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Original article

A novel approach to ultrasound-guided percutaneous native renal biopsy: a better tissue sampling technique

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Background: Percutaneous renal biopsy (PRB) is an essential tool in diagnosis and management of various renal diseases. Conventional ultrasound-guided free-hand approaches to the lower pole of the kidney for PRB yield marginal tissue adequacy and causes a certain incidence of bleeding complications.

Objective: To describe a novel ultrasound-guided approach to the middle part of the kidney for PRB to obtain better tissue sampling.

Patients and methods: The plane angle between the renal biopsy needle and the skin was set at 30° for patients in the novel middle part approach group (n = 15) and 45° for patients in the conventional lower pole approach group (n = 15).

Results: The perpendicular distance between the needle tip and renal capsule in the middle part approach was significantly shorter than the lower pole approach group (0.92 ± 0.6 vs. 1.49 ± 0.4 cm, $p = 0.005$). The middle part approach to PRB yielded a significantly higher number of glomeruli (22.8 ± 7.2 vs. 15.3 ± 4.1, $p = 0.002$) and arcuate arteries (0.9 ± 0.6 vs. 0.5 ± 0.1, $p = 0.02$). The bleeding complications in the middle part approach seemed to be less than in the lower pole approach technique. Pain scores between the two methods as assessed using a visual analog scale were not different.

Conclusion: This novel approach to the middle part of the kidney for PRB provides comparable patient satisfaction and a superior adequacy of renal tissue when compared with the conventional lower pole approach with its consequent lower post biopsy bleeding complications. Larger studies to confirm this finding are warranted.

Keywords: Middle part approach, percutaneous native renal biopsy

Renal biopsy is an essential intervention for tissue diagnosis in several renal diseases. Of various renal biopsy methods including blind, percutaneous, open, transvenous, laparoscopic, and transurethral techniques [1-4], percutaneous renal biopsy (PRB) remains the most popular choice [5, 6]. Since the original description of PRB in the 1950s [7], there have been several modified techniques for increasing diagnostic yields and minimizing complications [8]. However, there is still no standard recommendation regarding the anatomical approach [9]. The most preferred approach is using lower pole of the left kidney as the localized landmark. With this approach, several studies still report marginal tissue adequacy results and a high incidence of bleeding complications following the procedure [10-12]. The angle between the needle and the skin in the conventional lower pole approach makes the biopsy needle with an approximately 1.9 cm length of sample notch penetrate too deeply in the kidney and this might result in inadequate renal tissue and/or bleeding complications. Moreover, the recess of the lower pole of the kidney and the surrounding quadratus lumborum muscle can cause difficulty in applying effective direct pressure to renal capsule immediately after the needle is withdrawn. This architecture also provides an easily expansible hematoma formation. Herein, we report a novel ultrasound-guided free-hand approach to the middle part of the kidney for PRB that can provide a better yield of renal tissue and less bleeding complications, as well as comparable patient satisfaction.

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Methods

Participants and procedures

This prospective, case-control study was conducted in 30 patients who underwent renal biopsy at King Chulalongkorn Memorial Hospital. Indeed, the most appropriate study design should be a randomized controlled trial. The case-control design was performed because of the high failure rate in patient consent and a limitation in total case numbers. The study was approved by the Ethics Committee of Chulalongkorn University, Bangkok, Thailand. Each patient gave written informed consent. Indications for PRB comprised further evaluation of proteinuria, microscopic hematuria, renal manifestation of systemic disease, and unexplained renal failure. Exclusion criteria were anatomical abnormality, especially multiple cysts or solitary kidney, and urinary tract obstruction by ultrasonography. Patients with a high diastolic blood pressure (DBP more than 95 mmHg), high blood urea nitrogen (BUN more than 80 mg/dL), low platelet counts (less than $80 \times 10^3/\mu L$), or coagulopathy (INR more than 1.2) were deferred and corrected until the conditions were well controlled. 1-Deamino-8-D-arginine vasopressin (DDAVP) at a dose of 0.3 mg/kg was prescribed prior the intervention at least 30 minutes in patients with blood urea nitrogen (BUN) levels above 60 mg/dL or creatinine clearance by MDRD formula below 30 mL/min/1.73 m^2. Hemodialysis for BUN removal was performed in patients with BUN levels over 80 mg/dL. The bleeding time was tested and was required to be less than 10 minutes before biopsy. At least 7-day cessation was recommended in patients with concurrent antiplatelet or anticoagulant medication. The participating patients were randomized into two groups using: (1) a conventional lower pole approach (n = 15) and (2) a novel middle part approach (n = 15). The plane angle between the biopsy needle and the skin was 45□ in the conventional lower pole approach PRB group and 30□ in the novel middle part approach PRB group (**Figure 1**).

