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Comparison of native and transplant kidney biopsies: diagnostic yield and complications

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ABSTRACT

Background. The safety and adequacy are established for the native percutaneous renal biopsy (PRB) but no prospective studies exist that directly compare these with transplant PRB.

Methods. From 1995 to 2015, 1705 adults underwent percutaneous native [native renal biopsy (NRB)] or transplant renal biopsy (TRB) by the Nephrology service. Real-time ultrasound and automated biopsy needles (NRB, 14 or 16 gauge; TRB, 16 gauge) were used. Patients were observed for 24 h (NRB) or 8 h (TRB) post-procedure. Adequacy was defined as tissue required for diagnosis plus glomerular yield. Complications were defined as those resulting in the need for an intervention, such as surgery, interventional radiologic procedure, readmission, blood transfusion and death. Data were collected prospectively in all biopsies.

Results. At the time of biopsy, NRB patients were younger (mean $\pm$ SD, 47 ± 17 versus 50 ± 14 years, $P < 0.0001$) and more often female (62 versus 48%, $P < 0.0001$) compared with TRB. A fellow supervised by an attending performed the procedure in 91% of NRB compared with 63% of TRB ($P < 0.0001$). TRB patients were more hypertensive [systolic blood pressure (SBP) 140 ± 22 versus 133 ± 18 mmHg, $P < 0.0001$] and had a higher serum creatinine (3.1 ± 1.8 versus 2.3 ± 2.2 mg/dL, $P < 0.0001$), activated partial thromboplastin time (28 ± 4.3 versus 27 ± 5 s, $P < 0.0001$) as well as lower hemoglobin (Hgb) (11.2 ± 1.8 versus 11.7 ± 2.1 g/dL, $P < 0.0001$) compared with NRB. Adequate tissue for diagnosis was obtained in $>99\%$ of NRB and TRB ($P = 0.71$). Compared with TRB, NRB had a greater drop in Hgb after the biopsy (0.97 ± 1.1 versus 0.73 ± 1.3 g/dL, $P < 0.0001$), a higher complication rate (6.5 versus 3.9%, $P = 0.02$) and higher transfusion rate (5.2 versus 3.3%, $P = 0.045$). There was one death in each group attributed to the biopsy.

Conclusions. Although death is equally rare, the complication rate is higher in NRB compared with TRB despite TRB having more of the traditional risk factors for bleeding. Differences in technique, operator (fellow or attending) or needle gauge may explain this variability.

Keywords: bleeding, complication, kidney biopsy, kidney transplantation

INTRODUCTION

Since the initial description of the percutaneous renal biopsy (PRB) in 1951 by Iversen and Brun [1] and subsequent modifications by Kark and Muehrcke [2], it has remained an integral procedure for the field of nephrology. In the era of transplantation, use of the PRB has also been essential for the detection of disease in the renal allograft [3]. Without the renal biopsy, our understanding of the pathophysiology of native and transplant diseases would never have advanced to where it is today.

For a procedure to be successful, it must be performed safely and add diagnostic value [4]. For the native renal biopsy (NRB), the rate of catastrophic complications resulting in death has decreased from 0.12% to 0.02% over the last 65 years [5]. However, clinically significant bleeding, requiring either a blood transfusion or a procedure to stop the bleeding can still occur and is as high as 25% in some series with high risk patients, but in most reports is <5% [6–14]. Diagnostic yield for the NRB is focused on the amount of glomeruli per specimen, with at least 10 being required for an adequate specimen, but ideally up to 20 if the disease is focal in nature [8, 15]. Since the use of automated needles and real time ultrasound, the NRB has provided adequate material for a diagnosis in over 95% of biopsies [8]. The number of glomeruli in the specimen is also dependent on the needle gauge, with the smaller 18 gauge providing the least compared with 16 or 14 gauge [4].

The measures of success, that is, safety and diagnostic yield, are just as important in the percutaneous transplant renal biopsy (TRB) as in the NRB. For the TRB, death is equally rare [16]; in three large observational series [17–19] life-threatening complications occurred in 0.19%, and serious complications were 1–2% [17, 19]. An adequate specimen for a TRB has been considered to be anywhere from 10 to 25 glomeruli [20–23], but the definition for adequacy is evolving to include tubulointerstitial and vascular lesions in the specimen [24–26].

