Percutaneous Kidney Biopsy Under Guidance of Ultrasound, A Point of Care Ultrasound Gift: A Review article

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Abstract
After the application of autopsy as the only method for assessing pathophysiology of renal disease, over 50 years ago, the kidney biopsy has become an essential tool for diagnosis and management of renal diseases. To perform an appropriate kidney biopsy, some steps should be considered. In this review, the authors aimed to mention thorough details regarding percutaneous kidney biopsy under the guidance of ultrasound.

Keywords: Kidney Biopsy; Real time Ultrasonography; Child; Complications.

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Introduction
After the application of autopsy as the only method for assessing the pathophysiology of renal diseases, over 50 years ago, the kidney biopsy has become an essential tool for the diagnosis and management of renal diseases. At first, an open kidney biopsy was performed and then in an accident at the time of a liver biopsy, needle obtained a kidney tissue. This accident motivated physicians to do percutaneous kidney biopsy under guidance of intravenous pyelograms on a sitting or supine positioned patient. A percutaneous kidney biopsy which is commonly performed to take small pieces of kidney tissue, is a safe and valuable method to define the reason, severity, and possible treatment of a kidney disorder. The obtained tissue which is looked under a microscope, can have considerable diagnostic and prognostic values about kidney diseases (1).

The advancement in the kidney biopsy by the use of new needles configurations, real-time ultrasonography and microscopic evaluations including light (LM), immunofluorescence (IF), and electron (EM) microscopies decreases its risk, increases the chance of successful tissue sampling, and provides further information. This considerable change provided the percutaneous kidney biopsy as the center of recent nephrology field.

Indications for Renal Biopsy
As a main principal, a renal biopsy is ideally used when new information is needed for identifying an accurate diagnosis, showing the level of disease and determining the rapid and concise decision. Kidney biopsy is performed for renal diseases including isolated glomerular hematuria, isolated non-nephrotic proteinuria, nephrotic syndrome in adults, acute kidney injury, acute nephritic syndrome, renal dysfunction resulting from systemic disease, and renal transplant dysfunction (2).

Non-Nephrotic Range Proteinuria
There is a controversy regarding the use of renal biopsy in patients with non-nephrotic proteinuria. Although it is not a method of choice for changing the management, it can occasionally promote the prognosis.
Nephrotic Syndrome
In the absence of systemic disease in prepubertal and adult patients with nephrotic syndrome, performing a kidney biopsy is needed. Also a kidney biopsy is needed in children with atypical features of the nephrotic syndrome such as hematuria, decreased levels of serum complements, renal dysfunction, steroid resistance, and steroid dependent nephrotic syndrome.

Acute Kidney Injury
A renal biopsy is not necessary for detecting acute kidney injury in patients with a history of chronic kidney disease. Other methods are adequate for detecting obstruction, reduced renal perfusion, and acute tubular necrosis (ATN). However, a renal biopsy is needed in the minority of patients, including patients with acute tubular injury and acute interstitial nephritis in the presence of elevated serum creatinine for more than 10-14 days or after removing offender drug. It helps physicians administer appropriate treatment before the occurrence of irreversible renal injury.

Systemic Diseases
Diabetic nephropathy and its associated diseases commonly does not need a kidney biopsy, however in some atypical presentations, kidney biopsy can be helpful.
Although, Lupus nephritis is diagnosed by clinical and laboratory examinations, a kidney biopsy is needed for detection of pathologic lesions, extent of chronic fibrosis, level of active inflammation, and accurate treatment.
Viral induced nephropathies are detected by the presence of glomerular lesion in accordance with evidence of active viral infection. However, by immune- and molecule- pathologic techniques, renal biopsy can be used to identify virus-specific protein or DNA or RNA in the tissue.

Renal Allograft Dysfunction
Renal biopsy is needed to detect the cause of renal allograft dysfunction when there is no urinary tract infection, ureteral obstruction, renal artery stenosis, or toxic levels of calcineurin inhibitors. Differentiating rejection from ATN and BK virus nephropathy is performed by biopsy in the early post-transplantation period. Also, acute rejection from calcineurin inhibitor toxicity, chronic allograft nephropathy, recurrent or de novo glomerulonephritis (GN) can be differentiated by renal biopsy.

Hematuria
Hematuria and proteinuria are common findings in various kidney diseases (3). The prognosis of patients with hematuria is good and no kidney biopsy is needed when there is no nephrotic proteinuria, renal dysfunction, or high blood pressure.