The patients were placed in a prone position. Renal size, cortical thickness, corticomedullary appearance, cortical cysts, and renal parenchyma echogenicity were reexamined by using a 3C-RS (3.5 MHz) convex/abdominal transducer probe (GE LogiqBook XP portable ultrasound machine, Milwaukee, Wisconsin, USA). Then, the skin above the left kidney was marked. Following infiltration with 2% lidocaine anesthetic under ultrasound guidance, biopsies were performed by a single nephrologist using a free-hand approach with real-time ultrasound guidance and a 16-gauge × 16 cm biopsy needle with a 1.9 cm sample notch (MC1616; Bard Peripheral Vascular, Tempe, AZ, USA). Confirmation of needle angle was achieved by comparing the ultrasound transducer parallel to the needle axis. Because the transducer line cannot be set below 45□, we set this as the referenced line in each case (**Figure 1**). As the needle was advanced to the renal capsule, the patients were advised to breath normally until a proper position such that the selected part was just beneath the needle tip and then advised to stop breathing. Within this single breath-hold, the needle was advanced using an automatic gun fired under direct ultrasound visualization and simultaneously frozen for photography. According to previous studies, approximately three passes of the needle were required for adequate renal tissue collection [11, 13-15] and so three needle passes were used in the present study. If insufficient tissue was obtained, further passes of needle were allowed. Pressure was directly applied to the biopsied kidney by the investigator for at least five minutes after each pass of needle. After evaluating immediate postprocedure complications and wound dressing, the patient was rolled directly in their own hospital bed for 8-hours absolute bed rest with regular clinical observation.

Although tissue samples were routinely examined by electron microscopy (EM), only the total number of glomeruli seen under light microscopy (LM) and immunofluorescence (IF) were counted for tissue adequacy because only one glomerulus is routinely allocated for EM. Postprocedure hematoma was assessed by ultrasound imaging either immediately after biopsy or within 24 hours of the procedure. Follow-up for hemoglobin level change was performed only in patients experiencing perinephric hematoma and/or hematuria. Patient satisfaction in each PRB procedure was assessed using a visual analog scale pain score.

Statistical analysis

Quantitative parameters were presented as mean ± standard deviation, while qualitative parameters were expressed as counted numbers and percentages. Categorical variables were compared using a Chi-square or a Fischer exact test where appropriate.

