KIDNEY RESEARCH AND CLINICAL PRACTICE

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Needle guides enhance tissue adequacy and safety of ultrasound-guided renal biopsies

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Background: Needle guides have recently come into use for ultrasound-guided percutaneous renal biopsies; however, it is not yet clear if the use of needle guides leads to decreased post-biopsy complication rates and improved tissue yields. Thus, we conducted a retrospective single center study comparing biopsy yield, adequacy, and rates of complications before and after utilization of a needle guide device.

Methods: A retrospective analysis was performed on all native kidney biopsies performed before and after June 2015 corresponding to the start of needle guide use. All biopsies in the latter period of the study were performed by a single operator. We compared clinical characteristics, indications, type of investigation, tissue yield, adequacy of procedure, and rates of major and minor complications.

Results: A total of 343 biopsies were analyzed, 140 in the pre-needle guide use period (Period I) and 203 in the needle guide use period (Period II). Biopsy yields were similar, irrespective of the use of needle guides. Tissue adequacy was better in Period II (93.7% vs. 84%, $P < 0.001$, with respect to pathologist-reported inconclusive biopsies. There were no differences in terms of major complications (1.7%) for the two periods; however, the rate of minor complications (8.4%) was significantly reduced in Period II ($P = 0.006$). According to multiple logistic regression analysis, not using a needle guide (odds ratio, 3.70; $P < 0.001$) along with low hemoglobin level, higher pre-dialysis serum creatinine level, and high urinary red blood cell count were significant predictors of biopsy complications.

Conclusion: Use of a needle guide improves biopsy adequacy and is associated with reduced rates of minor complications in native renal biopsies. Therefore, needle guides may be recommended in percutaneous renal biopsies, especially when transitioning to single-operator performed procedures.

Keywords: Image-guided biopsy, Interventional ultrasonography, Kidney, Needle biopsy, Renal insufficiency

Introduction

Renal biopsy is an important tool in the diagnostic armamentarium available to the nephrologist. First de-

scribed by Iversen and Brun [1], percutaneous renal biopsy has undergone several modifications over the years, with the introduction of the Vim-Silverman needle [2] in the 1950s followed by spring-loaded automated biopsy gun [3] and now widespread use of ultrasound guidance in the last two decades [4]. Most renal biopsies are carried out under ultrasound guidance, with computed tomography guidance accounting for only a minority of cases. With presently available expertise, complication rates of < 5% have been achieved [4–6]. The specific types of bleeding complications can vary depending on the site of hemorrhage, and include perinephric hematomas, arteriovenous fistulas, and aneurysms, which can present as local pain, an asymptomatic drop in hemoglobin, he-

maturia, bladder clots, and obstructive symptoms if the bleeding occurs in the pelvicalyceal system. The need for a subsequent invasive procedure such as angiography, cystoscopy, blood transfusion, or surgery is seen in 0.3% to 6.6% cases [4]. Given the acceptably low risk of complications, a vast number of centers have started to perform renal biopsies as day-care procedure in recent years. However, when procedure-related complications do occur, they inevitably lead to increased treatment costs as well as prolonged and unanticipated hospital stays. Several risk factors are known to be associated with a higher risk of bleeding, including older age, female sex, uncontrolled hypertension, poor renal function, and deranged coagulation profiles. Therefore, careful risk-stratification may help in identifying patients where extra caution is required [4–6].

Needle guides were developed to allow passage of the needle via a predetermined track, and it has been hypothesized that decreased path deviation translates to improved outcomes. Employment of a needle guide represents a one-time procurement cost of the bracket, and regular disinfection of the needle guide to maintain sterility. While the use of needle guides is common in prostate and breast biopsies, it is not clear whether their use in renal biopsies improves biopsy yields and decreases rates of complications. Indeed, only two other studies on this topic have been publish, and their results are contradictory [7,8].

