

Percutaneous Renal Biopsy: Comparison of Blind and Real-time Ultrasound Guided Technique

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ABSTRACT

Background: Percutaneous renal biopsy is performed for diagnosis and prediction of prognosis of renal diseases. Adequacy of tissue and clinically significant bleeding are the main issues of the procedure. We aimed to compare these issues in renal biopsy by blind and real time ultrasound guided technique.

Methods: It was a cross sectional, randomized study conducted between June 2016 to December 2016. In blind technique, marking for biopsy was done by ultrasound. Two attempts were performed for all and more if tissue was inadequate. Patients kept in bed rest for 24 hours, observed for post procedure hematuria and ultrasound done at 6 hours and 24 hours to diagnose perinephric hematoma.

Results: Total 75 biopsies (blind = 37 and Ultrasound -guided = 38) were evaluated. Blind and Ultrasound-guided technique had significant difference of number of attempt (mean±SD) 2.4 ± 0.6 and 2.1 ± 0.3 ($p<0.01$) respectively with no difference of number of glomeruli in light microscopy. Bleeding complications were macroscopic hematuria (11(30%)vs15(40%)) and perinephric hematoma (5(13.5%)vs3(7.9%)) in blind and Ultrasound-guided technique respectively with no significant difference. Those patients who developed perinephric hematoma was observed in all at 6 hours.

Conclusions: Ultrasound-guided technique of percutaneous renal biopsy is superior with fewer attempts and equivalent in adequacy of tissue and bleeding complication than blind technique.

Keywords: Biopsy complications; percutaneous renal biopsy; perinephric hematoma; ultrasound-guided renal biopsy.

INTRODUCTION

Percutaneous renal biopsy (PRB) and histopathological evaluation is a mandatory tool for definitive diagnosis and prediction of prognosis of renal parenchymal diseases.

Adequate tissue yield with at least 8-10 glomeruli with no or minor bleeding complications have always been the goal.^{1, 2} Historically, PRB was performed blindly by radiography³ and later ultrasound (USG) guided surface marking. Gradually the whole procedure of PRB has been performed by real-time USG guidance with better tissue yield and increased safety.^{4, 5}

Similarly, PRB started in 1973 by nephrologist in Nepal had evolved from blind technique via radiography⁶ and then USG guided surface marking to real-time USG guided technique and histopathological diagnosis of kidney disease been reported after 2000.⁷⁻⁹ So, present study

was conducted to compare the efficiency, adequacy of tissue and bleeding complications between blind and real time USG-guided PRB.

METHODS

This was a cross sectional, randomized, comparative study conducted in the Department of Nephrology, Bir Hospital, Kathmandu, Nepal from June 2016 to December 2016. Ethical approval was obtained from Institutional Review Board (IRB) of National Academy of Medical Sciences (NAMS).

Patients decided for kidney biopsy by consultant nephrologist with bilateral normal sized kidneys and normal bleeding profiles (BT, CT, PT, APTT, and Platelets) were included after obtaining informed written consent and patients with single kidney and allograft was excluded.

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Detail history including drug history was taken and blood pressure recorded. Patients on antiplatelet or anticoagulant drugs were asked to stop it for 5 days after approval from concerned physician and follow up for enrolment. All patients undergoing PRB were admitted. The laboratory parameters including bleeding profiles and renal function tests and clinical indications for PRB were recorded in predesigned pro-forma. The first patient was randomized by a coin-toss and underwent blind biopsy: subsequent patients were randomized alternately.

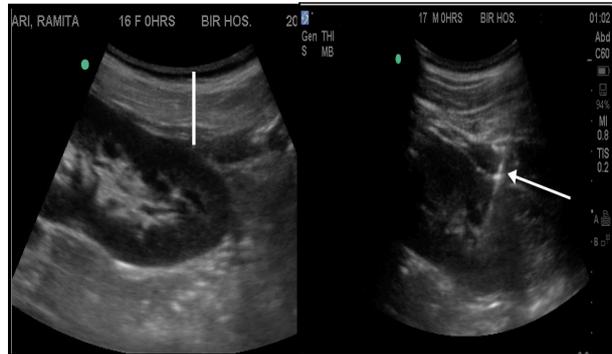
All PRB were performed by second year nephrology residents who were trained for the procedure already. The patients were kept on prone position. A routine preliminary USG with 3.5 MHZ transducer had scanned both kidneys for complete evaluation of cortical and sinus echogenicity by longitudinal and transverse images and exclusion of any structural abnormalities prior to the biopsy. All PRB were performed by Bard gun “max-core” disposable core biopsy instrument (Bard Peripheral Vascular, Inc, USA), size 18G*16 cm length, with 1.8cm sample notch length.