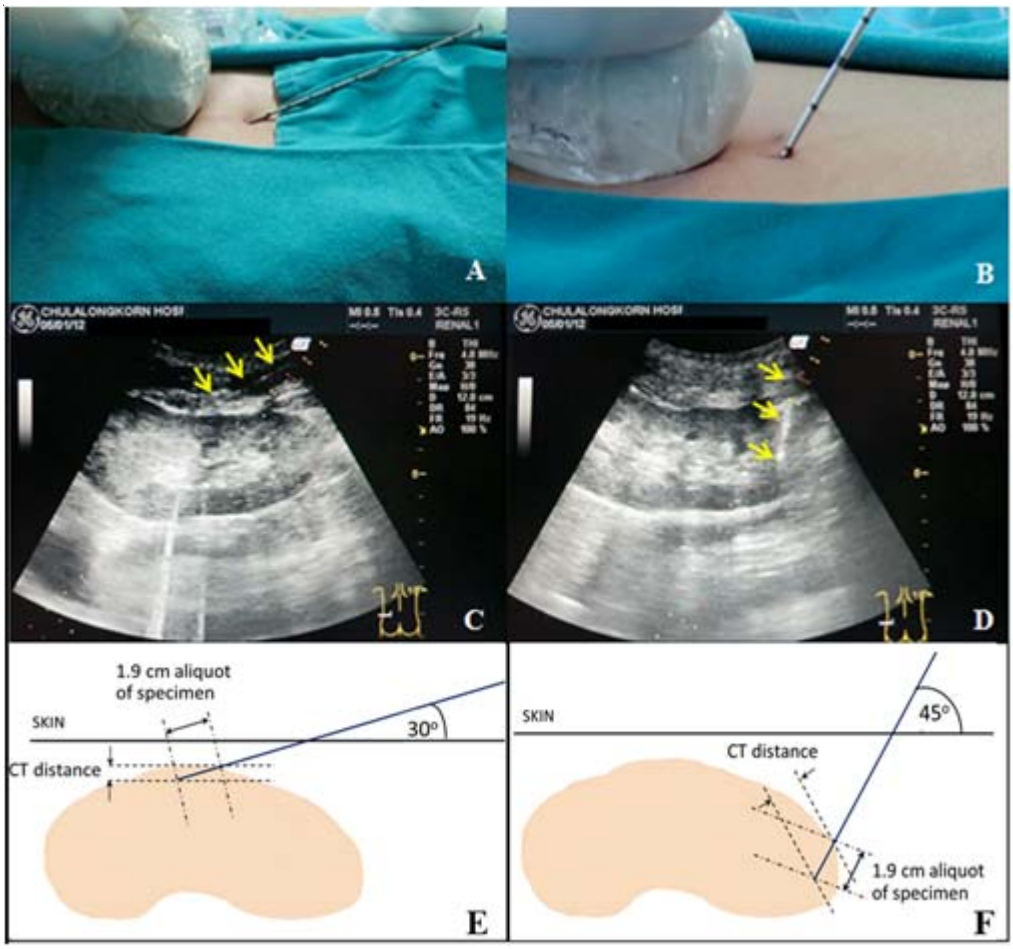

Figure 1. Demonstration of the long axis set up for ultrasound-guided percutaneous renal biopsy (PRB). The ultrasound is scanned along the long axis of biopsy needle. The trajectory of the needle puncture site was marked during a preprocedural scan. The biopsy needle is inserted at the edge of the transducer ultrasound probe. In the novel middle part approach to PRB, the needle was maintained on a 30° angle **(A)** and maintained on a 45° angle in the conventional lower pole approach to PRB **(B)**, between the needle and the skin by using a 45° ultrasound transducer dotted line as a referenced line during advancement of the needle (arrow) into the renal parenchyma **(C, D)**. The novel middle part approach to PRB **(E)** showed less perpendicular, more oblique penetration beyond the renal capsule (CT distance) than the conventional lower pole approach PRB **(F)**.

Results

Clinical characteristics

As seen in **Table 1**, both groups showed nonsignificant differences in baseline characteristics except body mass index (BMI). Patients in the middle part approach to PRB group had a significantly higher BMI. Women were slightly, but not significantly, predominant in both groups. There were no significant differences in the number of patients with each indication for PRB between the groups (**Table 1**).

Procedure and adequacy outcomes

The average perpendicular distance between the needle tip and the renal capsule, CT distance, in the middle part approach PRB group was significantly less than in the lower pole approach PRB group (0.92 ± 0.6 vs. 1.49 ± 0.4 cm, $p = 0.005$) (**Figure 1** and **Table 2**).

All of the patients underwent only three passes at each procedure. All biopsies (100%) provided adequate tissue for definitive diagnoses. The middle part approach to PRB yielded a significantly greater number of glomeruli than the lower pole approach PRB [22.8 ± 7.2 (range 10–34) vs. 15.3 ± 4.1 (range 7–22), $p = 0.002$]. This occurred although there was more incidence of advanced interstitial fibrosis and tubular atrophy and diabetic nephropathy in the middle part approach to PRB group (**Table 2**). IgA nephropathy was the main etiology in the lower pole approach PRB group while lupus nephritis was the most frequently diagnosed lesion in the middle part approach to PRB group.