Unknown Chronic Kidney Disease
Some underlying cause of Chronic Kidney Disease (CKD) cannot be detected by clinical and usual laboratory examinations. Biopsy is complementary tool in CKDs with unknown cause or normal sized kidneys.
In patients with a small kidney size (<90 mm length), there is a high risk of kidney biopsy complications consequent to glomeruli and interstitial fibrosis. Therefore, the physician will determine the necessity of gathering more information by IF study for detecting pathology such as IgA nephropathy in expense of increasing biopsies risks.

Inherited kidney disease
In Inherited kidney diseases, kidney biopsy of one member of the family may be used for other family members and decrease the need for further assessments.

Repeated Kidney Biopsy
A repeated biopsy is needed in patients with the pathologic changes in lupus nephritis or steroid-resistant/dependent and frequently relapsing minimal change disease, and rapidly progressive glomerulonephritis. The repeated biopsy is used commonly for better management and predicting outcome.

Contraindication for Renal Biopsy
To perform kidney biopsy, there are absolute and relative contraindications. Absolute contraindications are uncontrolled severe hypertension, uncontrollable bleeding diathesis, uncooperative patient, severe hydronephrosis, and a solitary native kidney. In addition, relative contraindications include small hyperechoic kidneys (less than 9 cm for adults), solitary native kidney, multiple, bilateral cysts or a renal tumor,
Uncorrectable bleeding diathesis, severe hypertension, small shrunken kidneys, obesity, ascites, hydronephrosis, active renal or perirenal infection, anatomic abnormalities of the kidney, skin infection over the biopsy site, and uncooperative patient (4).

**Biopsy Needles**

The type of kidney biopsy needles has developed over time. An aspiration needle was first used for percutaneous renal biopsy. It is then changed from Vim Silverman needle to the manually operated side cut needles. More recently, spring-loaded devices are the default standard of care. Although, there is no definite knowledge regarding the ideal needle types in kidney biopsy, generally comparing manual, automated and semi-automated spring-loaded devices show that enough samples and lower level of complications may be obtained by these. There are 3 different sizes of needles including 14 gauge (G), 16G and 18G. Although there are different configurations of cutting surfaces, there is fixed throw of needles which is specific for each device. As so far various throws are available to be used, the length of the needle at the time of biopsy can be chosen by the operator and there is no definite adjustment. Currently, no information has been published regarding the suitable devices for smaller kidneys or thinner cortices (5).

Each biopsy needle has an outer sheath and an inner stylet/trocar. While, the obtained tissue is collected in the inner stylet, the outer sheath creates the core sample by cutting through the tissue. Side Cut Needle is the most common type of needle cutting pattern. The Tru-Cut biopsy needle is a common type of a side cut needle. It is noteworthy that the coaxial Tru-Cut needle is a considerable advancement in the new kidney biopsies. It is located in the target organ and can decrease the damage to the surrounding tissue and performing multiple samplings, however the non-coaxial technique needs repeated insertion for each sampling (6).

**The Biopsy Tissue**

In kidney biopsy, obtaining at least 2 biopsy cores are commonly needed. Appropriate samples in standard preparation consisted of fixative for LM, IF, and EM. As samples from random locations has no variable pathology, it is assumed that there is no sampling bias if the physician obtains the core from the same general area. Cortical tissue is predominantly needed to be obtained because there are many glomeruli located there. Dividing cores in a manner can help to enlarge the obtained glomeruli in each sample. Needle size can also affect the obtained glomeruli count. The diameter of a 14-16- and 18-gauge needles is respectively 1,000 μm, 700 μm; and 350 μm. Insufficient samples and fragmented glomeruli may be induced if an 18-gauge needle was used in an adult with a 250 μm average diameter of glomerulus. Hematoma formation and no difference in glomeruli may be increased by the use of a 14 compared to 16-gauge needles. Minimal bleeding complications and adequate sample are noted by a 16-gauge needle as well. It seems that despite the variability of the amount of needed glomeruli for a diagnosis by light microscopy, 15 to 20 of them are enough. The 1.5- to 2-cm-long cores of tissue can usually provide this amount. Dissecting scope or magnifying glass after cores collection by the operator can assess the presence of the glomeruli in sample. In the case of inadequacy, up to 5 passes can be performed. More than 5 can increase the risk of hemorrhage (7).