For blind biopsy, USG surface marking for PRB over the lower pole of the left kidney by default were done and the perpendicular distance from the skin to the renal cortex were measured. The skin was disinfected with povidone-iodine, draped with a sterile sheet and anesthetized with 1% lignocaine. A probe was used to locate the kidney depth. Patients were asked to take deep breath in and hold and probe inserted perpendicularly until it penetrated the muscle and reached the expected distance estimated by the initial USG. Then patients were asked to take deep breath in and out to see the movement of the probe. If it was not moving with respiration, again patient was asked to hold deep breath in and probe pushed slightly more. The process repeated until the probe penetrated the kidney and moved with respiration. Then the probe was removed and depth measured in Bard gun and it was inserted blindly up to that depth with breath hold in deep inspiration, gun fired and tissue obtained.

USG probe was covered with a sterile cover and sterile jelly applied. Local anesthesia with 1% lignocaine was injected under USG guidance from the skin to the renal capsule. The Bard gun was advanced under USG guidance along the anesthetized tract. Biopsies were performed free hand and biopsy adapter was not used. Before the renal capsule reached, the patient was instructed to take a breath and hold it such that the lower pole comes

under the needle tip, and then it was advanced and the gun was fired.

The USG surface marking with depth measurement from skin in blind biopsy and real time biopsy needle visualization at the renal capsule in USG-guided technique is shown in Figure 1.



The distance to the biopsy point from the skin surface was determined (white line). Real time biopsy needle visualization (arrow)

Figure 1. B mode ultrasonographic image of a kidney.

In general, 2 cores of tissues were taken. A minimum of two attempts and a maximum of four attempts were performed in each of these patients. After the procedure, a firm pressure was applied.

The renal tissue obtained was sent for light-microscopy and direct immunofluorescence (DIF). Wound was closed with dressing.

After the procedure, all patients were advised for strict bed rest lying flat on the back for 6 to 8 hours and then remained in bed for 24 hours of observation. Patients were monitored closely after biopsy for signs or symptoms of complications, such as hematuria, flank pain, or hypotension. Vital signs was checked every 15 min for 1 h, every hour for 2 h, every 2 h for 4 h, and then every 4 h thereafter. Each urine void was checked for hematuria visually, and the result was recorded. Hemoglobin levels were checked at approximately 18 to 24 h after the procedure. Data was entered first in excel spread sheet and later analysed using SPSS software package 19.0 and $p < 0.05$ was taken as the level of significance. Data for continuous variables was expressed as mean \pm standard deviation and t-test was used to compare the mean difference of each group. Test suitable for 2 x 2 contingency table (chi-square) was used for test of independence.

RESULTS

Total 76 patients had undergone PRB of native kidneys during study period with blind biopsy in 38 (15 male and 23 female) and USG -guided in 38 (24 male and 14 female) patients. But one patient in blind group was excluded from the study as there was no tissue even after 4 attempts with 75 PRB for analysis.

The comparison of clinical and laboratory parameters of patient with blind and USG-guided biopsy (Table 1) has shown no difference in age, hemoglobin, platelet counts, BT, PT and APTT and significantly higher baseline systolic and diastolic blood pressure and lower CT in USG guided group though all within normal limit and the patients were of more female gender in blind group. The indications for PRB were nephrotic syndrome (44%), glomerulonephritis (GN) with nephritic syndrome (16%) and others (40%) with no difference between two groups (Fig 2).

Table 1. Clinical and laboratory baseline demographic data of PRB patients.

