical manifestations, pathology, and diagnosis", section on 'Diagnosis'.)

Acute nephritic syndrome — The acute nephritic syndrome—hematuria, cellular casts, proteinuria, and, frequently, hypertension and kidney function impairment—is often caused by a systemic disease that requires a kidney biopsy to establish the diagnosis and guide treatment. However, there are situations in which the initiation of therapy is required while awaiting the kidney biopsy. Examples include microscopic polyangiitis, granulomatosis with polyangiitis, or anti-glomerular basement membrane (GBM) disease. These are disorders that are associated with rapidly progressive glomerulonephritis and, in the appropriate clinical setting, are suggested serologically by the presence of circulating antineutrophil cytoplasmic autoantibodies (ANCA) or anti-GBM antibodies. Although a classic clinical presentation of one of these diseases accompanied by the appropriate positive serologic tests could be considered confirmatory to make the diagnosis, we typically will still perform a biopsy in this setting to determine prognosis and guide treatment as well as to exclude the rare possibility of an unexpected diagnosis. (See "Overview of the classification and treatment of rapidly progressive (crescentic) glomerulonephritis".)

The reason for a biopsy is variable in lupus nephritis. Patients with acute kidney injury and an active urine sediment may have any number of lesions and require a kidney biopsy to establish a diagnosis, determine prognosis, and guide therapy. A repeat biopsy may also be performed for late progression of the disease to distinguish between active lupus (which may require immunosuppressive therapy) and scarring of previous inflammatory injury (which may warrant antihypertensive therapy with an angiotensin-converting enzyme [ACE] inhibitor). These issues are discussed in detail elsewhere.

Glomerulonephropathy also may be associated with HIV, hepatitis C or B virus, positive cultures for fungi or parasites, or a chronic bacterial abscess. The authors and reviewers of this topic **would** perform a kidney biopsy in such patients as long as the presumptive treatment would not be contraindicated. (See "Overview of kidney disease in patients with HIV" and "Overview of renal disease associated with hepatitis C virus infection" and "Kidney disease associated with hepatitis B virus infection".)

Kidney biopsy is usually **not** performed in patients with a presumptive diagnosis of poststreptococcal glomerulonephritis based upon the clinical history of recent pharyngitis or skin infection and a positive streptozyme test and/or throat or skin culture for group A beta-hemolytic streptococcal infection. Resolution of poststreptococcal glomerulonephritis is usually rapid if there is resolution of the infection. A diuresis typically begins within one week, and the serum creatinine returns to the previous baseline in three to four weeks. Other causes of glomerulonephritis should be considered and kidney biopsy performed if there are recurrent episodes of hematuria, which is suggestive of immunoglobulin A (IgA) nephropathy; persistent hypocomplementemia at six weeks after appropriate therapy; and/or a progressive increase in serum creatinine. (See "Poststreptococcal glomerulonephritis", section on 'Diagnosis'.)

Kidney biopsy is also **not** usually performed in patients with glomerulonephritis associated with endocarditis or shunt nephritis in whom control of the infection usually leads to rapid resolution of the kidney disease. (See "Kidney disease in the setting of infective endocarditis or an infected ventriculoatrial shunt".)

Unexplained acute kidney injury — The most common causes of acute kidney injury—prerenal disease, acute tubular necrosis, and urinary tract obstruction—can be diagnosed clinically without kidney biopsy. Biopsy is indicated in those settings in which the diagnosis is uncertain, as may sometimes be the case with acute interstitial nephritis secondary to drugs [4]. By comparison, patients with small kidneys or slowly progressive chronic kidney disease over a period of years are generally not biopsied, since there is little likelihood of finding a treatable disease.

Findings that do not require biopsy — The following clinical presentations generally do **not** require a kidney biopsy:

- **Isolated glomerular hematuria** – In patients with asymptomatic microscopic hematuria (ie, persistent microscopic hematuria with dysmorphic red blood cells, negative "dipstick" for proteinuria, normal serum creatinine concentration, and normal blood pressure), the kidney biopsy may not alter therapy, as such patients generally have a good prognosis. When biopsies are performed, they typically demonstrate either a normal kidney biopsy or

one of three disorders: IgA nephropathy, Alport syndrome, or thin basement membrane nephropathy. Most patients with IgA nephropathy and thin basement membrane nephropathy without proteinuria have a good long-term prognosis and, other than ACE inhibitors, there is no clear effective therapy for any of these conditions. However, some patients (such as those with Alport syndrome) may desire a histologic diagnosis for genetic counseling purposes. (See "Urinalysis in the diagnosis of kidney disease" and "Isolated and persistent glomerular hematuria in adults".)

As a result, a kidney biopsy is not routinely performed to establish a specific diagnosis, at least in the United States, unless there is coexisting proteinuria (albuminuria) or evidence of kidney function impairment [4]. In a prospective study of 276 native kidney biopsies, for example, biopsy for isolated hematuria changed a management decision in only 1 of 36 patients [3].

If a biopsy is not performed, ongoing follow-up to monitor for the development of proteinuria or disease progression is warranted. This is particularly true with IgA nephropathy since the majority of patients who are first seen with isolated hematuria have progressive disease (eg, development of proteinuria, hypertension, or kidney function impairment) over many years [12]. (See "Treatment and prognosis of IgA nephropathy".)