Presently, there are no prospective studies comparing diagnostic yield and complication rates of native and transplant PRBs. We report a large single center prospective series comparing complication rates and adequacy for these procedures over a 20-year time period.

MATERIALS AND METHODS

PRBs of native ($n = 767$) and transplant ($n = 938$) kidneys were performed in adult patients from January 1995 to April 2015 at Rush University Medical Center by a nephrology attending or a nephrology fellow with attending supervision. Imaging was performed by a radiologist using real-time ultrasound as previously described [27]. Automated biopsy needles (Bard Biopty gun, CR Bard Inc., Covington, GA, USA) were used for all procedures. For NRB, nephrologist discretion allowed for either a 14 or 16 gauge needle, and for TRB, only 16 gauge was used. No TRB patients were biopsied for protocol purposes (all were biopsied for indication). Beginning in February 2002, routine 1-h post-biopsy ultrasound was performed for all NRB ($n = 486$) and TRB ($n = 886$). Surgical and non-percutaneous biopsies were not included in the study. Once obtained, specimens were routinely evaluated for light (LM), immunofluorescence (IF) and electron microscopy (EM) for NRB, and only LM and IF for TRB unless EM was specifically requested. Glomerular yield and adequacy was recorded.

Native renal biopsy procedure

Information collected at the time of NRB included age, gender, race, systolic and diastolic blood pressures (BP), serum creatinine (SCr), bleeding time (BT), prothrombin time (PT), activated partial thromboplastin time (aPTT) and hemoglobin concentrations (Hgb). In general, it is our practice to perform NRB in patients with a normal BT, PT and PTT and stable BP. In patients with a prolonged BT, the use of desmopressin acetate was at the discretion of the attending nephrologist. The procedural technique was as described previously [27]. Following the biopsy, patients lay flat on their back for 4–6 h and then remained in bed for 23–24 h of observation. Patients were monitored following the biopsy for signs or symptoms of complications, such as gross hematuria, flank pain and hypotension. Vital signs were checked every 15 min for 2 h, every hour for 4 h, every 2 h for 6 h and then every 4 h thereafter. Hgb levels were checked at ~5–8, 10–13 and 18–20 h after the procedure, and the lowest post-biopsy Hgb level was recorded. The need for additional studies or treatment was determined by each nephrologist. Patients were reevaluated in the outpatient setting ~1 week after discharge.

TRB Procedure

Information collected at the time of TRB was the same as NRB with the exception of BT. Once in the biopsy suite, the patient was placed in the supine position. The skin overlying the transplant kidney was sterilized using Betadine, and 1% lidocaine was used for local anesthesia. The renal cortex was identified using real-time ultrasound, and the biopsy needle was advanced to the level of the cortex. The sample was obtained and confirmed to be renal cortex via a 10× microscope. Following the biopsy, pressure was applied to the area for 5 min, and a sand bag was placed over the kidney for at least 1 h. Patients lie flat on their back for 4–8 h and were discharged after 8 h if no clinical complication was apparent. Patients were monitored following the biopsy for signs or symptoms of complications, such as gross hematuria, flank pain and hypotension. Vital signs were checked every 15 min for 2 h and every hour for 6 h. The need for additional studies, observation or treatment was determined by each nephrologist but the intent was for the procedure to be a 'same-day' procedure in all cases. Patients were reevaluated in the outpatient setting ~1 week after discharge.

For both procedures, a complication was defined as those resulting in the need for an intervention, such as a transfusion of blood products or an invasive radiologic or surgical procedure, or those resulting in severe hypotension, acute renal obstruction or failure, septicemia, the need for readmission or death. The timing of any post-PRB complication was noted and recorded.

Data were collected prospectively in all biopsies. Statistical analysis was performed using the Mann–Whitney test for continuous data or the Fisher's exact test for categorical data. Data are reported as mean ± SD, and a $P < 0.05$ was considered statistically significant.

This study was approved by the institutional review board at Rush University Medical Center.

