Diagnosis

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Critical review

The percutaneous native kidney biopsy: a nephrologist's perspective

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Abstract

Introduction

Kidney biopsy is one of the most important diagnostic tools in a nephrologist's armamentarium. It has been shown that performance of a kidney biopsy in the appropriate clinical setting has the potential to alter the clinical diagnosis as well as change the therapy in many cases. Current biopsy practice is very safe with minimal complications and has the ability to obtain adequate tissue for histological diagnosis in more than 95% of cases. It is important for nephrologists to know about the various indications, contraindications and modifications in the procedure as well as the complications. All the trainees are supposed to learn the proper technique of kidney biopsy not only because of the importance of the procedure, but because of the fact that kidney biopsy is one of the triggers that enable the development of nephrology as a separate subspecialty. In this article, we critically review various aspects of a kidney biopsy that is important for practice by nephrologists.

Conclusion

Percutaneous kidney biopsy is a relatively safe procedure because of the development of many advances like ultrasound-guided and automated biopsy needles. Complication rates following the procedure are minimal and have been decreasing over a period of time.

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Introduction

The procedure of obtaining the renal tissue for histopathological examination, 'the kidney biopsy', is perhaps one of the turning points in nephrology practice that enabled it to develop as a separate subspecialty[1]. The widespread acceptance and performance of this procedure has been brought about by refinements in the existing practices and introduction of newer developments. This has led to a more successful tissue yield that resulted in a more accurate histological diagnosis and has also made the procedure reasonably safe.

The kidney biopsy is used for evaluation of many renal diseases and occasionally becomes the only answer to many complex disorders. The aim of this critical review is to discuss the native kidney biopsy through a nephrologist's perspective.

Discussion

In this review, the authors have referenced some of their own studies. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees associated to the institutions in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in the studies.

Evolution of the biopsy procedure

The earliest histological examinations of the renal tissue were secondary to examination of tissues obtained during renal decapsulation procedures performed between 1900 and 1930[1]. Kidney biopsy as an acceptable and valid medical procedure started to evolve following the seminal work published by Iverson and Brun[2] in 1951 and Alwall[3] in 1952. These initial reports were aspiration biopsies performed with the patient in the sitting position and using imaging (X-ray or intravenous pyelogram) for surface marking of the kidney. Adequate tissue collection in these two initial reports was found to be only 50% and 77%, respectively. In 1954, Kark and Muehrcke used an exploring needle to localise the kidney after placing the patient in the prone position and used the Franklin-modified Vim-Silverman needle for biopsy. The technique used by them can be described as a 'blind procedure'[4]. This modification resulted in development of more successful biopsies and a larger core of tissue for examination.

Subsequently imaging modalities have been used for localising the kidneys and ultrasound-guided (USG) is used most commonly. Initially used for surface marking and approximating the needle direction and depth, the USG has gradually been adopted to conduct the entire biopsy procedure under real-time guidance. Biopsies conducted under the USG management are safer than a blind procedure and can also result in more successful biopsies with a better tissue sample[5,6].

The automated biopsy devices

In the 1980s, the spring loaded, automated, cutting-needle biopsy guns were developed[7]. The advantages of safety, better tissue yield with minimal tissue disruption and ease of the procedure enabling use of a real-time USG imaging with one hand and the biopsy gun with another, made these automated devices readily acceptable and the Tru-Cut needles were gradually phased out[8–12]. Adequate tissue for a

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successful diagnosis can now be obtained using a real-time USG guidance and automated biopsy needles in more than 95% of cases[13].

A variety of sizes of these automated devices are generally manufactured, but only 14 gauges through 18-gauge devices have been traditionally used for kidney biopsies. It is generally seen that bleeding complications are observed more often with a 14-gauge needle, without any additional advantage regarding the adequacy of the tissue[14]. A 16-gauge device has an internal diameter that is approximately thrice the diameter of an adult glomerulus and thus, could theoretically result in a better glomerular yield with lesser 'fragmented' glomeruli and lesser number of cores. The safety of the 16-gauge needle has also been shown to be as good as the smaller 18-gauge needle[15,16]. Thus, it is advisable to use a 16-gauge needle for adults and an 18-gauge needle for children. The larger 14-gauge needle is not recommended for a kidney biopsy.