Kidney biopsies are not indicated in patients with persistent nonglomerular hematuria; such patients need a thorough urologic evaluation. If a complete urologic evaluation is negative, a kidney biopsy would be indicated if the patient with isolated microscopic hematuria is a potential living donor for kidney transplant. (See "Etiology and evaluation of hematuria in adults".)

- **Isolated non-nephrotic proteinuria** – A kidney biopsy is generally **not** performed in a patient who presents with low-grade proteinuria (<500 mg/day or mg/g creatinine) or albuminuria (<300 mg/day or mg/g creatinine), absence of glomerular hematuria, normal kidney function (adapted to age), and an absence of clinical or serologic evidence of a systemic disease that can cause glomerulonephritis (eg, systemic lupus erythematosus, vasculitis, or a paraproteinemia) (see "Assessment of urinary protein excretion and evaluation of isolated non-nephrotic proteinuria in adults"). Some of these patients will have primary FSGS, IgA nephropathy, or membranous nephropathy [13]; however, immunosuppressive therapy would not be indicated in this setting, since the prognosis with non-nephrotic proteinuria is often excellent. Other patients will have secondary FSGS as a response to ischemic injury (as in nephrosclerosis) or to nephron loss (as in reflux nephropathy). (See "Secondary factors and progression of chronic kidney disease".)

Many nephrologists routinely perform a kidney biopsy in patients with somewhat higher degrees of non-nephrotic proteinuria (0.5 to 2 g/day), except in the setting where this may be explained by another condition, such as longstanding diabetes mellitus. If such a patient is reluctant to undergo biopsy, indications for further encouragement of the patient to consent to the procedure include increasing proteinuria or serum creatinine concentrations or the new onset of hypertension.

Contraindications — Percutaneous kidney biopsy for the detection of primary kidney disease is generally not pursued in the following settings:

- Small hyperechoic kidneys (generally less than 9 cm in length by ultrasound but adjusted for height, weight, and/or body mass index [14]), which are generally indicative of chronic irreversible disease
- Solitary native kidney (relative contraindication)
- Multiple, bilateral cysts or a kidney tumor (relative contraindication)
- Uncorrectable bleeding diathesis
- Severe hypertension (ie, systolic blood pressure >170 mmHg [15,16]) that cannot be controlled with antihypertensive medications
- Hydronephrosis
- Active renal or perirenal infection
- Anatomic abnormalities of the kidney that may increase risk (such as polycystic kidney disease or horseshoe kidney)
- Skin infection over the biopsy site
- An uncooperative patient
- When a skilled operator (nephrologist or interventional radiologist, experienced in performance of the procedure) or appropriate pathology support is not available

Advanced age is not a contraindication to the procedure. Several studies have shown that percutaneous kidney biopsy can be performed safely and revealed unanticipated diagnoses in 15 to 33 percent of cases in older adults (over age 60 to 65 years) [17-20]. Even among the very old (over age 80 years), kidney biopsy may provide valuable diagnostic and prognostic data [21].

Pregnancy is not a contraindication to percutaneous kidney biopsy. Several series have shown complication rates of the percutaneous approach in the prone position similar to those reported in nonpregnant patients [22,23], and there are reports of percutaneous biopsies performed in the sitting or lateral decubitus position during later gestation [24]. However, despite the safety, as there is always potential for maternal-fetal morbidity, consideration should be given to avoid or defer the procedure until the postpartum period unless it may change management prior to delivery [25-27].

A solitary native kidney is not an absolute contraindication to undergoing percutaneous kidney biopsy. In the past, a solitary native kidney had been considered an absolute contraindication to percutaneous biopsy because of the concern that marked bleeding may lead to nephrectomy and loss of all of the patient's functioning kidney mass. However, percutaneous biopsy of a solitary native kidney has been performed successfully in a few selected cases, and it has been suggested that the risk of surgery and nephrectomy with percutaneous biopsy is so low that it may be less than the risk of general anesthesia [1,24,28,29]. As the data are limited, if a biopsy is necessary in the setting of a solitary kidney, it should be performed by experienced operators.

CHOICE OF BIOPSY METHOD

For most patients, a percutaneous kidney biopsy is the preferred approach because it is less invasive compared with other approaches. A percutaneous kidney biopsy is usually performed under real-time ultrasonic guidance; however, a computed tomography (CT) scan is an alternative when the kidneys cannot be well visualized, as with marked obesity or small echogenic kidneys [30]. (See 'Description of procedure' below.)

Other, nonpercutaneous biopsy approaches may be used in specific settings:

- **Open kidney biopsy** – An open (surgical) kidney biopsy can be considered when there is an uncorrectable bleeding diathesis, when there is a solitary kidney, or after failed attempts at percutaneous kidney biopsy. A large core or wedge of kidney cortex can usually be obtained, the incidence of severe bleeding is very low, and mortality is rare. Other relatively minor postoperative complications can occur, including fever, atelectasis, and ileus. In addition, an open biopsy under general anesthesia is associated with a longer hospital stay and a larger surgical scar.

- **Laparoscopic kidney biopsy** – Laparoscopic kidney biopsy is an alternative to open kidney biopsy for patients who are unable or unwilling to undergo percutaneous kidney biopsy. In one series of 32 patients who underwent laparoscopy for a variety of indications, all biopsies were successful and associated with minimal complications [31]. Another series of 21 patients provided similar results, suggesting that this may be a safe and effective alternative to the open kidney biopsy [32].