**Preparation**

Before kidney biopsy, patients need laboratory assessments for blood clotting abnormality or infection. Tests are prothrombin time, complete blood count, complete biochemical profile, partial thromboplastin time, platelet count, and bleeding time. Furthermore, to decrease the risk of bleeding and considering its safety, reviewing drugs with health care provider is needed. In the case of taking warfarin (Coumadin), heparin, clopidogrel (Plavix), or other drugs that prevent blood clots, clinicians should inform patients about the appropriate time for medications before biopsy (8).

**Equipment**

For performing kidney biopsy needed instruments are:

1. A spinal 23-gauge needle for infiltration
2. A 5 mL syringe
3. 1% lidocaine for topical anesthesia
4. Number 11 Scalpel
5. Topical antiseptic solution
6. Sterile gauzes
Perforated gown
8. Sterile gloves
9. A blanket roll
10. An automated 16 or 18 gauges needles with or without coaxial introducer
11. 3 containers for light microscopy (LM), immunoflurescent (IF), and electromiroscopy (EM).
12. An ultrasound with curvilinear or linear probes.

Analgesia
Commonly light sedation and local anesthesia under using 1% Lidocaine should be applied. Also, for uncooperative adults or children, deep anesthesia may be needed.

Marking proper kidney biopsy site
Historically kidney biopsy was performed under real time guidance of intravenous pyelogram. Then Ultrasound was introduced and initially marked the proper site of kidney outside of or in the operating room. It developed to real time guidance by radiologists. Recently by the advent of point of care ultrasound (POCUS) which is the use of ultrasound at the bedside by physicians can be used for diagnosis and procedural aims (9) such as kidney biopsy, pleural and ascites tap, suprapubic aspiration (10), etc. Furthermore, CT guided kidney biopsy can be used in some circumstances as well.

Procedure
The common biopsy site is the lower pole of the left kidney, but clinicians prefer performing biopsy on a kidney with the highest level of visibility and accessibility.

In percutaneous renal biopsy under real-time ultrasound guidance, patient is placed in prone position and a pillow is put under the upper abdomen. Although in a cooperative patient, there is no need for sedative administration, in anxious adults and children, mild sedative or even anesthesia may be needed (11).

To perform an appropriate kidney biopsy, following steps should be considered.
First, the Physician and his/her assistant wear sterile gowns and gloves. Then the Patient lay in a prone position on a firm table and lay over the blanket roll. The lower pole of left kidney is the best site of needle insertion because of its lower vessels composition. In sagittal plane, while probe’s indicator to the patient's head, probe is slowly sliding from left midscapular line of lower ribs until the desired point. The desired point is achieved when the middle part of the probe is located exactly on the lower pole of left kidney. This point is marked as the needle biopsy insertion site. In a cooperative patient, there is no need for sedative administration. But, in anxious adults and children, mild sedative or even anesthesia may be needed. Therefore, clinicians should inform the possibility of its complications to patients and/or guardians. In this step, Anti-septic solution is used and local anesthesia by lidocaine 1% is injected. To insert the needle, clinician makes a small incision. After incision, needle biopsy should be advanced by the direct and real time guidance of ultrasound. For real time kidney visualization, sterile ultrasound probe cover should be used. Ultrasound is used for better visualization of coaxial or needle pathways. Based on patients’ size, physicians can use linear probe as the preferred probe for thin adults and children. Otherwise, they should apply curvilinear probe for overweight and obese patients. To decrease the damage to the surrounding tissue and performing multiple samplings, the coaxial Tru-Cut needle can be recommended if available. It is better to be used in all patients especially high risk ones. It is placed just to the outer cortex of the kidney. The patient should hold his/her breath during coaxial or needle insertion into the renal tissue. As it is shown in the attached video, by US guide, the coaxial needle is slowly introduced next to the kidney cortex. Automated 16-18 gauges needles can be applied and inserted in the coaxial introducer. After firing, the first sample is obtained and the needle is withdrawn but coaxial introducer is preserved for further samplings. Two to three obtained cores should be used for different pathological assessments. If the samples were adequate, the coaxial will be removed. The incision site should be pressed and dressed and the patient have adequate rest for 12-24 hours. Recent investigation demonstrated that there is no need for overnight hospitalization for patients undergoing kidney biopsy.

Complications
The patient should be closely observed for complications including flank pain, growth hematuria, hypotension, and blockage of urination during observation period (12).
You can find the complementary educational video in this issue which is entitled Incorporating Real time ultrasound guidance to kidney biopsy by the nephrologist.

**Conflict of Interest**
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**References**