RESULTS

PRB was performed in 1705 adult patients with the use of real-time ultrasound. NRB ($n = 767$) was performed by a fellow more often than TRB ($n = 938$) (fellow, NRB, 91% versus fellow, TRB, 63%, $P < 0.0001$) (Table 1). All TRB procedures were performed with a 16 gauge needle, but for NRB, 88% were 14 gauge and 12% 16 gauge. There was no difference in complication rates or adequacy between these two needle gauges [28]. Patients

Table 1. Baseline demographic, clinical and laboratory features

	Transplant	Native	P
n	938	767	
Fellow (%)	63	91	<0.0001
Age (years)	50 ± 14	47 ± 17	<0.0001
Male (%)	52	38	<0.0001
Race (%)			
White	25	35	<0.0001
African American	45	35	<0.0001
Hispanic	24	16	<0.0001
Asian/other	6	5	0.28
BP			
Systolic (mmHg)	140 ± 22	133 ± 18	<0.0001
Diastolic (mmHg)	78 ± 13	79 ± 13	0.01
SCr (mg/dL)[a]	3.1 ± 1.8	2.3 ± 2.2	<0.0001
>1.5 mg/dL (%)	89	47	<0.0001
>3.0 mg/dL (%)	36	22	<0.0001
>5.0 mg/dL (%)	13	10	0.05
PTT (s)[b]	28 ± 4.3	27 ± 5.0	<0.0001
>33 s (%)	8.4	7.9	0.78
Pre-PRB Hgb (g/dL)	11.2 ± 1.8[c]	11.7 ± 2.1	<0.0001
Post-PRB Hgb (g/dL)[d]	10.1 ± 1.8	10.7 ± 2.1	<0.0001
Change in Hgb (g/dL)[d]	0.73 ± 1.3	0.97 ± 1.1	<0.0001
>1 g/dL (%)	32	43	0.0002
>2 g/dL (%)	7.4	11	0.04
>3 g/dL (%)	2.5	2.2	0.84
>4 g/dL (%)	1.4	0.9	0.57

[a]Available in 917 of transplant biopsies.
[b]Available 717 of transplant biopsies.
[c]Available in 917 of transplant biopsies.
[d]Available in 759 of native and 443 of transplant biopsies.
Data are presented as mean ± SD unless otherwise indicated.

Table 2. Adequacy of biopsy

	Transplant	Native	P
n	938	767	
LM			
≥10 glomeruli (%)	88	92	0.002
≥20 glomeruli (%)	59	56	0.15
Number of glomeruli	25 ± 14	23 ± 11	0.008
IF			
Number of glomeruli	8.2 ± 5.4[a]	8.6 ± 4.8	0.005
Total glomeruli (LM + IF)	33 ± 17[a]	31 ± 13	0.11
≥10 glomeruli (%)	98	99	0.11
≥20 glomeruli (%)	80	81	0.76
QNS (%)	0.3	0.5	0.71

[a]IF not performed (not ordered) in 25 biopsies, only available in 913.
Data are presented as mean ± SD unless otherwise indicated.
QNS, quantity not sufficient.

Table 3. Biopsy complications

	Transplant	Native	P
n	938	767	
Complications, *n* (%)	37 (3.9)	50 (6.5)	0.02
Gross hematuria	6	4	
Hematoma	24 (includes 1 death)	35 (includes 1 death)	
Both of the above	1	9	
Death	1	2[a]	
Other	6	1	
Procedures/readmissions, *n* (%)	36 (3.8)	46 (5.9)	0.04
IR procedure	2	10	
With transfusion	1	9	
Cystoscopy and/or surgery	6	1	
With transfusion	3	0	
Readmission	3	5	
With transfusion	2	1	
Transfusion	25	30	
Total transfusions, *n* (%)	31 (3.3)	40 (5.2)	0.045

[a]Two deaths, one as a result of the biopsy.

undergoing TRB were more often older, male and minority race (Black and Hispanic) compared with NRB. TRB also had higher systolic blood pressure (SBP) (TRB, 47% >140 versus NRB, 31% >140 mmHg, P < 0.0001), increased PTT (28 ± 4.3 versus 27 ± 5.0 s, P < 0.0001) and higher SCr (3.1 ± 1.8 versus 2.3 ± 2.2 mg/dL, P < 0.0001). For TRB, the SCr was >3.0 mg/dL in 36% of biopsies compared with only 22% for NRB (P < 0.0001). At the time of biopsy, the baseline Hgb concentration was lower for TRB compared with NRB (11.2 ± 1.8 versus 11.7 ± 2.1 g/dL, P < 0.0001). The average decrease in Hgb after the biopsy was less in TRB compared with NRB (0.73 ± 1.3 versus 0.97 ± 1.1 g/dL, P < 0.0001), but large drops (>4 g/dL) were equally rare (TRB, 1.4% versus NRB, 0.9%, P = 0.57). However, only 45% of TRBs had a post-biopsy Hgb measured.