- **Transjugular kidney biopsy** – A transjugular kidney biopsy is generally performed by an interventionalist in the angiography suite and requires a small amount of intravenous contrast. The major indication for this modality is an uncorrectable clotting disorder; other

indications include the requirement for combined liver or heart and kidney biopsy, morbid obesity, or a solitary kidney [33-41].

The risk of perinephric bleeding is theoretically reduced since the renal capsule is not intentionally penetrated [33,34,42]. In centers with experience, the complication rate of this technique is similar to the percutaneous approach [35-37,43]. However, intrarenal bleeding due to arterial trauma may still occur, and some centers have reported high rates of bleeding due to capsular perforation [34,35,37]. Contrast-induced acute kidney injury has also been reported [43]. Another limitation of the procedure is that obtaining adequate tissue for establishing a diagnosis ranges from only 73 to 97 percent but improves with increased operator experience [44].

Contraindications to a transjugular kidney biopsy include bilateral internal jugular vein thrombosis, allergy to contrast media, and the lack of experienced clinicians [39]. The greater cost in time, personnel, and radiologic guidance make this procedure impractical for routine kidney biopsy but may be an option in selected circumstances when the appropriate expertise is available.

PREBIOPSY CONSIDERATIONS

Patient evaluation — Prior to a percutaneous kidney biopsy, a history, a physical examination, and selected laboratory tests should be performed to determine whether a patient is at increased risk for complications (eg, bleeding) [30]. The skin overlying the biopsy site should be free from signs of infection, and the blood pressure should be well controlled. We suggest controlling blood pressure before and after the biopsy to a goal of less than 140/90 mmHg. As hypertension is a risk factor for bleeding complications, we generally will not perform an elective kidney biopsy if the patient has a systolic blood pressure of >170 mmHg [15,16]. The patient should also be able to follow simple directions.

Recommended laboratory tests include a complete biochemical profile, complete blood count, platelet count, prothrombin time (PT) and international normalized ratio (INR), and activated partial thromboplastin time (aPTT). Some experts, including the authors of this topic, also routinely obtain a bleeding time; however, the value of this practice continues to be debated, and not all centers obtain this test prior to kidney biopsy [44-47]. A bleeding diathesis, if discovered, should be appropriately evaluated and treated prior to undertaking an elective kidney biopsy. (See "Approach to the adult with a suspected bleeding disorder" and 'Thrombocytopenia' below.)

A kidney ultrasound should precede the biopsy to assess the size of and/or presence of any anatomic abnormalities that may preclude the performance of a percutaneous biopsy (eg, solitary kidney, polycystic kidney, malpositioned or horseshoe kidney, small echogenic kidneys, or hydronephrosis). The kidney ultrasound is often performed at the time of the biopsy (unless the biopsy is done under computed tomography (CT) guidance or as an open procedure by a surgeon).

Thrombocytopenia — Thrombocytopenia (ie, platelet count of <140,000/microL) has been shown to increase the risk of bleeding after kidney biopsy [48,49]. In one study, the risk of developing a symptomatic hematoma was highest (40 percent) in patients with a platelet count of <100,000/microL [48]. Thus, a platelet count of <100,000/microL should be corrected by the appropriate therapy if possible prior to undergoing an elective percutaneous kidney biopsy.

Medication management

Antiplatelet and antithrombotic agents — Patients who are taking antiplatelet or antithrombotic agents (eg, aspirin, omega-3 fatty acids [50], glycoprotein (GP) IIb/IIIa inhibitors, dipyridamole, and nonsteroidal antiinflammatory drugs) should ideally discontinue these medications if possible for **at least one to two weeks** prior to a scheduled elective biopsy and remain off of them for one to two weeks after the biopsy if possible. However, one retrospective study of 2563 patients undergoing percutaneous kidney biopsy reported no increased bleeding risk in a subset of 327 patients who continued aspirin at the time of biopsy [51], providing some supportive data for the continuation of these agents if necessary.

Anticoagulants — The management of patients on chronic anticoagulation must be individualized, often in consultation with hematology and cardiology, as appropriate. A full discussion of the relevant issues is presented separately. (See "Perioperative management of patients receiving anticoagulants".)

Issues that must be considered in patients on chronic anticoagulation include the following:

- Whether a kidney biopsy is essential for diagnosis, prognosis, and/or management.
- The indications for chronic anticoagulation and risk of thrombosis if anticoagulation is temporarily stopped (eg, venous versus arterial thrombosis, mechanical heart valve).
- The risk for bleeding after the kidney biopsy. Factors other than anticoagulation that increase the risk of bleeding postbiopsy include the level of kidney function (and associated platelet dysfunction), anemia, and blood pressure [52,53]. (See 'Bleeding' below.)

The following is a general guide concerning the management of such patients:

- **Patients on** warfarin – Stop warfarin to allow the INR to drift below 1.5 or reverse it with vitamin K if the biopsy must be performed urgently. Whether heparin is required prior to the biopsy once the INR falls below 2, and after the biopsy until oral anticoagulation is restarted, depends upon the perceived risk of thrombosis or embolism (eg, type of event and frequency and remoteness of prior events). (See "Perioperative management of patients receiving anticoagulants", section on 'Estimating thromboembolic risk'.)