Percutaneous kidney biopsy procedure

Even though kidney biopsy is a relatively safe procedure, it is still an invasive one and should be performed only when indicated. Even then its importance cannot be undermined. This is because performing a kidney biopsy has been shown to change the pre-biopsy clinical diagnosis in 44% of cases and has also been shown to change therapy in 30% of cases[17]. Thus, a kidney biopsy can be very aptly labelled as a 'necessary evil'.

The indications of a kidney biopsy include a diverse spectrum of illnesses (Table 1). However, the choice of patients depends on the prevalent practices and is not absolute. For example, even though a kidney biopsy is considered necessary in all adult nephrotic syndrome patients, it is performed only in selected childhood cases e.g., in steroid-resistant or atypical cases. Similarly, in cases where the renal function has acutely worsened, the need and timing of a kidney biopsy depends on various factors like presence of a correctable underlying cause, manifestations of systemic diseases, unsatisfactory recovery etc.

Pre-biopsy evaluation

A proper history and a good physical examination is a must in all patients. Laboratory examinations that are essential before biopsy include a complete blood count, complete biochemical test, coagulation parameters [activated partial thromboplastin time (APTT), prothrombin time (PT), bleeding time and clotting time] and urinalysis. In addition, further tests have to be performed according to the underlying renal syndrome. All patients should have a USG examination, which is mainly to rule out small kidneys or any anatomic abnormalities or other contraindications to biopsy.

There is a lot of controversy surrounding kidney biopsy in patients with deranged coagulation function test (PT and APTT). Abnormal coagulation test did not predict increased bleeding risks in many clinical situations, including kidney biopsy according to a systematic review[18]. In a recent literature review by Jecko Thachil[19], bleeding risk from the abnormal clotting screen was minimal in the absence of prior bleeding history in patients with renal disease. Administration of fresh frozen plasma (FFP) in these cases is probably unnecessary and often causes delay in the procedure. Similarly, platelet transfusions may not be appropriate in those with platelet dysfunction. The author of this review concluded that patients without any prior bleeding history and with PT/APTT less than 1.5 times upper limit of normal can safely undergo a kidney biopsy. The rest of the patients should undergo alternate tests that

Table 1. Indications and contraindications of percutaneous native kidney biopsy.

Indications	Contraindications
Nephrotic syndrome. Renal involvement in systemic illnesses. Unexplained kidney dysfunction (acute or chronic). Microscopic haematuria with proteinuria. Subnephrotic proteinuria >1g/day. Familial renal diseases.	Absolute contraindications: Uncontrolled hypertension Bleeding diathesis Widespread renal disease or renal malignancy Hydronephrosis Unco-operative patient Relative contraindications: Single kidney Anti-platelet or anti-coagulation therapy Anatomic abnormalities Small kidneys Active urinary or skin sepsis Obesity

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include thrombin generation tests or thromboelastography methods before considering FFP transfusions. Large trials are required to investigate the extent to which deranged coagulation tests along with renal dysfunction predicts bleeding following kidney biopsy and probably, this will remain only a myth.

After selecting and investigating the patients who require a kidney biopsy, it is imperative to look for various situations where performing a biopsy is contraindicated or requires special modifications in the procedure (Table 1)[20,21]. The aim should be to always control many of these contraindications before a biopsy is performed. In certain situations, it becomes necessary to perform a biopsy urgently regardless of these circumstances when some alternate strategies like open (surgical) biopsy, transjugular (transvenous) biopsy and laparoscopic biopsy can be used[21].

Performing a percutaneous native kidney biopsy

After the patient has been selected and evaluated, an informed consent is taken (from the guardian in case of minors). The patient is instructed to lie prone with a pillow below the abdomen at the level of the umbilicus. A preliminary USG is performed to localise the surface marking of the position of the lower urinary pole. We routinely perform renal biopsies from the left kidney by default as it is away from the major vessels and organs and it is easier to handle the biopsy guns in case of right-handed operators. The skin is then cleaned with povidone-iodine/chlorhexidine and is draped with a sterile sheet. The USG probe is covered with a sterile cover and is placed on the skin after applying some sterile jelly. It is generally enough to perform the procedure under local anaesthesia. Occasionally, in children or in anxious individuals, mild sedation can be used. Local anaesthesia in the form of 1%–2% lignocaine is injected under USG guidance from the skin, down to the renal capsule, along the biopsy tract.