The number of operators involved in performing the renal biopsy is another under-studied factor that can potentially affect biopsy success both in terms of adequacy and complications. Indeed, procedure protocols vary by center, with some utilizing either two nephrologists, one nephrologist and one radiologist, or a single radiologist or nephrologist. At our center, prior to the procurement of a needle guide in June 2015 (Period I), our standard biopsy procedure involved two trained nephrologists, with one handling the ultrasound probe and the other responsible for obtaining cores. Following procurement of a needle guide (Period II), a single nephrologist was able to handle both the probe and biopsy gun. While large tertiary care referral centers do not have a dearth of trained (and in-training) nephrologists, the same is not true for the majority of nephrology practitioners, who must often rely on radiologists' assistance and schedule their biopsies accordingly. Thus, we undertook the present study to compare biopsy yields and complication rates at our center before and after the use of a needle guide (two operators vs. a single operator, respectively) over two time periods (2013–2015 vs. 2015–onwards).

Methods

The study was approved by the institute's ethical committee (IEC 6/17). In this retrospective, observational study, we compared biopsy yields and complication rates before and after the introduction of needle-guiding device corresponding to July 2013–May 2015 (Period I) and June 2015–April 2017 (Period II), respectively. A total of 359 biopsies were performed during the study period in the Department of Nephrology. Biopsies performed in the radiology suite (8), allograft biopsies (4), and post-mortem biopsies (4) were excluded from our analysis.

All patients were admitted prior to the procedure and underwent blood pressure recording and a basic set of investigations, including hemoglobin level, platelet count, coagulation profile, and bleeding time, and deranged parameters were corrected prior to the procedure. Pre-biopsy hemodialysis was performed for patients with a serum creatinine above 5 mg/dL, and intranasal desmopressin at a dose of 150 μg was also administered one hour prior to transfer to the biopsy room. Informed consent was obtained prior to the procedure in all cases. Procedures were performed under real-time ultrasound guidance (Sono Site M-TURBO® [Fujifilm Sonosite, Bothell, WA, USA], using the curvilinear probe of 3.5 MHz) using an automated spring-loaded biopsy gun, BARD® Max Core (Bard Peripheral Vasc Inc., Tempe, AZ, USA), either 16G or 18G, with a side notch of 18 mm and length of 16 cm in most cases, although a 10 cm length was used for children and adults of small build. The needle guide is shown in Fig. 1A, attached to the ultrasound probe.

The biopsy procedure involved placing the patient in prone position, with a pillow under the abdomen, after which the patient surface was cleaned with 2% povidone iodine, covered with a sterile drape, and infiltrated with 10 mL of 2% lignocaine for local anesthesia (as marked by pre-procedure ultrasound). During Period I, without the needle guide, one nephrologist would localize the lower pole of the left kidney, while the second, under real-time ultrasound, would advance the biopsy gun in a tangential approach and obtain samples upon reaching the desired
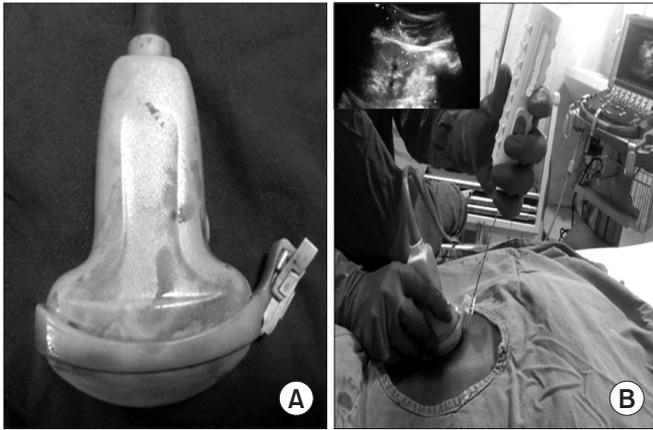
Figure 1. (A) The needle guiding device attached via a bracket to the curvilinear ultrasound probe. (B) Single-operator technique of performing renal biopsy with the needle guide. Inset: pathway of the needle shown during renal biopsy.

area. During Period II, a sterilized needle guide (Ultra-Pro II™; Civco, Coralville, IA, USA) was attached to the ultrasound probe, and samples were obtained through a predetermined track by a single operator. Fig. 1B demonstrates the single-operator performed biopsy using a needle guide. Two cores were taken in all cases, with division of the second core for electron microscopy. In pediatric cases, general anesthesia was administered where necessary, and all procedures were performed in the operating room. The right kidney was biopsied in all cases, as the left kidney was typically more difficult to access due to polar cysts, scars, and stones.