- **Patients on intravenous (IV) heparin** – IV heparin should be stopped for at least six hours prebiopsy to allow the aPTT to normalize and, if possible, should be only resumed without a bolus after at least 12 to 24 hours. Although most clinically significant bleeding is recognized in the first 12 to 24 hours postbiopsy, bleeding may occur up to several days after the procedure [54]. Patients on heparin should be closely monitored for signs of bleeding (vital signs, serial hematocrit).

- **Patients on low-molecular-weight heparin (LMWH)** – Patients on LMWH should have this stopped the day prior to the procedure, and it can be resumed 48 to 72 hours after the procedure for those at high risk of thromboembolic events [24]. (See "Perioperative management of patients receiving anticoagulants", section on 'Estimating thromboembolic risk'.)

- **Patients on a direct oral anticoagulant (DOAC)** – As there are no data on the use of DOACs and bleeding complications in patients undergoing percutaneous kidney biopsy, we hold the DOAC for five days prior to the procedure in those with low thromboembolic risk and use an IV heparin bridge for those at high risk. (See "Perioperative management of patients receiving anticoagulants", section on 'Estimating thromboembolic risk' and "Perioperative management of patients receiving anticoagulants", section on 'Bridging anticoagulation'.)

Most clinicians would resume oral anticoagulation with warfarin or a DOAC approximately seven days postbiopsy if there is no evidence of clinically significant bleeding as determined in part by serial monitoring of hemoglobin or hematocrit.

An open or, if available, transjugular kidney biopsy can be considered if the percutaneous approach is not feasible. (See 'Choice of biopsy method' above.)

Use of desmopressin (dDAVP) — Use of desmopressin prior to a biopsy to prevent bleeding is controversial. In general, we reserve desmopressin for patients with an elevated bleeding time. Although this test has not been shown to reliably predict surgical bleeding [47,55], an elevated bleeding time has been associated with a higher risk of complications (mostly bleeding) in a prospective study of patients undergoing percutaneous kidney biopsy [15] and can help

determine bleeding risk in patients with underlying kidney disease. In the absence of a bleeding time or another accurate measure of platelet function, administration of desmopressin can be considered on a **case-by-case** basis, and the risk of bleeding should be weighed against the risks of desmopressin administration, such as thrombosis and hyponatremia [56,57].

The role of desmopressin was evaluated in a single-center trial that randomly assigned 162 patients to receive either desmopressin or placebo prior to an ultrasound-guided biopsy of a native kidney [58]. All patients were low risk for bleeding: all had an estimated glomerular filtration rate (eGFR) greater than 60 mL/min per 1.73 m^2, blood pressure less than 140/90 mmHg, and normal coagulation parameters including normal bleeding times. Fewer patients in the desmopressin group had a hematoma detected on postbiopsy screening ultrasound (13.7 versus 30.5 percent in the placebo group). The hematomas were clinically silent as there was no difference between groups in hemoglobin following the biopsy, and no patient in either group had gross hematuria or required a transfusion or intervention. The clinical benefit of preventing an ultrasound-detected hematoma that causes no symptoms is not clear; in addition this study was not powered to detect adverse effects of desmopressin [56].

PERCUTANEOUS KIDNEY BIOPSY

Description of procedure — All patients should provide informed consent for the biopsy. Possible allergy to local anesthetics and iodine-containing solutions should be elicited. Just prior to the procedure, peripheral intravenous access is placed, and the patient is usually placed prone with a pillow under the abdomen. If the patient is pregnant or very obese, the biopsy can be performed in the seated, lateral decubitus, or supine anterolateral position [22,23,59]. Some anxious patients may require mild sedation, but when prescribing sedatives, caution should be taken and side effects considered.

Percutaneous kidney biopsy is usually performed under ultrasonic guidance with local anesthesia (usually 1 percent lidocaine hydrochloride). Ultrasonography can localize the desired lower pole site (at which the risk of puncturing a major vessel is minimized), determine kidney size, and detect the unexpected presence of cysts that might necessitate using the contralateral kidney. As previously mentioned, a computed tomography (CT) scan is an alternative when the kidneys cannot be well visualized, as with marked obesity or small echogenic kidneys [30]. (See 'Choice of biopsy method' above.)

After the lower pole is localized, a skin mark is made to identify where the biopsy needle will be inserted. The site is subsequently prepped and anesthetized. Under ultrasound guidance, a

spinal needle can be used to locate the capsule of the lower pole and to provide anesthesia for the biopsy needle tract.

After a small skin incision is made to facilitate passage, real-time ultrasonography is most commonly used to guide the biopsy needle directly into the lower pole [30,60]. This somewhat more cumbersome procedure has the advantage of direct visualization of the location of the needle as the core of tissue is obtained.

The use of real-time ultrasound has been compared with the "blind" approach (using ultrasound for localization only). A retrospective study demonstrated a higher diagnostic yield (100 versus 84 percent) as well as a lower major hemorrhagic complication rate (0 versus 11 percent) in the group using real-time ultrasound [61]. A second retrospective study in 2138 patients reported similar findings; diagnostic yield was higher with ultrasound guidance, and the rate of major complications was lower (2.1 versus 6.7 percent) [62]. We therefore recommend the use of real-time ultrasonography rather than ultrasonography for localization only.

Choice of needle — A variety of different biopsy needles are available, including manual needles and automated spring-loaded biopsy needles. The choice of biopsy needle is largely one of individual preference. We prefer the use of a spring-loaded needle with real-time ultrasonic guidance for native and transplant kidney biopsies given its superior ease of use and possible increase in diagnostic yield [2,30]; however, the choice is often determined by local resources and availability. For native kidney biopsies, we suggest the use of a 16-gauge needle rather than an 18-gauge needle.