The appropriate biopsy needle is then advanced under USG guidance along the anesthetised tract. We prefer a 16-gauge biopsy needle for adults and 18-gauge needle for children as described above. Before the renal capsule is reached, the patient is instructed to take a deep inspiration and hold it such that the lower pole comes under the needle tip, and then it is advanced with the needle passing the capsule and after this the triggering mechanism of the needle is released. The needle is then withdrawn immediately and the patient is instructed to start breathing. In general, 2 to 3 cores of tissue are sufficient for an adequate yield.

The biopsy sample is then inspected under either a dissecting microscope or under a light microscope by making a wet mount of the core with normal saline with or without a cover slip. This is essential to ensure that the sample contains an adequate number of glomeruli, which can be seen as reddish dots. If this facility is not available, then the individual cores can be divided. One acceptable protocol for this is to send the terminal 1 mm from both sides of the biopsy core for electron microscopy (EM). The remaining sample is then divided and the larger of the first and smaller of the second core is sent for light microscopy (LM) and the remaining tissue is used for immunofluorescence (IF)[22]. Samples should be handled with extreme care to avoid development of artefacts. Desiccation of the sample should be avoided and normal saline should be used to wash off the tissue cores from the biopsy needle, which should be placed on saline soaked gauze rather than dry or water soaked gauze. An 18-gauge needle of a wooden stick should then be used to handle the samples and if they are divided, the scalpel should be fresh and sharp. The samples are then placed in fixatives and transport media for LM, IF and EM, and are dispatched immediately along with the relevant clinical and laboratory details.

Post-biopsy observation

After the biopsy, strict bed rest lying flat on the back is advised for 6 to 8 hours and patients are generally restricted to bed for the next 24 hours. The duration of the strict bed rest is unclear, but in one study decreasing this period of strict bed rest from 7 to 2 hours decreased the incidence of back pain without increasing the complication rate[23]. Vitals are frequently monitored and every voided urine sample is examined for visible haematuria and patients are observed for any complications.

Due to the occurrence of delayed bleeding complications, kidney biopsy is generally performed as an inpatient procedure as it is believed that ≥33% complications occur beyond 8 hours of observation[24,25]. However, there are many studies conducted in both adult and paediatric populations[26–30], including our own experience[31], where a shorter observation time enabled an outdoor procedure that was safe and reported no deaths. This can also prove to be cost effective. Maripuri et al.[32] have reported that the overall cost was much lower for outpatient biopsies compared with inpatient observation even when the additional costs accounted for the treatment of complications or possible death was considered.

Performing additional tests such as haemoglobin, haematocrit or USG as a routine for all patients may not be cost effective. Waldo et al.[33] showed that on a 1-hour post-biopsy USG, absence of a perirenal haematoma predicted no complications, but presence of one also could not significantly predict the development of complications. Thus, careful clinical observation is good enough.

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Complications

The current practice of percutaneous native kidney biopsy is a relatively safe procedure with life threatening complications occurring in <0.1% of biopsies[13,24,34,35]. Complications are generally divided into those that resolve spontaneously without interventions (minor complications) and those that require interventions-like transfusions or invasive procedures or are life or organ threatening (major complications) (Table 2).

Significant macroscopic haematuria has been variably reported from 0.3%–14.5%, but a recent meta-analysis of 34 studies from 1980 till 2011 comprising 9,474 biopsies showed that the overall rate was 3.5% with 0.9% requiring blood transfusions and angiographic intervention is only 0.6%[14]. New data from the Norwegian Kidney Biopsy Registry show that this complication rate may still be lower with macroscopic haematuria reported in 1.9% of the patients; 0.9% of patients requiring blood transfusion and 0.2% of patients requiring surgical intervention/catheterisation[36].

Multiple factors have been considered predictive of complications after biopsy. However, a meta-analysis showed that out of the many variables considered, a higher blood transfusion requirement was observed when a 14-gauge needle was used for biopsy compared with 16-gauge and 18-gauge needles, in patients with higher serum creatinine values, in biopsies performed for acute kidney injury, lower baseline haemoglobin and also in older patients and hypertensives[14]. Another study showed that biopsies in patients with a serum creatinine ≥5.0 mg/dL were 2.3 times more likely to have a complication after renal biopsy[25].

The non-invasive kidney biopsy?

There are many limitations of a kidney biopsy. The non-uniform parenchymal involvement in many renal diseases, which can be missed by biopsy taken from a very small section of the kidney, might miss detection of the pathological changes. Many times, there are situations, when a biopsy cannot be safely performed or can result in complications. A non-invasive method of assessment is the urinary proteomics, which is study of the protein profile in the urine using complicated procedures, like liquid chromatography and tandem mass spectrometry. The precursor peptides and fragment ion masses are analysed by complex search programmes to identify proteins from genomic databases[37]. This can serve as a theoretically sound alternative to a kidney biopsy, but is still in the developmental stage. Till this new method becomes one of the validated and economically acceptable methods, the percutaneous kidney biopsy is here to stay.