	Blind PRB (n=37)	USG Guided PRB (n=38)	p-values
Age (Years)	32.97 ± 15.56	33.92±15.41	0.792
Male gender n (%)	15 (41%)	24 (63%)	0.05
SBP (mm of Hg)	123.19±17.18	130.42±10.56	0.031
DBP	79.03±10.12	83.68±8.63	0.035
Platelet count (x1000 /mm3)	274±93	267±125	0.777

BT (Min)	2.88±0.82	2.64±0.74	0.241
CT (Min)	7.65±1.25	6.89±1.37	0.016
PT (s)	12.51±1.61	12.37±1.30	0.686
APTT (s)	32.39±8.10	33.87±10.31	0.493

Analysis of renal biopsy efficiency and adequacy of tissue (Table 2) has shown real time USG- guided technique being more efficient than blind technique with mean number of attempts (2.11 versus 2.41, p=0.008) and patients with more than 2 attempt needed in (4 versus 13, p=0.011) respectively. But there was no difference in adequacy of tissue with similar number of tissue bits per attempt, average size of the bits and average total number of glomeruli in both techniques. Moreover, tissue adequacy with > 8 glomeruli was found in 94.6% of blind and 92.1% of USG guided biopsies. But in one case of blind biopsy, there was only medullary tissue with no glomeruli in DIF study and repeat biopsy was done.

The bleeding complications (perinephric hematoma and / or macroscopic hematuria), as shown in Table 3 were observed in 35.1% of blind and 42.1% of USG guided PRB with macroscopic hematuria being the predominant complication in 29.7% vs 39.5% patients respectively and none of the patients in both group had persistent macroscopic hematuria till 24 hours after PRB. The perinephric hematoma was found only in 13.5% of blind and 7.9% of USG group and associated with macroscopic hematuria in 8.1% and 5.3% patients respectively. Moreover, the hematomas developed in all patients by 6 hours except one in blind technique that showed 2 cm hematoma at 24 hours and one patient in each group had persistent hematoma till 24 hours.

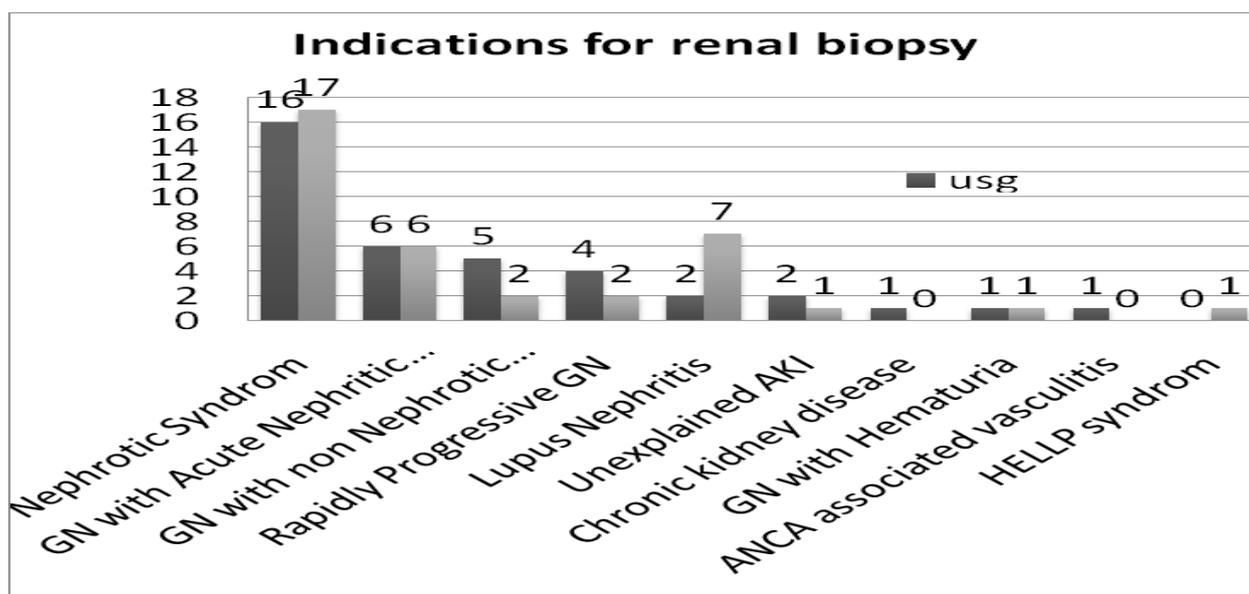


Figure 2. Indications for renal biopsy.