Syndromic diagnoses were made according to widely used syndromes in nephrology practice. "Nephrotic syndrome" was diagnosed in cases of proteinuria > 3.5 g/24 hours/1.73 m^2 along with hypoalbuminemia, edema and hyperlipidemia. "Nephrotic syndrome with renal dysfunction" was diagnosed in patients with nephrotic syndrome and a reduced glomerular filtration rate (GFR). "Nephritic syndrome" was diagnosed based on the presence of oliguria, hypertension, and edema along with azotemia and urinary findings of hematuria and/or red blood cells (RBC) casts. "Rapidly progressive renal failure" was diagnosed when patients presented with oliguria and had a documented acute decline in GFR. "Chronic renal failure" was diagnosed in cases of azotemia lasting greater than 3 months. A diagnosis of "Asymptomatic urinary abnormality" was made based on the presence of hematuria, proteinuria, and/or sterile pyuria, casts in the absence of edema, azotemia, and hypertension.

Complications were defined as major when an intervention such as blood transfusion, angiography with or without embolization, or cystoscopy was considered necessary. Conversely, minor complications consisted of any complication that resolved without the need for intervention, including gross hematuria and symptomatic perinephric hematomas [9]. Patients were observed in the hospital for a minimum of 24 hours after biopsy.

All biopsies were reported by a single pathologist, and biopsy adequacy was judged in two ways. First, the absolute number of glomeruli on light microscopy was determined, and biopsies with less than 5 glomeruli were considered inadequate. Secondly, biopsies were considered inadequate if the pathologist, in collaboration with the nephrologist, could not arrive at a diagnosis [10–13].

Statistical analysis

Data were analyzed using the SPSS software ver. 16.0 (SPSS Inc., Chicago, IL, USA). Data normality was tested using the Shapiro–Wilk test, and means were compared with student's *t* test in the case of normally distributed continuous variables. The Mann–Whitney test was used in cases of a non-normal distribution and medians were expressed in place of means. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test as appropriate. *P* values < 0.05 were considered significant. Logistic regression analysis was used to derive predictors of biopsy complications.

Results

A total of 343 biopsies performed over a period of 45 months were included in our analysis. Among the 343 biopsies, 140 were performed without the use of a needle guide and 203 were performed with a needle guide. The baseline clinical and laboratory characteristics of the two groups are presented in Table 1. Biopsy yields and complications in the two groups are presented in Table 2. Table 3 shows the biopsy yields and complications in the subgroup of patients with renal failure requiring dialysis.

There were no significant differences between patient groups with respect to baseline parameters, except for a higher number of diabetic biopsies performed in Period I. Approximately one-third of all biopsies were performed

Table 1. Baseline clinical and laboratory characteristics of the study population