Conclusion

Percutaneous kidney biopsy is one of the most important investigations in clinical nephrology and is a relatively safe procedure because of the development of many advances such as USG and automated biopsy needles. Complication rates following the procedure are minimal and have been decreasing over a period of time. It is important that all nephrology programmes train the trainees in performing biopsies, so that there is a wider clinical use of this important investigation.

Table 2. Complications of percutaneous kidney biopsy.

Pain
Macroscopic haemorrhage
Perirenal haematoma
Arteriovenous fistula
Blood transfusion
Surgery/embolization
Injury to other organs
Death

Abbreviations list

APTT, activated partial thromboplastin time; EM, electron microscopy; IF, immunofluorescence; LM, light microscopy; PT, prothrombin time; USG, ultrasound-guided.

References

1. Cameron JS, Hicks J. The introduction of renal biopsy into nephrology from 1901 to 1961: a paradigm of the forming of nephrology by technology. Am J Nephrol. 1997;17(3–4):347–58.
2. Iverson P, Brun C. Aspiration biopsy of the kidney. Am J Med. 1951 Sep;11(3):324–30.
3. Alwall N. Aspiration biopsy of the kidney, including i.a. a report of a case of amyloidosis diagnosed through aspiration biopsy of the kidney in 1944 and investigated at an autopsy in 1950. Acta Med Scand. 1952 Sep;143(6):430–5.
4. Kark RM, Muehrcke RC. Biopsy of kidney in prone position. Lancet. 1954 May;266(6821):1047–9.
5. Maya ID, Maddela P, Barker J, Allon M. Percutaneous renal biopsy: comparison of blind and real-time ultrasound-guided technique. Semin Dial. 2007 Jul–Aug;20(4):355–8.
6. Hergesell O, Felten H, Andrassy K, Kühn K, Ritz E. Safety of ultrasound-guided percutaneous renal biopsy-retrospective analysis of 1090 consecutive cases. Nephrol Dial Transplant. 1998 Apr;13(4):975–7.
7. Lindgren PG. Percutaneous needle biopsy. A new technique. Acta Radiol Diagn. 1982;23(6):653–6.
8. Burstein DM, Korbet SM, Schwartz MM. The use of the automatic core biopsy system in percutaneous renal biopsies: a comparative study. Am J Kidney Dis. 1993 Oct;22(4):545–52.