Table 2. Efficiency and adequacy of tissue.

Efficiency and adequacy of tissue	Blind PRB (n=37)	Real time USG guided PRB (n=38)	p-values
Total Number of Attempts	2.41±0.6	2.11±0.3	0.008
>2 Attempts needed	13 (35.13%)	4(10.52%)	0.011
Number of tissue bits per attempt	0.95±0.13	0.98±0.08	0.198
Average size of the bits (cm) per sample	1.07±0.25	1.14±0.31	0.281
Total number of glomeruli	23.54±8.32	23.89±10.01	0.868
Average number of glomeruli per sample	10.72±4.07	11.76±5.09	0.331
>8 glomeruli in light microscopy	35(94.6%)	35(92.1%)	1.0

Table 3. Bleeding Complications of PRB.

Bleeding complications		PRB techniques		P value
Blind (n=37)				
USG -guided (n=38)				
No		32	35	
Perinephric Hematoma (a)	At 6 hours	4 (10.8%)	3 (7.9%)	0.97
	New at 24 hours	1 (2.7%)	0 (0%)	
	Total	5 (13.5%)	3 (7.9%)	0.68
Macroscopic hematuria (b)	Only hematuria	8 (21.6%)	13 (34.2%)	0.21
	With hematoma	3 (8.1%)	2 (5.3%)	
	Total	11 (29.7%)	15 (39.5%)	
Total bleeding complication (a) + (b)		13 (35.1%)	16 (42.1%)	
Post PRB interventions		0%	0%	

The mean hemoglobin level (gm/dl) at baseline and 18-24 hours post PRB of blind (12.2±2.2 vs 12.0±2.0, p=0.10) and USG guided (12.1±2.0 vs 11.9±1.9, p=0.11) showed insignificant blood loss in both techniques though there was reduction of hemoglobin in both group. There were no severe complications like blood loss requiring blood transfusion, loss of kidney function or death in any patients of both groups.

DISCUSSION

Percutaneous renal biopsy (PRB) with light and immunofluorescence examination of renal tissue can diagnose majority of renal parenchymal diseases. Addition of electronic microscopy with ultra-structural analysis provides invaluable information for accurate diagnosis of some specific renal diseases.¹⁰ PRB by blind technique is performed only by nephrologists and USG guided done by both nephrologist and radiologists or radiologist alone in different institutes as per their expertise.

In Nepal, this process was performed by nephrologists in the very beginning by blind technique through skin surface marking from X-ray KUB (Kidney, Ureter, Bladder) or nephrogram film by themselves and later through USG surface marking made by radiologists. Currently, with the availability of portable USG machines and development of expertise, it is either performed by real-time USG guidance by nephrologists or with assistance of radiologist or solely by radiologist. Although, histopathological diagnosis of glomerular disease,⁷⁻⁹ cast nephropathy¹¹ and allograft nephropathy¹² has been reported, there are few reports describing the PRB technique by radiologists and/or by nephrologist along with efficiency and complication of technique.^{13, 14}

We found that real-time ultrasound- guided renal biopsy was more efficient than blind technique with significantly less number of attempts to yield two adequate tissues (p=0.008) for light microscopic and immunofluorescence study and two tissue bits were obtained by two attempts in 89% of patients in USG guided group compared to 65% in blind group (p=0.011). Technical advantage of real time USG guided renal biopsy with two attempts in 91% patients were also observed by Maya and Allon in biopsy of 100 patients.¹⁵

Moreover, superiority of USG guided technique in adequacy of tissue with significantly higher number of glomeruli and success in 100% compared to 84% needing repeat biopsy in blind group was reported on a retrospective analysis.⁵ But in our study, there was no difference of adequacy of tissue as measured by number of tissue bits per attempt, average size of the bits per sample, total number of glomeruli, average number of glomeruli per sample and more than 8 glomeruli in sample for light microscopy in both technique and repeat biopsy was needed only in one patient in blind group for IF study indicating not inferiority of USG marked blind technique in tissue yield.