Characteristic	Period II (n = 203)	Period I (n = 140)	*P* value
Age (yr)	33.6 ± 16.2	33.2 ± 16.4	0.73
Sex (n), male/female	127/76	94/46	0.38
Hypertension (%)	32.3	25.0	0.10
Diabetes mellitus (%)	3.9	10.0	0.06
Duration of illness (mo)	3.4 ± 3.1	3.2 ± 2.7	0.40
Systolic blood pressure (mmHg)	127.3 ± 14.2	127.3 ± 13.6	0.16
Diastolic blood pressure (mmHg)	76.9 ± 8.3	74.7 ± 8.7	0.45
Pre-biopsy serum creatinine (μmol/L)	243.16 ± 168.88	225.47 ± 168.88	0.35
	187.45 (86.65−401.43)	160.04 (86.65−372.45)	
Pre-dialysis serum creatinine (μmol/L)	404.96 ± 417.34	372.45 ± 459.78	0.23
	197.18 (88.42−698.52)	174.19 (86.65−908.07)	
Hemodialysis done prior to biopsy (%)	32.4	25.7	0.10
Hemoglobin (g/dL)	10.7 ± 2.2	10.8 ± 2.3	0.49
Blood transfusion prior to biopsy (% of patients)	25.6	25.7	0.98
Platelet count (×10^3/μL)	249.14 ± 105.62	248.62 ± 101.55	0.37
Prothrombin time (sec)	13.9 ± 1.7	14.1 ± 1.7	0.51
aPTT (sec)	28.9 ± 2.4	28.7 ± 2.1	0.36
International normalized ratio	1.09 ± 0.17	1.09 ± 0.17	0.58
Serum albumin (g/dL)	2.42 ± 0.86	2.33 ± 0.95	0.25
Urinalysis			
Urine RBCs (cells/HPF)	8 (1−20)	10 (3−15)	0.08
Urine WBCs (cells/HPF)	5 (2−10)	4 (1−5)	< 0.01
24-hour urine protein (g/day)	4.56 ±3.56	4.50 ± 3.48	0.84
Syndromic diagnosis (%)			
Nephrotic syndrome	35.9	37.1	
Rapidly progressive renal failure	33.0	28.6	
Chronic renal failure	4.4	2.7	
Nephrotic proteinuria with renal dysfunction	22.2	20.7	
Asymptomatic urinary abnormalities	1.5	0.0	
Kidney length by ultrasound (cm), left/right	10.06 ± 0.75/9.99 ± 0.67	10.17 ± 0.93/10.01 ± 0.81	0.38/0.31
Use of 16G needle (%)	53.6	50.7	0.20

Values are presented as mean ± standard deviation or median (interquartile range).

aPTT, activated partial thromboplastin time; HPF, high power field; RBC, red blood cells; WBC, white blood cells.

in patients with advanced renal dysfunction requiring hemodialysis, and nearly one-fourth of all patients required blood transfusion prior to the biopsy procedure. The number of biopsies performed with a 16G or 18G needle was nearly equal, and although there was an increased use of 16G needles in Period II, the difference was not significant compared between the two periods.

Biopsy yield in terms of number of glomeruli on light and immunofluorescence microscopy were similar in both the periods, although biopsy adequacy was significantly better in Period II. The total number of inadequate biopsies as reported by the pathologist was 31 (9%), and

adequacy was significantly associated with the use of a needle guide and use of a 16G needle for the biopsy (*P* < 0.001).

The rate of complications in our study was 1.7%, with five cases requiring angiography and two cases requiring blood transfusion. The rate of minor complications was 8.4% for all biopsies. Occurrence of complications was significantly associated with low baseline hemoglobin level, need for blood transfusion, need for pre-biopsy hemodialysis, increased prothrombin time, higher international normalized ratio (INR), higher number of urinary RBC and white blood cells (WBC), use of an 18G needle,

Table 2. Biopsy yield and rates of complications in the study population

Variable	With needle guide (n = 203)	Without needle guide (n = 140)	P value
Number of glomeruli			
Light microscopy	11.9 ± 6.3	11.5 ± 7.2	0.45
Immunofluorescence	5.5 ± 3.5	4.9 ± 3.3	0.85
Pathologist-reported inadequate biopsies	9 (6.3)	22 (15.7)	0.00
Inadequate biopsies according to number of glomeruli*	23 (11.3)	38 (27.1)	0.05
Major complication (n)			0.06
Embolization/angiography	1	3	
Blood transfusion	0	2	
Minor complication (n)			0.01
Perinephric hematoma/ drop in Hb†	3	7	
Gross hematuria	6	13	
Hospital stay (d)	5.53±6.85	5.43±4.17	0.87

Values are presented as mean ± standard deviation or number (%).
*< 6 glomeruli in light microscopy, < 1 in immunofluorescence.
†Decrease in hemoglobin (Hb) < 1 g/dL.

Table 3. Complications in patients requiring dialysis

Variable	With needle guide (n = 66)	Without needle guide (n = 36)	P value
Major complication (n)			0.19
Embolization/angiography	1	2	
Blood transfusion	0	1	
Major complication (n)			0.05
Perinephric hematoma/ drop in Hb*	3	6	
Gross hematuria	3	3	
Hospital stay (d)	8.23±3.02	10.34±4.19	0.12

*Decrease in hemoglobin (Hb) < 1 g/dL.

and not using the needle guide. Likewise, univariate logistic regression analysis (Table 4) showed that low hemoglobin, advanced renal dysfunction, longer prothrombin time, higher INR, higher urinary RBCs and WBCs, using an 18G needle, and not using a needle guide were significant predictors of biopsy complications. A model based on hemoglobin level, urinary RBCs, pre-dialysis serum creatinine, and non-use of needle guide was able to predict 17% of the variance of the occurrence of biopsy complications and correctly classified 90.7% of cases.