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9. Kim D, Kim H, Shin G, Ku S, Ma K, Shin S, et al. A randomized, prospective, comparative study of manual and automated renal biopsies. Am J Kidney Dis. 1998 Sep;32(3):426–31.
10. Kumar A, Mitchell MJ, Aggarwal S, Fraser DB, Trillo AA. Ultrasonography-directed native renal biopsy: comparison of an automated biopsy device with a needle system. Can Assoc Radiol J. 1992 Oct;43(5):359–63.
11. Mahoney MC, Racadio JM, Merhar GL, First MR. Safety and efficacy of kidney transplant biopsy: Tru-Cut needle vs sonographically guided Biopty gun. AJR Am J Roentgenol. 1993 Feb;160(2):325–6.
12. Nyman RS, Cappelen-Smith J, al Suhaibani H, Alfurayh O, Shakweer W, Akhtar M. Yield and complications in percutaneous renal biopsy. A comparison between ultrasound-guided gun-biopsy and manual techniques in native and transplant kidneys. Acta Radiol. 1997 May;38(3):431–6.
13. Korbet SM. Percutaneous renal biopsy. Semin Nephrol. 2002 May;22(3):254–67.
14. Corapi KM, Chen JL, Balk EM, Gordon CE. Bleeding complications of native kidney biopsy: a systematic review and meta-analysis. Am J Kidney Dis. 2012 Jul;60(1): 62–73.
15. Van Damme B, Van Damme-Lombaerts R, Waer M. Biopty device for obtaining kidney specimens. Pediatr Nephrol. 1990 Jan;4(1):94–5.
16. Mai J, Yong J, Dixson H, Makris A, Aravindan A, Suranyi MG, et al. Is bigger better? A retrospective analysis of native renal biopsies with 16 Gauge versus 18 Gauge automatic needles. Nephrology. 2013 Jul;18(7):525–30.
17. Turner MW, Hutchinson TA, Barré PE, Prichard S, Jothy S. A prospective study on the impact of the renal biopsy in clinical management. Clin Nephrol. 1986 Nov;26(5):217–21.
18. Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. Transfusion. 2005 Sep;45(9): 1413–25.
19. Thachil J. Abnormal coagulation tests before kidney biopsies—what next? Clin Kidney J. 2013;6(1):50–4.
20. Salama AD, Cook T. The renal biopsy. In: Taal MW, Chertow GM, Marsden PA, Skorecki K, Yu ASL, Brenner BM editors. Brenner & Rector's The Kidney, 9th ed. Philadelphia: Saunders; 2012.p.1006–14.
21. Stiles KP, Yuan CM, Chung EM, Lyon RD, Lane JD, Abbott KC. Renal biopsy in high-risk patients with medical diseases of the kidney. Am J Kidney Dis. 2000 Aug; 36(2):419–33.
22. Walker PD, Cavallo T, Bonsib SM. Practice guidelines for the renal biopsy. Mod Pathol. 2004 Dec;17(12):1555–63.
23. Ishikawa E, Nomura S, Obe T, Katayama K, Oosugi K, Murata T, et al. How long is strict bed rest necessary after renal biopsy?Clin Exp Nephrol. 2009 Dec;13(6):594–7.
24. Marwah DS, Korbet SM. Timing of complications in percutaneous renal biopsy: what is the optimal period of observation? Am J Kidney Dis. 1996 Jul;28(1):47–52.
25. Whittier WL, Korbet SM. Timing of complications in percutaneous renal biopsy. J Am Soc Nephrol. 2004 Jan;15(1):142–7.
26. Mahajan V, Suri D, Saxena A, Nada R. Should ultrasound guided percutaneous renal biopsy in children be done in a day care setting? Indian J Nephrol. 2010 Jan;20(1):21–4.
27. Simckes AM, Blowey DL, Gyves KM, Alon US. Success and safety of same-day kidney biopsy in children and adolescents. Pediatr Nephrol. 2000 Sep;14 (10–11):946–52.
28. McMahon GM, McGovern ME, Bijol V, Benson CB, Foley R, Munkley K, et al. Development of an outpatient native kidney biopsy service in low-risk patients: a multidisciplinary approach. Am J Nephrol. 2012 May;35(4):321–6.
29. Lin WC, Yang Y, Wen YK, Chang CC. Outpatient versus inpatient renal biopsy: a retrospective study. Clin Nephrol. 2006 Jul;66(1):17–24.
30. Maya ID, Allon M. Percutaneous renal biopsy: outpatient observation without hospitalization is safe. Semin Dial. 2009 Jul–Aug;22(4):458–61.
31. Golay V, Sarkar D, Thomas P, Trivedi M, Singh A, Roychowdhary A, et al. Safety and feasibility of outpatient percutaneous native kidney biopsy in the developing world: experience in a large tertiary care centre in Eastern India. Nephrology. 2013 Jan;18(1):36–40.
32. Maripuri S, Penson DF, Ikizler TA, Cavanaugh KL. Outpatient versus inpatient observation after percutaneous native kidney biopsy: a cost minimization study. Am J Nephrol. 2011;34(1):64–70.
33. Waldo B, Korbet SM, Freimanis MG, Lewis EJ. The value of post-biopsy ultrasound in predicting complications after percutaneous renal biopsy of native kidneys. Nephrol Dial Transplant. 2009 Aug;24(8):2433–9.
34. Burstein DM, Schwartz MM, Korbet SM. Percutaneous renal biopsy with the use of real-time ultrasound. Am J Nephrol. 1991;11(3):195–200.
35. Mendelssohn DC, Cole EH. Outcomes of percutaneous kidney biopsy, including those of solitary native kidneys. Am J Kidney Dis. 1995 Oct;26(4):580–5.
36. Tøndel C, Vikse BE, Bostad L, Svarstad E. Safety and complications of percutaneous kidney biopsies in 715 children and 8573 adults in Norway 1988-2010. Clin J Am Soc Nephrol. 2012 Oct;7(10):1591–7.
37. Bramham K, Mistry HD, Poston L, Chappell LC, Thompson AJ. The non-invasive biopsy--will urinary proteomics make the renal tissue biopsy redundant? QJM. 2009 Aug;102(8):523–38.

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