Several studies have compared the adequacy and safety of different needle gauges and types. The automated needles and larger gauge needles (14 and 16 gauge as compared with 18 gauge) have provided more glomeruli per core and per biopsy [63-66]. There is no difference in complication rate between a manual needle and an automatic needle of the same gauge [65].

Two different prospective, single-center studies have reported no difference in frequency of complications or number of glomeruli obtained between automated needles of 14 gauge compared with 16 gauge [67,68]. In addition, a nationwide registry study in Norway of 9288 biopsies revealed no difference in complications between 14- and 16-gauge needles, although there was a higher rate of complications with 18-gauge needles [69]. There were more glomeruli per biopsy with use of either of the larger needles (14 or 16 gauge) as compared with 18-gauge needles. However, a meta-analysis of 34 retrospective (n = 21) and prospective (n = 13) studies, including 9474 biopsies, revealed an increased need for erythrocyte transfusion in studies using a 14 gauge as compared with either 16 or 18 gauge [70].

As more percutaneous kidney biopsies are being performed by interventional radiologists [69,71,72], there has been an increasing use of the smaller 18-gauge needle [69]. However, use of this needle may jeopardize the diagnostic success of the biopsy without enhancing safety. Given that the glomerular yield with a 16-gauge needle is comparable to that of a 14-gauge needle and superior to that of an 18-gauge needle without a difference in complication risk, the use of a 16-gauge needle is preferred for performing a kidney biopsy in adults [16,24,73-77].

Tissue sampling — Obtaining two cores of kidney tissue is generally recommended [1,2,30], and the tissue should be assessed for the presence of glomeruli with a 10x lens. However, the quantity of tissue required varies with the likely diagnosis. As an example, the distinction of focal (arbitrarily defined as fewer than 50 percent of glomeruli affected on light microscopy) from diffuse proliferative lupus nephritis may require up to 100 glomeruli to make the diagnosis with a reasonable degree of statistical certainty [1]; obtaining this quantity of kidney tissue is rare with percutaneous biopsy, and sampling error may therefore explain the seeming variability in clinical outcome in patients with focal disease.

Although obtaining two cores with two passes is ideal, up to five passes has not been shown to increase the complication rate [15,16]. One study showed an increased rate of complications with greater than five passes [78]. When less tissue is obtained, the tissue may need to be prioritized for either light microscopy, immunofluorescence microscopy, or electron microscopy depending upon the suspected diagnosis. (See 'Evaluation of the biopsy specimen' below.)

Postbiopsy observation — Following the procedure, the patient should be supine for four to six hours and then remain at bedrest overnight. To help detect bleeding and other complications (see 'Complications' below), vital signs are closely monitored. At our center, vital signs are monitored every 15 minutes for the first hour, then every 30 minutes for the next four hours, then per routine if the patient remains stable. A complete blood count is obtained at various time points postbiopsy, the first generally within six hours after the procedure. To minimize the risk of bleeding, blood pressure should be well controlled (goal of <140/90 mmHg) [52]. Although practice varies at different centers, we obtain a routine screening ultrasound at one hour after the procedure in all patients. Although the presence of a hematoma by this test is not predictive of an eventual complication, the absence of one is predictive of an uneventful course [79].

For most patients who have undergone a percutaneous kidney biopsy, we suggest an extended period of postbiopsy inpatient bedrest and observation [54,80,81]. In our practice, we observe patients for 24 hours in the hospital, although other experts prefer a 6- to 12-hour period of observation. Our rationale is based upon a study of 750 native kidney biopsies in adults with a normal bleeding time, no evidence of coagulopathy, and a stable blood pressure that found

that clinical recognition of a major complication (bleeding severe enough to require a transfusion or invasive procedure, septicemia, acute kidney obstruction or failure, or death) occurred within 4, 8, 12, and 24 hours among 38, 67, 89, and 91 percent of patients, respectively [54]. It was concluded that observation for 24 hours was optimal, with more than 90 percent of major complications being identified within this period. However, in low-risk patients (eg, serum creatinine concentration <2.5 mg/dL [221 micromol/L], blood pressure of <140/90 mmHg, and no evidence of coagulopathy), a shorter observation period has been described [52,82,83].

Clinical findings that should raise suspicion for a significant postbiopsy bleed include the development of abdominal and/or flank pain, especially if sudden, as well as passing blood clots in the urine. Tachycardia and hypotension are other signs of a potential significant bleed. In patients with suspected bleeding, a complete blood count should be obtained and abdominal imaging (either ultrasound or CT) should be performed. If the patient is hemodynamically unstable, urgent referral for angiography or surgery without imaging may be indicated.

Complications

Bleeding — Bleeding is the primary complication of kidney biopsy (image 1) [1,2]. Compared with biopsy of other sites, biopsy of the kidney has the greatest risk of postprocedure hemorrhage (1.2 percent) [84]. Bleeding after the kidney biopsy can occur at three sites:

- Into the collecting system, leading to microscopic or gross hematuria and possible ureteral obstruction
- Underneath the renal capsule, leading to pressure tamponade and pain
- Into the perinephric space, leading to hematoma formation and a possibly large fall in hematocrit (image 2)

Rarely, severe bleeding may occur due to puncture of the renal artery, aorta [85], or venous collaterals (in patients with renal vein thrombosis). Most clinically significant bleeding is recognized within 12 to 24 hours of the biopsy [54,86]. (See 'Postbiopsy observation' above.)