Table 1. Baseline characteristics in the conventional lower pole and novel middle part approach groups

Characteristics	Conventional lower pole approach (n = 15)	Novel middle part approach (n = 15)	*p*
Age (years)	50.4 ± 14.3	56.7 ± 18.2	0.30
Sex (F:M)	10:5	8:6	0.88
BMI (kg/m^2)	20.1 ± 2.2	22.5 ± 3.5	0.03
Systolic blood pressure (mmHg)	151.2 ± 14.1	148.4 ± 12.8	0.57
Diastolic blood pressure (mmHg)	89.2 ± 6.4	90.6 ± 5.7	0.53
Hemoglobin (g/dL)	10.4 ± 1.2	11.2 ± 2.4	0.26
Platelets (×10^3/μL)	249.0 ± 86.8	213.7 ± 54.3	0.19
BUN (mg/dL)	57.5 ± 14.9	62.8 ± 15.8	0.35
Creatinine (mg/dL)	3.1 ± 1.5	3.6 ± 1.1	0.31
eGFR (mL/min/1.73m^2)	41.8 ± 23.2	35.4 ± 18.7	0.44
Albumin (g/dL)	3.8 ± 0.4	4.2 ± 1.1	0.19
Prothrombin time (seconds)	10.2 ± 2.2	11.4 ± 1.6	0.10
INR	1.2 ± 0.1	1.3 ± 0.5	0.45
Bleeding time (minutes)	6.7 ± 0.3	7.1 ± 1.2	0.22
Indications for kidney biopsy, n (%)			
Proteinuria	6 (40)	5 (33)	0.99
Undetermined renal failure	4 (27)	6 (40)	0.70
Microscopic hematuria	3 (20)	2 (13)	0.99
Renal manifestation of systemic disease	1 (7)	3 (20)	0.59
Preoperative management, n (%)			
DDAVP (0.3 μg/kg)	3 (20)	4 (27)	0.99
PRC transfusion	1 (7)	1 (7)	0.47
Platelet transfusion	2 (13)	1 (7)	0.99
Cryoprecipitate transfusion	0	0	
Hemodialysis	0	1 (7)	0.99

BMI = body mass index, BUN = blood urea nitrogen, DDAVP = 1-deamino-8-D-arginine vasopressin, eGFR = estimated glomerular filtration rate, F = female, INR = international normalized ratio, M = male, PRC = packed red cell

Table 2. Results of kidney biopsy

Results	Conventional lower pole approach (n = 15)	Novel middle part approach (n = 15)	*p*
Renal biopsy intervention parameters			
Renal length (cm)	10.3 ± 2.4	11.5 ± 2.2	0.16
Renal width (cm)	4.5 ± 1.8	5.2 ± 2.2	0.35
Cortical thickness (cm)	1.3 ± 0.5	1.4 ± 0.2	0.48
Depth of the kidney from skin (cm)	5.4 ± 2.1	6.2 ± 2.6	0.36
Capsule to needle tip (CT) distance (cm)	1.49 ± 0.4	0.92 ± 0.6	0.005
Number of needle passes per case	3	3	
Number of core obtained per case	3	3	
Adequacy parameters			
Number of glomeruli	15.3 ± 4.1 (7–22)	22.8 ± 7.2 (10–34)	0.002
Number of arcuate arteries	0.5 ± 0.1	0.9 ± 0.6	0.02
Number of interlobar arteries	1.8 ± 0.5	1.6 ± 0.2	0.16
Adequacy for diagnosis, n(%)	15 (100)	15 (100)	

Table 2. Results of kidney biopsy (Continue)

Results	Conventional lower pole approach (n = 15)	Novel middle part approach (n = 15)	*p*
Diagnosis, n (%)			
IgA nephropathy	4 (27)	3 (20)	0.99
Lupus nephritis	3 (20)	5 (33)	0.68
Focal segmental glomerulosclerosis	3 (20)	1 (7)	0.59
Membranous nephropathy	2 (13)	0	0.47
Minimal change disease	1 (7)	0	0.99
Diabetic nephropathy	1 (7)	4 (27)	0.33
Pauci-immune glomerulonephritis	1 (7)	1 (7)	0.47
Interstitial nephritis	0	1 (7)	0.99
Severity of interstitial fibrosis and tubular atrophy, n (%)			
Less than 25%	8 (53)	7 (47)	0.99
25 to 75%	3 (20)	1 (7)	0.59
Over 75%	4 (27)	7 (47)	0.45

Safety outcomes

The novel middle part approach provided slightly, but not significantly, lower bleeding complications than the conventional lower pole approach (**Table 3**).