Adequate specimens for a diagnosis was available in >99% of PRBs (quantity not sufficient TRB 0.3% versus NRB 0.5%, P = 0.71) (Table 2). The average number of glomeruli per biopsy, including LM and IF, was 33 ± 17 for TRB and 31 ± 13 for NRB, P = 0.11. For NRB, part of the specimen was routinely sent for EM, which was not included in the analysis. Less than 2% of PRBs had <10 glomeruli.

Complications are reviewed in Table 3 and were exclusively related to bleeding. Use of the 1-h screening ultrasound did not change the detected rate of complications for PRB. Compared with TRB, more patients who underwent NRB had a bleeding complication requiring a change in standard management (NRB, 6.5% versus TRB, 3.9%, P = 0.02). Of these complications, there were more transfusions (NRB, 5.2% versus TRB, 3.3%, P = 0.05) and interventional radiology procedures to stop the bleeding and/or readmissions (NRB, 5.9% versus TRB, 3.8%,

P = 0.04) with NRB compared with TRB. One death in each group was attributed to hemorrhagic complications, both noted within 4 h after the procedure. Nephrectomy of a native or allograft kidney was not required after any biopsy.

Risk factors predictive of complication for TRB are shown in Table 4. The operator (fellow versus attending) was not predictive of a complication, nor was patient factors such as age, race and gender. There was a trend towards a higher BP, SCr and PTT in those patients with a complication. The Hgb at the time of biopsy was the main predictive factor of a complication (including transfusion). The baseline Hgb was nearly 1 g/dL less in those with a complication compared with those without (10.1 ± 1.7 versus 11.2 ± 1.7 g/dL, P < 0.0001). Furthermore, more patients with a complication had a baseline Hgb of <9.0 g/dL compared with only those without a complication with the same degree of anemia (Hgb <9.0, complication: 24% versus no complication, 8%, P = 0.003). The drop in Hgb was greater in those with complications (P < 0.0001), but follow-up Hgb was only available in 45% of TRB. There was no difference in complication rate based on the number of passes or cores.

Risk factors predictive of complication for NRB are in Table 5. Black patients (P = 0.03) and women (P = 0.002) were more likely to have a complication. Patients with complications post-NRB

Table 4. Characteristics predictive of complication in transplant biopsies

Complication status	None	Complication	P
$n = 938$	901	37	
Fellow (%)	62	73	0.23
Age (years)	50 ± 14	53 ± 14	0.33
Male (%)	52	46	0.51
Race (%)			
White	25	30	0.77
Black	45	41	0.65
Hispanic	24	26	0.64
Asian/other	6	3	0.68
BP (mmHg)			
Systolic	141 ± 22[a]	146 ± 16	0.16
>140 mmHg (%)	47	54	0.41
Diastolic	78 ± 13[a]	81 ± 12	0.3
SCr (mg/dL)	3.4 ± 5.9[b]	3.4 ± 1.5	0.91
>1.5 mg/dL (%)	88	97	0.11
PTT (s)	28 ± 4.2[c]	29 ± 4.6	0.25
>33 s (%)	8	9	0.98
Pre-PRB Hgb (g/dL)	11.2 ± 1.7[b]	10.1 ± 1.7	<0.0001
<9.0 g/dL (%)	8	24	0.003
9.0–11.0 g/dL (%)	41	57	0.06
>11.0 g/dL (%)	51	19	0.0001
Post-PRB Hgb (g/dL)	10.4 ± 1.7[d]	7.6 ± 1.4	<0.0001
Change in Hgb (g/dL)	0.6 ± 0.9[d]	2.7 ± 2.0	<0.0001
>1 g/dL (%)	27	84 <0.0001	<0.0001
>2 g/dL (%)	3	60 <0.0001	<0.0001
>3 g/dL (%)	1	16 <0.0001	<0.0001
>4 g/dL (%)	0.4	11 <0.0001	<0.0001
Passes	3.2 ± 0.9[e]	3.0 ± 0.6 (3, 2–4)	0.16
Cores	2.8 ± 0.7[f]	2.6 ± 0.8 (3, 1–4)	0.1

[a]Available in 888.
[b]Available in 885.
[c]Available in 684 with no complications, 33 with complications.
[d]Available in 407 (45%).
[e]Available in 459.
[f]Available in 878.
Data are presented as mean ± SD unless otherwise indicated.