As previously mentioned, the incidence of bleeding is minimized with normal activated partial thromboplastin time (aPTT), prothrombin time (PT), platelet count, and bleeding time [80]. Additional clinical risk factors for bleeding include hypertension, reduced glomerular filtration rate (GFR), anemia, older age, the use of a larger (14 gauge) biopsy needle, and when biopsy is performed in a patient with acute [87,88], as well as chronic, kidney disease [30,52,54,70,78,89].

In a systematic review of 87 studies, including 118,604 native, percutaneous kidney biopsies [90], the approximate incidence of the different bleeding complications was as follows:

- Pain at the biopsy site – 4.3 percent
- Transient macroscopic hematuria – 3.5 percent
- Perinephric hematomas – 11 percent
- Requirement for erythrocyte transfusion – 1.6 percent
- Requirement for intervention to control bleeding – 0.3 percent
- Requirement for nephrectomy to control bleeding – 0.01 percent [70]
- Death – 0.06 percent

Rates of bleeding complications in this review varied according to certain risk factors, such as hospitalized patients and those with acute kidney injury demonstrating higher risk compared with those undergoing outpatient biopsies. Another meta-analysis assessed risk factors for requiring erythrocyte transfusion, which were on average significantly higher in patients with the following characteristics [70]:

- Systolic blood pressure greater than or equal to 130 mmHg – 1.4 versus 0.1 percent
- Serum creatinine greater than or equal to 2 mg/dL (177 micromol/L) – 2.1 versus 0.4 percent
- Hemoglobin concentration less than 12 g/dL – 2.6 versus 0.5 percent
- Age over 40 years – 1 versus 0.2 percent

Prior reports suggested an increased risk of bleeding complications in certain disorders, such as autoimmune disease, end-stage kidney disease, acute tubular necrosis, and amyloidosis [67,78,91]. However, subsequent studies did not show an increased risk of hemorrhagic complications among patients with systemic amyloidosis [92,93] or monoclonal gammopathies [94]. The presence of anemia also increases the risk of complications; preprocedure anemia is a stronger predictor of receiving a blood transfusion as opposed to the development of actual postprocedure bleeding after percutaneous kidney biopsy [53,95].

The risk of bleeding might be decreased by the administration of desmopressin prior to biopsy. This is controversial and is discussed elsewhere in this topic. (See 'Use of desmopressin (dDAVP)' above.)

Other complications — Other potential complications of kidney biopsy that may or may not be related to bleeding include:

- Pain lasting more than 12 hours in 4 percent; this problem may be due to ureteral obstruction from a blood clot in patients with gross hematuria or to stretching of the renal capsule by a subcapsular hematoma.

- Arteriovenous fistulas form in up to 14 percent of cases due to damage to the walls of an adjacent artery and vein (image 3) [1,96,97]. Postbiopsy fistulas are usually clinically silent and resolve spontaneously over one to two years. Symptomatic fistulas, causing hematuria, hypotension, or high-output heart failure, are now rare. The diagnosis can be established by color Doppler ultrasonography or arteriography [96]. Either transcatheter arterial embolization or surgical ligation can be used to close a symptomatic fistula [96].

- Another rare complication is chronic hypertension due to the "Page kidney" [98-100]. In this setting, pressure-induced ischemia from a large subcapsular hematoma can lead to hypertension due to persistent activation of the renin-angiotensin system.

- Perirenal soft tissue infection may occur in 0.2 percent of cases, most often in patients with active parenchymal renal infection [1,101].

- Rarely, puncture of the liver, pancreas, spleen, or even aorta may occur, as well as urinoma formation from puncture of the urinary tract [102].

EVALUATION OF THE BIOPSY SPECIMEN

The routine evaluation of a percutaneous kidney biopsy involves examination of the tissue under light, immunofluorescence (and immunoperoxidase in some laboratories [103]), and electron microscopy. Each component of the evaluation can provide important diagnostic information. The routine immunofluorescence examination of biopsy specimens should include (at a minimum) evaluation of immunoglobulin G (IgG), immunoglobulin M (IgM), IgA, C3, C4, C1q, albumin, fibrin, and kappa and lambda immunoglobulin chains. Special studies, including evaluation of serum amyloid A deposits, IgG subclasses (IgG1 to 4), phospholipase A2 receptor (PLA2R), collagen chains (alpha 3, 4, and 5), DnaJ heat shock protein family (Hsp40) member B9 (DNAJB9), and mass spectrometry may be helpful in some cases where available. Immunofluorescence microscopy on pronase-digested paraffin sections may help to salvage a diagnosis if glomeruli were not present in the original sample.

- (See "Membranous nephropathy: Clinical manifestations, pathology, and diagnosis".)

- (See "Thin basement membrane nephropathy (benign familial hematuria)".)

- (See "Genetics, pathogenesis, and pathology of Alport syndrome (hereditary nephritis)".)

Justification for the routine application of electron microscopy comes largely from studies in the 1960s and 1970s that showed that this technique provided substantive diagnostic information beyond that obtained from light microscopy in nearly 50 percent of cases. Although most of

these studies were performed at a time when immunofluorescence microscopy was not widely available, similar findings have been reported in more recent studies assessing the utility of electron microscopy [104].