Patient satisfaction

The mean value of 10-point visual analog scale pain score was comparable between both groups (3.5 ± 2.2 and 4.3 ± 1.6 in lower pole and middle part approach PRB groups, respectively; $p = 0.26$) (**Figure 2**).

Discussion

Here we report a case-controlled study of a novel ultrasound-guided approach to the middle part of the kidney for PRB and compared the tissue sampling adequacy and postprocedure complications, as well as patient satisfaction, of this novel method and the conventional technique using a lower pole approach. The lower pole approach has been long introduced into clinical practice. However, several studies using this lower pole landmark reported inadequate tissue for diagnosis and/or bleeding complications after the procedure [5, 16-19]. The minimum renal tissue sample size adequate for diagnosis may vary greatly with the specific diagnosis [20]. For example, membranous glomerulonephritis can be diagnosed from a single glomerulus. By contrast, 25 glomeruli may be needed for light microscopic (LM) examination to detect focal lesions that involve a small number of glomeruli. In general, 8 to 10 glomeruli are required for most LM assessments to adequately verify severity and distribution of lesions. In addition, vessels including the arcuate or interlobar artery should be present in the tissue sample [20]. Taken together, a greater the number of renal structures obtained from PRB would potentially provide better information regarding the renal lesions.

Table 3. Complication outcomes following renal biopsy procedure

Complications, n (%)	Conventional lower pole approach (n = 15)	Novel middle part approach (n = 15)	*p*
Total bleeding-related complications	2 (13)	1 (7)	0.68
Gross hematuria	2 (13)	1 (7)	0.99
Perinephric hematoma	0	0	
Retroperitoneal hematoma	0	0	
Bleeding requiring blood transfusion	0	0	
30-Day gross hematuria	0	0	