Similarly, comparison of tissue yield by blind (n=271) and USG guided (n=170) renal biopsy performed by nephrologist in Korea also showed no difference though significantly better yield by both techniques compared to USG technique performed by radiologist.¹⁶ Total number of PRB attempt, mean size of renal tissue and average number of glomeruli was also reported to be significantly higher in USG guided PRB performed by nephrologist when compared with historic biopsies performed with radiology assistance indicating nephrologist should take up this simple but vital procedure.¹⁷ There are reports on USG guided PRB by radiologist with adequate tissue yield in 98.9% and by nephrology resident who were assisted by radiologist if unsuccessful with total adequate tissue yield in 92.3% from teaching institutes of Nepal.^{13, 14} But in our institute as PRB has been always performed by nephrologist and trained the junior, the PRB by nephrology resident by self USG marking and self USG guided technique found to be efficient and effective with success rate of 98.7% of total biopsy.

The current practice of percutaneous native kidney biopsy is a relatively safe procedure with life threatening complications occurring in <0.1% of biopsies.¹⁸ Bleeding complications as measured by macroscopic hematuria, perinephric hematoma, reduction of hemoglobin and need of intervention including blood transfusion or embolization revealed no significant difference in both techniques irrespective of needle bore size¹⁹ or irrespective of the specialty of the PRB performer.¹⁶ But better safety profile of USG guided technique compared to blind technique was observed in terms of large hematoma (0% vs 11%), vascular intervention (0% vs 8%) and significantly higher 24 hour post biopsy hematocrit (p=0.04) in study by Maya et al,⁵ and lower frequency of perinephric hematoma with smaller hematoma volume by Kim et al.²⁰ We found perinephric hematoma in 10.7% patients all being minor needing no intervention with no difference between two techniques indicating blind technique is equally safe if performed by well-trained person.

Macroscopic hematuria is the most common and usually transient complication²¹ and may be associated clots, colicky pain, urinary obstruction and in the most severe case hemorrhagic shock. Puncture of the renal calyceal system, large vessel damage, arteriovenous fistulas and aneurysms are the main causes. In our study frank hematuria occurred in 30% of blind and 40% of USG guided biopsies with no statistical difference and all resolved by 24 hours.

Lower hemoglobin value clinically predicts a major

bleed. Some study shows each 1gm/dl decrease in the baseline hemoglobin doubled the likelihood of a major bleed²² and other shows drop in hemoglobin by >1 g/dl after biopsy is common and has been reported to occur in almost 50% of cases.^{23, 24} Our study also showed mild decrease in hemoglobin by 0.2 gm/dl in both groups needing no blood transfusion. The cause of the non-hemorrhagic change in hemoglobin is not known but may be the result of multiple factors, including the frequent development of a small subclinical perinephric hematoma, hemodilution as a result of the more water intake,²⁵ or postural hemodilution resulting from the resorption of interstitial fluid in severely edematous patients after prolonged bed rest after biopsy.²⁶ Thus, an initial decrease in hemoglobin concentration after renal biopsy must raise suspicion for a possible complication, but it is not a reliable predictor of outcome.

In a smaller retrospective series, Simard-Meilleur et al. found that 100% of complications in outpatients undergoing PRB occurred within 8 hours versus 72% of complications in inpatients and that 10% of inpatients had complications >24 hours after PRB.²⁷ The most recent large biopsy series found that 91% of major complications occurred within 12 hours of PRB, with 7.4% occurring between 12 and 24 hours and 1.85% occurring after 24 hours²⁸ where as other study shows only two hours post-PRB observation is optimal time to assess the safety of PRBs and prediction of late complications.²⁹ In our study also perinephric hematoma was observed in all at 6 hours except one in blind technique who showed it in 24 hours and none needed any intervention.

CONCLUSIONS

Compared with the blind technique, real time USG-guided percutaneous renal biopsy was superior in terms of fewer attempts; however there was no difference in the adequacy of sample and bleeding complications.

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