Diagnoses that commonly require electron microscopy include minimal change disease, focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis, membranous nephropathy, thin basement membrane nephropathy and Alport syndrome, postinfectious glomerulonephritis, HIV-associated nephropathy, amyloidosis, immunoglobulin deposition diseases, fibrillary glomerulonephritis, and immunotactoid glomerulopathy.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Glomerular disease in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Kidney (renal) biopsy (Beyond the Basics)" and "Patient education: The nephrotic syndrome (Beyond the Basics)" and "Patient education: IgA nephropathy (The Basics)")

SUMMARY AND RECOMMENDATIONS

- A percutaneous kidney biopsy may be obtained to establish a diagnosis, help guide therapy, and ascertain the degree of active and chronic changes. The routine evaluation of a percutaneous kidney biopsy involves examination of the tissue under light, immunofluorescence, and electron microscopy. (See 'Introduction' above and 'Evaluation of the biopsy specimen' above.)

- The indications for performing a kidney biopsy vary among nephrologists, being determined in part by the presenting signs and symptoms:

    - Among patients with the nephrotic syndrome, a biopsy is usually performed in those with lupus nephritis to determine the type of disease that is present. We also usually perform a biopsy in patients with the nephrotic syndrome and no evidence of systemic disease, both to determine treatment and to occasionally make an unexpected diagnosis. (See 'Nephrotic syndrome' above.)

    - The acute nephritic syndrome is often caused by a systemic disease that requires a kidney biopsy to establish the diagnosis and guide treatment. Even in the absence of a systemic disease, the acute nephritic syndrome often requires a biopsy to ascertain a diagnosis and direct treatment. (See 'Acute nephritic syndrome' above.)

    - Among patients with unexplained acute kidney injury, a biopsy is indicated in those settings in which the diagnosis is uncertain. (See 'Unexplained acute kidney injury' above.)

- A kidney biopsy is generally **not** routinely performed to establish a diagnosis in patients with the following:

    - Isolated glomerular hematuria, unless there is evidence of progressive disease such as increasing proteinuria or a rising serum creatinine concentration

    - Low-grade proteinuria (less than 500 mg/day), the absence of glomerular hematuria, normal kidney function, and an absence of clinical or serologic evidence of a systemic disease that can cause glomerulonephritis (see 'Findings that do not require biopsy' above)

- For most patients, a percutaneous kidney biopsy is the preferred approach because it is less invasive compared with other approaches. Other kidney biopsy methods include open (surgical) biopsy, laparoscopic biopsy, and transjugular biopsy. (See 'Choice of biopsy method' above.)

- Prior to a percutaneous kidney biopsy, a history, physical examination, and selected laboratory tests should be performed to determine whether a patient is at increased risk for complications (eg, bleeding). Recommended laboratory tests include a complete biochemical profile, complete blood count, platelet count, prothrombin time (PT) and international normalized ratio (INR), and activated partial thromboplastin time (aPTT). Some experts also routinely obtain a bleeding time, but the value of this practice continues to be debated. A kidney ultrasound should precede the biopsy to assess the size and/or presence of any anatomic abnormalities that may preclude the performance of a percutaneous biopsy. (See 'Patient evaluation' above.)

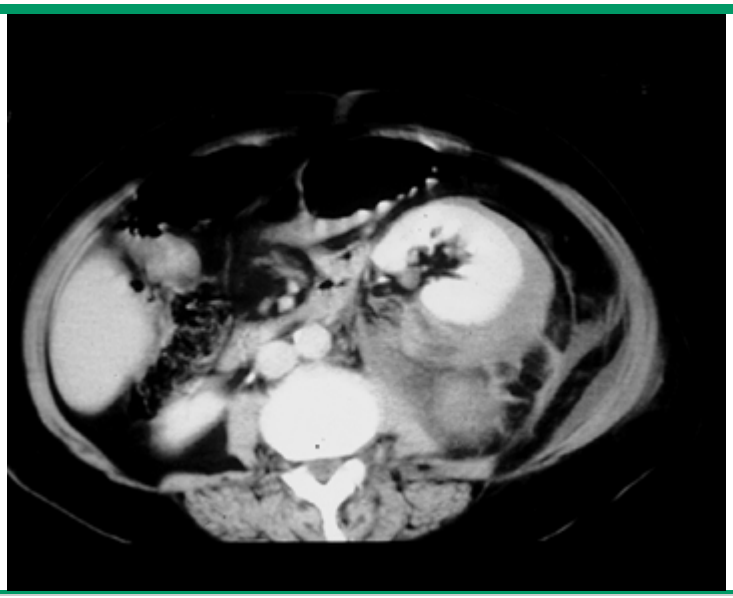
- Percutaneous kidney biopsy is usually performed under ultrasonic guidance with local anesthesia. We recommend the use of real-time ultrasonography rather than the blind approach in which ultrasound is used for localization only (**Grade 1B**). Real-time ultrasonography leads to fewer important complications and a higher diagnostic yield. We prefer the use of a spring-loaded needle for native kidney biopsies given its superior ease of use and possible increase in diagnostic yield; however, the choice is often determined by local resources and availability. For native kidney biopsies, we suggest the use of a 16-gauge needle rather than an 18-gauge needle (**Grade 2C**). We try to obtain two cores of kidney tissue. (See 'Description of procedure' above and 'Choice of needle' above and 'Tissue sampling' above.)