Table 4. Predictors of biopsy complications

Variable	P value	OR (95% CI)
Univariate logistic regression		
Pre-biopsy serum creatinine	0.042	1.207 (1.007–1.446)
Maximum serum creatinine	0.001	1.102 (1.039–1.170)
Hemoglobin	0.002	0.705 (0.568–0.875)
Prothrombin time	0.033	1.220 (1.017–1.465)
INR	0.044	6.334 (1.050–38.194)
Urine RBCs	0.009	1.023 (1.006–1.041)
Urine WBCs	0.016	1.059 (1.017–1.102)
Use of needle guide	0.004	0.325 (0.151–0.697)
Use of 16G needle	0.013	0.349 (0.152–0.800)
Multivariate logistic regression		
Hemoglobin	0.002	0.707 (0.589–0.925)
Urine RBCs	0.018	1.022 (0.998–1.038)
Use of needle guide	0.001	0.270 (0.105–0.552)

The variables used in the multivariate logistic regression analysis consisted of hemoglobin, prothrombin time, international normalized ratio (INR), urinary red blood cells (RBCs), white blood cells (WBCs), use of 16G needles, use of a needle guide, and performance of pre-biopsy hemodialysis.
CI, confidence interval; OR, odds ratio.

Finally, we found that use of a needle guide reduced the likelihood of complications to one-third.

Discussion

The use of needle guides in ultrasound-assisted biopsies has become fairly widespread in recent years. Placing a guide over the ultrasound probe is thought to prevent deviation of the biopsy needle from its predetermined track which, conceptually, should lead to fewer complications. Our study showed similar yields of glomeruli, improved biopsy adequacy as well as better safety, similar major complications, with significantly lower minor complication rates after the use of needle guides, even when the biopsies were performed by a single operator in the needle guide use period. Besides low hemoglobin, baseline presence of renal dysfunction, a higher number of urinary RBCs (indicating nephritic syndrome), and not using a needle guide remained significant predictors of biopsy complications according to multiple logistic regression.

Biopsy adequacy may be judged by either core size, absolute number of glomeruli and vessels (again depending on the nature of the disease, focal or diffuse, and varying between native and allograft biopsies) or by the patholo-

gist's ability to arrive at a diagnosis with a given specimen [10–13]. In the present study, based only on absolute number of glomeruli, 82% of biopsies were considered adequate, and the number of inadequate biopsies was significantly higher in the period before a needle guide was used. When only biopsies where the pathologist and clinician were unable to make a diagnosis were considered inadequate, 91% of the biopsies were adequate, and adequacy defined in this way was significantly higher with the use of a needle guide. Owing to an approximately 50% usage of an 18G needle in both periods, a slightly lower yield of glomeruli was noted compared to similar studies, although the overall rate of adequacy was similar [7,8,10].

Several large studies have analyzed complication rates of ultrasound-guided renal biopsies according to major complications such as urinary tract obstructions and perinephric hematomas requiring blood transfusion, angiographic interventions, or surgery. The reported complication rates range from < 1% to up to 7% in large studies involving > 500 subjects. On the other hand, rates of minor complication such as perinephric hematoma, self-limited gross hematuria, and asymptomatic decreases in hemoglobin can vary more significantly, ranging from 2% to 25%, and depend partly on the length of observation after biopsy and whether routine post-biopsy ultrasound was used to detect asymptomatic hematomas [5,6,14,15]. The overall rate of major complications in the present study was 1.7%, with four cases requiring angiography, one of which required subsequent embolization, and two cases requiring blood transfusion. The rate of minor complications was 8.4%, with symptomatic perinephric hematomas accounting for 2.9% and self-limited gross hematuria account for 5.5% of cases. The overall complication rate, evaluated by combining both major and minor complications, was reduced significantly after the introduction of the needle guide. However, when analyzed separately, use of the needle guide led to a significant reduction only in the rate of minor complications, and not major complications.