Table 5. Characteristics predictive of complication in native biopsies

Complication status	None	Complication	P
$n = 767$	717	50	
Fellow (%)	90	98	0.08
Age (years)	47 ± 17	49 ± 17	0.32
Male (%)	40	18	0.002
Race (%)			
White	36	18	0.01
Black	44	60	0.03
Hispanic	15	22	0.22
Asian/other	5	0	0.17
BP (mmHg)			
Systolic	133 ± 18	141 ± 22	0.003
>140 mmHg (%)	30	44	0.01
Diastolic	79 ± 13	83 ± 13	0.02
SCr (mg/dL)	2.2 ± 2.0	3.5 ± 3.5	0.01
>1.5 mg/dL (%)	45	64	0.01
PTT (s)	27 ± 5.0	28 ± 3.8	0.16
>33 s (%)	8	4	0.42
BT (min)	7.2 ± 1.9	8.1 ± 1.8	0.0002
>9 min	9	16	0.13
Pre-PRB Hgb (g/dL)	11.8 ± 2.1	10.2 ± 1.7	<0.0001
<9.0 g/dL (%)	9	24	0.003
9.0–11.0 g/dL (%)	29	48	0.006
>11.0 g/dL (%)	62	28	<0.0001
Post-PRB Hgb (g/dL)	10.9 ± 2.0[a]	8.2 ± 1.6	<0.0001
Change in Hgb (g/dL)	0.9 ± 1.1[a]	2.0 ± 1.2	<0.0001
>1 g/dL (%)	40	82	<0.0001
>2 g/dL (%)	9	42	<0.0001
>3 g/dL (%)	1	16	<0.0001
>4 g/dL (%)	0.8	0.2	0.38
Passes	2.9 ± 1.0[b]	3.2 ± 1.3	0.21
Cores	2.3 ± 0.6[c]	2.4 ± 0.8	0.45

[a]Available in 709.
[b]Available in 240 biopsies.
[c]Available in 432 biopsies.
Data are presented as mean ± SD unless otherwise indicated.

were more often hypertensive (44% >140 versus 30% >140 mmHg SBP, P = 0.01), had higher SCr (3.5 ± 3.5 versus 2.2 ± 2.0 mg/dL, P = 0.01) and prolonged BT (8.1 ± 1.8 versus 7.2 ± 1.9 min, P = 0.0002) compared with those without. Lower baseline Hgb (10.2 ± 1.7 versus 11.8 ± 2.1 g/dL, P < 0.0001) and greater change in Hgb post-NRB (2.0 ± 1.2 versus 0.9 ± 1.1 g/dL, P < 0.0001) were also predictive of complication. There was no difference in complication rate based on the number of passes or cores.

The timing of complications was prospectively evaluated following the PRB (Table 6). Of patients with post-biopsy complications, ~75% were discovered in ≤8 h. For TRB, 26% of complications were not discovered until after the 8 h protocol observation period, but 61% of these occurred in inpatients (39% required readmission). For NRB, 14% were discovered after the standard 24 h protocol observation period, but 37% of these occurred in inpatients (63% required readmission).

DISCUSSION

We conclude that both the NRB and TRB are successful procedures, defined by diagnostic yield and safety. Both NRB and TRB had equal amount of glomeruli per biopsy, with a diagnostic accuracy of over 99%. However, despite the higher clinical hemorrhagic risk profile of patients undergoing TRB, they experienced fewer bleeding complications, required fewer interventions and received fewer blood transfusions compared with NRB.