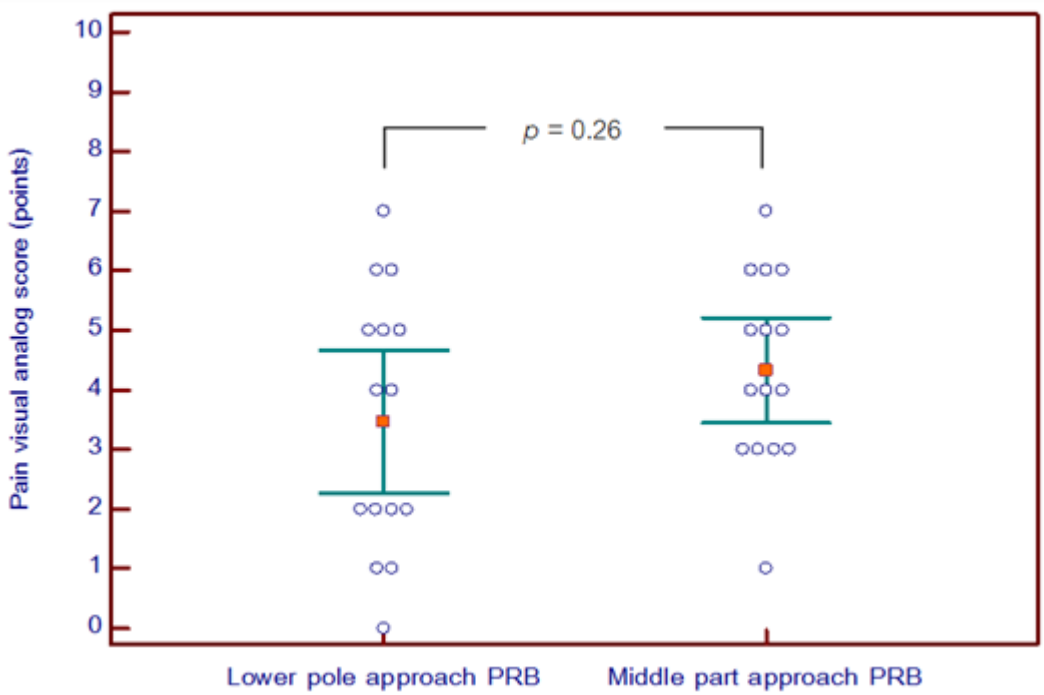

Figure 2. Comparison of the visual analog scale pain score after the lower pole approach and middle part approaches to percutaneous renal biopsy (PRB).

As shown in **Table 2**, the novel middle part approach to PRB yielded a greater number of glomeruli and arcuate arteries than the conventional lower pole approach to PRB. In this regard, one might postulate that the greater BMI of patients in the novel middle part approach PRB group might result in a larger renal tissue sample. This postulation is incorrect because the cortical thickness of renal tissue and the number of cores per case were comparable between the two groups. As seen in **Figure 1 E** and **F**, the angle of 30□ set in the novel middle part approach to PRB group allowed the biopsy obtain a greater number of renal structures than the biopsy in the conventional lower pole approach to PRB group. A previous study of patients with high BMI showed that the supine anterolateral position technique provided a better renal tissue sample than the conventional lower pole approach to PRB [21]. Thus, the present study additionally showed that the novel middle part approach to PRB might be an alternative approach in population of patients with high BMI.

As seen in **Figure 1** and **Table 2**, the CT distance in the middle part approach is significantly shorter than in the lower pole approach. As such, the more adequate tissue sampling is clearly explained by the fact that the 1.9-cm length of sample notch of the biopsy needle in the middle part technique samples the renal cortical area, while a portion of the sample notch penetrated the renal medulla in the lower pole method (**Figure 1**).

Although many centers generally have a good preoperative strategy for minimizing the risk of bleeding complications, there are literature reports that from 3% to 13% of patients developed bleeding complications. Approximately one in 10 patients will develop spontaneous resolving macroscopic hematuria, one in 100 will have serious bleeding that requires blood transfusion, one in 1000 will need an invasive procedure to stop the bleeding, and less than 0.0001% develop the most serious complication, bleeding that requires surgical nephrectomy [22]. In the present study, the bleeding complications in both groups were quite low and comparable to earlier reports. Of interest, the novel middle part approach provided slightly, although not significantly, lower bleeding complications than the conventional lower pole technique (**Table 2**). Previous studies showed that the risk factors for bleeding complications after PRB included advanced renal failure, poor control hypertension, amyloidosis, and bleeding diathesis [6]. Of note, there was a trend of greater severity of interstitial fibrosis and tubular atrophy in patients of the middle part approach group (**Table 2**).

There are several explanations for the lower number of bleeding complications in the middle part approach group patients. The penetration of renal tissue, mostly in the renal cortex, in the middle part group might cause less injury to large vessels including interlobular artery when compared with the lower pole technique in which the renal medulla is also injured. Furthermore, as seen in **Figure 1**, the distance from the skin to the position of biopsy needle in the middle part approach is shorter than the lower pole approach, resulting in more effective direct pressure to the renal capsule and possibly less bleeding complications in the middle part approach to PRB.

This novel middle part approach to PRB can be conducted by any surgeons who routinely perform PRB using the conventional lower pole approach. No additional special training is needed. Admittedly, the number of patients in the present study is quite low and this is only a single center study. Small sample sizes may limit the precision of the study outcome when extrapolated to other population groups. However, with its impressive outcomes, this novel middle part approach to PRB appears to provide better diagnostic and therapeutic benefit to the patients. Thus, a larger multicenter study is warranted to confirm the findings of the present study.

In conclusion, the novel middle part approach to PRB provides superior renal tissue sampling over the conventional lower pole approach with less post biopsy bleeding complications and comparable patient satisfaction.

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