- For most patients who have undergone a percutaneous kidney biopsy, we suggest an extended period of postbiopsy inpatient bedrest and observation (**Grade 2C**). In our practice, we observe patients for 24 hours in the hospital, although other experts prefer a 6- to 12-hour period of observation. Bleeding is the primary complication of kidney biopsy. (See 'Postbiopsy observation' above and 'Complications' above.)

Topic 3067 Version 29.0

GRAPHICS

Renal hematoma



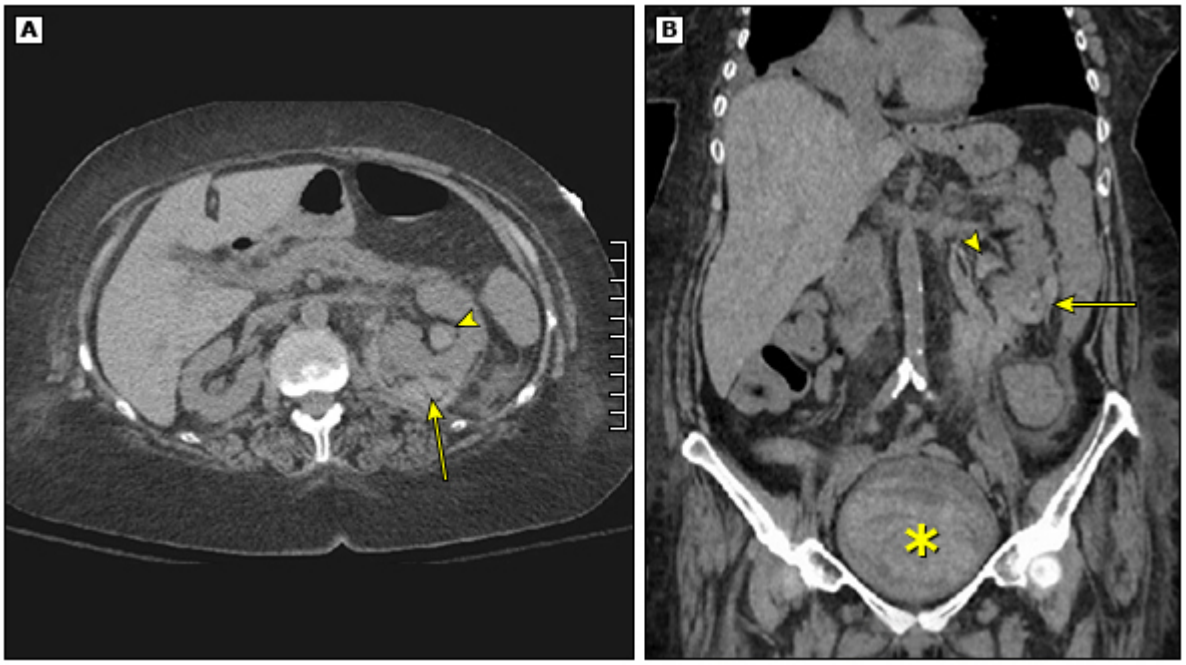
CT scan shows hemorrhage into the left perirenal and pararenal spaces following percutaneous biopsy of the left kidney. The hematoma has displaced the kidney anteriorly.

CT: computed tomography.

Courtesy of Jonathan Kruskal, MD.

Graphic 54874 Version 3.0

Hemorrhage into collecting system post kidney biopsy on CT

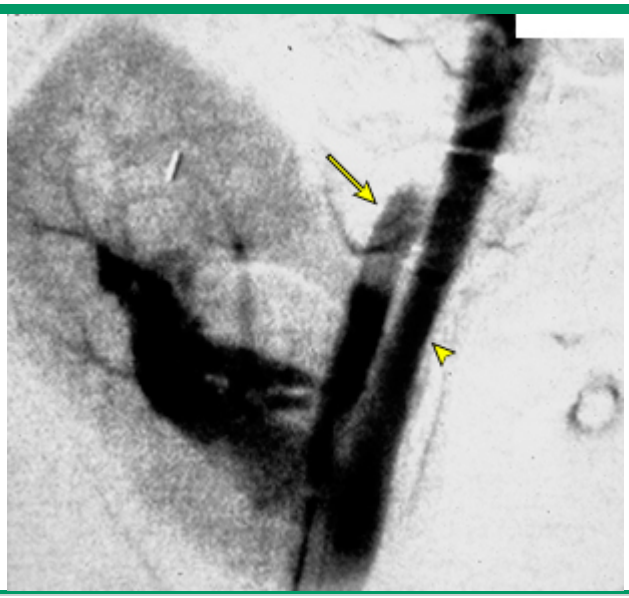


A CT scan following a kidney biopsy (A) shows high density blood in the perinephric space (arrow) and in the collecting system (arrowhead). Image B is a coronal reconstruction and shows high-density blood in the renal pelvis (arrowhead) and perinephric space (arrow) with a large amount of layering in the bladder (asterisk).

CT: computed tomography.

Graphic 91784 Version 2.0

Renal AV fistula



Arteriovenous (AV) fistula following biopsy of a transplanted kidney. Following injection of contrast material into the right common iliac artery (arrow), there is prompt filling of the iliac vein (arrowhead) with poor perfusion of the transplanted kidney.

Courtesy of Jonathan Kruskal, MD.

Graphic 59858 Version 5.0