Although serious complications were found in a minority of procedures, they still occurred, and the frequency in our study (5.1% overall) is consistent with other studies of PRB [6, 7, 9, 13, 14, 29]. For NRB, the complication rate can be as high as 27% in certain high-risk populations [10, 11, 30]. For TRB, based on observational studies (including stable patients with 'protocol' biopsies, which are known to be safer than biopsy for 'indication' [17]), the complication rate is 1–9 and includes gross hematuria, perinephric hematomas, urinomas, arteriovenous fistula (AVF) formation, blood transfusion, acute renal failure/obstruction, interventional or surgical procedures to stop hemorrhage, readmission, graft loss/nephrectomy and death [16–19, 31–36]. One prior report has directly compared complication rates of native and transplant biopsies [16]. In this single center retrospective study of 515 PRBs (NRB 170, TRB 345) using real-time ultrasound and 14 gauge needles, the overall complication rate was higher in native biopsies (NRB, 19.4% versus TRB, 8.7%, P < 0.001), but the rate of major complications was not different (NRB, 2.4% versus TRB, 2.9%, P = 0.944). For NRB, the major

Table 6. Timing of complications in native and transplant PRB

		Complication					
	n	≤4 h	≤8 h	>8 h	≤12 h	≤24 h	>24 h
Native	50	58%	72%	28%	82%	86%	14%
Transplant	37	69%	74%	26%	n/a	n/a	n/a

n/a, not available.

complications were requirement of blood transfusions, and for TRB, they were requirement of blood transfusions, embolization of AVF, urinoma, graft loss and death. Although serious and catastrophic complications can occur after both procedures, our prospective study with 1705 biopsies detected a higher rate of major complications with NRB compared with TRB.

The difference in complication rate for the biopsies could be explained by patient and/or procedural factors. Compared with TRB, a greater percentage of women underwent NRB, which is a known risk factor for complication [5, 6, 29, 37], although this may be partially explained by the higher frequency of anemia in women compared with men [38]. There were also baseline ethnic differences between the two groups in our study that may have affected the results. However, many of the other traditional patient-related risk factors for complication in NRB were present in a greater degree in patients undergoing TRB, yet TRB patients developed fewer complications. Compared with NRB, patients undergoing TRB were older, had higher PTT, SCr and BP and lower Hgb. Traditional risk factors for complications after NRB include these as well as thrombocytopenia [11, 30], prolonged BT [5, 13], bleeding diathesis, use of a 14 gauge needle [6] and inpatient status [11]. These risk factors have not been as widely studied in TRB, but higher complications have been associated with anticoagulation [17], increased age [17], blood urea nitrogen [17], thrombocytopenia [17], a greater drop in Hgb [17, 19, 36] as well as biopsy for 'indication' [17] (as opposed to 'protocol') and biopsy of the allograft within 1 week of transplantation [19].

In our study, when the traditional risk factors for complications of NRB were evaluated for TRB, there was a trend for higher complication rate with a higher BP, SCr and PTT, but only the pre/post-Hgb was found to be statistically significant to predict bleeding complications. This is similar to other studies of TRB when the post-biopsy Hgb was checked routinely [17, 19, 36]. However, the baseline Hgb itself may not be a reliable risk factor. It has been found only to be useful to predict receiving a blood transfusion as opposed to predicting hemorrhagic complications post-NRB [38]. In addition, in our study of TRB, although the pre-biopsy Hgb was available on most patients, the usefulness of the post-Hgb (and therefore the delta Hgb) is flawed by the fact that it was checked in only 47% of TRB procedures. It was ordered when there was a consideration for a hemorrhagic complication post-TRB, and is therefore a biased indicator of a complication for TRB in our study. Regardless of the validity of the specific risk factors, given that TRB had a higher frequency of them compared with NRB, yet was still safer, it is unlikely that patient related-factors played a role in the difference seen in complication rates.

Alternatively, procedural or protocol differences are more likely to have affected the complication rate. A greater percentage of fellows performed the NRB compared with TRB, and the experience of the operator or center can affect the rate of complications [6, 14, 39]. There are also several technical differences

in the procedures that may help explain the variability. Firstly, for the TRB, the patient is in the supine position and the allograft is typically more superficial compared with the prone positioning/retroperitoneal location of the kidney for the NRB, which also moves with respiration. Direct manual pressure and/or the use of a sand bag theoretically would be more likely to contain a forming hematoma or hemorrhage in a transplant, which is not feasible for the NRB.