To the best of our knowledge, only two studies to date have examined the biopsy yields and complication rates associated with the use of needle guides, albeit with conflicting results. Prasad et al [7] performed a retrospective analysis of biopsies done over a ten-year period with and without the use of a needle guide. They showed that the use of a needle guide led to improved biopsy yields as well as a reduction in complications to one-third that of the rate before the use of a needle guide. However, their study was confounded by the fact that biopsies in the pre-needle guide period were performed jointly with radiologists, while only nephrologists, including trainees, performed biopsies during the needle guide use period, although there were two operators in both periods. Nevertheless, it is impressive to note that major and minor complication rates (5.1% and 5.4% respectively) were reduced significantly in the latter aspect of their study, which was attributable, at least in part, to the use of a needle guide. However, in sharp contrast to the study by Prasad et al [7], Ali et al [8] published an analysis of over 500 renal biopsies with and without the use of a needle guide, all of which were day-cases performed by trained nephrologists. Although they did not specify the number of operators, their results indicated that needle guides do not improve biopsy yields and complication rates, except in cases utilizing a 14G biopsy gun. Likewise, they showed that minor complications were lower with the use of a needle guide, which was consistent with our findings. Of note however, while Prasad et al and the present study utilized 16G and 18G guns, Ali et al [8] compared 14G and 16G biopsy guns in their study. In addition, our study also showed significantly better biopsy adequacy and lower complications with the use of 16G needles compared to 18G needles. Consistently, other studies have reported higher rates of bleeding complications with 18G needles, which has been attributed to an increased number of passes and tangential deviation of the 18G needle from its track.

Renal dysfunction is consistently associated with a greater risk of bleeding complications [16–20]. The mean serum creatinine in our study (235.2 μmol/L with a pre-dialysis mean of 396.12 μmol/L) was higher than that of the studies by Prasad et al [7] and Ali et al [8] (226.36 μmol/L and 137.05 μmol/L, respectively). Furthermore, a subgroup analysis of 102 patients in our study with renal failure requiring dialysis showed that use of a needle guide was associated with a significantly lower rate of minor complications. In addition, the overall low rate of major complications may have had a masking effect on any true difference between the two groups. Indeed, in addition to the use of a needle guide, it is likely that standard pre-biopsy care, such as careful control of blood

pressure, hemoglobin, and coagulation parameters, as well as having procedures performed by adequately trained nephrologists, plays an important role in preventing complications. Our use of intranasal desmopressin, although off-label, may have contributed to decreased rates of post-biopsy bleeding, consistent with previous studies [21–24]. Overall, the clear improvement in biopsy adequacy and minor complication rates with the use of needle guides, as well as successful transition to single-operator handled biopsies as noted in our study, should encourage their use by nephrologists.

The main strength of the present study was the evaluation of a large number of patients with advanced renal failure requiring hemodialysis, which allowed us to evaluate the efficacy and safety of the needle guide in this high-risk population. Another strength of the study was the fact that the same nephrologists and pathologists were present during both periods, thereby limiting the role of observer bias. The retrospective study design was the prime limitation of our study. Nevertheless, even though the number of participants in the present study was relatively less compared to the two previous studies discussed above, our study included a comparatively greater number of "high-risk" biopsies, which allowed us to study the effect of the needle guide more effectively. The lower overall rate of complications in our study was attributed to optimal pre-biopsy patient preparation and use of well-trained operators compared to operators in-training, where there may be effects due to the learning curve of the procedure. We did not obtain information on the number of passes taken (typically 2–4), which prevented us from assessing the effect of pass number on rate of biopsy complications, although older studies do not support this effect. Lastly, our study did not utilize 14G biopsy needles, which are less common than 16G and 18G needles.

Our findings of a similar biopsy yield and complication rate after changing to the use of a needle guide by a single operator suggest that the transition to this device is both safe and successful, and allows more flexible scheduling of biopsies in centers run by a single nephrologist.

Conflicts of interest

All authors have no conflicts of interest to declare.

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