In addition, unless there was a noted complication, patients were out of bed with the intent to return home 8 h after the TRB, as opposed to staying at bed rest for 24 h after the NRB, and although this is counterintuitive, bed rest or prolonged observation could have contributed to detecting more complications as currently defined. It is possible that since NRB patients were observed for longer, a higher frequency of 'complications' could have been noted by routine lab draws in an otherwise uneventful biopsy. This in turn could lead to further testing, blood transfusions and/or a prolonged hospital stay. Thus, a longer observation period may increase the detected complication rate. Consistent with this is that the majority of complications discovered after 8 h for TRB occurred in inpatients, who by definition were observed for longer. However, the longer period (24 h) is justified for NRB, and should be considered for TRB, given that about one-quarter of all PRB complications (NRB 27%, TRB 24%) were detected after the initial 8 h of observation in our study. This delay in detecting complications for NRB is consistent with the reported literature where 28–33% of complications are detected after 8 h [5, 27]. In TRB, when timing of complications has been evaluated, a 4 h observation period is common. Reported serious complications that occur after 4 h have varied from none in one series of protocol biopsies [18] to 37.5% in another study [36]. In a retrospective series of 3738 biopsies with an 18 gauge needle by Redfield *et al.* [19] in 2016, 1.8% of biopsies developed complications, but 67% of the procedures that required surgical intervention presented after the initial 4 h observation period. Another study [17] evaluated 2514 TRB and noted a major complication rate of 1.9%. Only 53% of these were discovered on the same day. On Day 2, 17% more were detected, and the 30% remaining presented from Day 2 to 14. Thus, serious complications can occur after both procedures, and often present in a delayed fashion.

The last major procedural difference that could theoretically affect complications is needle gauge. Transplant nephrologists exclusively used a 16-gauge needle for TRB, as opposed to the larger 14 gauge for the majority (88%) of NRB, and both led to equal diagnostic accuracy (≥99.5%). For NRB, use of the 14 gauge has been shown in a large review to be associated with a higher complication rate [6]. However, when direct comparisons of needle gauges have been made in individual studies, the larger gauge has consistently shown no increase in complication rates or transfusion requirements [12, 14, 40–44], including a large report of 9288 PRBs in the Norwegian Kidney Biopsy Registry [14]. In addition to not increasing risk, a number of other studies of NRB have shown a greater diagnostic yield with the 14 gauge compared with 16 or 18 gauge, with a superior sample demonstrating more intact glomeruli with less 'crush or fragmentation' artifact [12, 14, 45, 41, 43, 46–48]. The use of 18 gauge has consistently led to fewer glomeruli and more nondiagnostic biopsies compared with 16 or 14, which has the potential to expose the patient to a second procedure. For TRB, serious complications occurred in one report by Redfield *et al.* [19] (0.21%, 0.19% life-threatening) despite the sole use of an 18 gauge. In another study by Schwarz *et al.* [35], 1171 TRB protocol biopsies were performed with a major complication rate of 1%.

In the beginning of the study, an 18 gauge was used, but due to a higher amount of inadequate specimens with this gauge (47%), the investigators switched to a 16 gauge. They noted no increase in complication rate with the large-gauge needle, and the sample from the 16 gauge needle more often (76%) demonstrated an adequate specimen. Nicholson *et al.* [48] performed the only randomized controlled trial of 14, 16 and 18 gauge needles for TRB. They demonstrated that use of a 14 gauge resulted in a significantly larger sample size (15 versus 11 versus 9 glomeruli, P < 0.05) and greater diagnostic accuracy (85 versus 76 versus 53%, P < 0.05). Although there was no difference in complications between the gauges, patients undergoing TRB with a 14 gauge had more pain compared with the smaller needles, leading to the recommendation of the investigators to use a 16 gauge for TRB. In the only other comparative study of TRB and NRB by Preda *et al.* [16], similar to our study, TRB demonstrated fewer complications. However, in this study [16], both TRB and NRB were performed with a 14 gauge. Thus, although in our study TRB may have fewer complications in part due to use of a smaller gauge needle, other factors besides needle gauge alone lead to TRB being safer.

In conclusion, the PRB remains a safe and successful procedure. Diagnostic accuracy remains excellent for both TRB and NRB, but the complication rate is higher for NRB despite TRB displaying more of the traditional risk factors for bleeding. Serious complications rarely occur in both procedures, and can present in a delayed fashion. It is likely that procedural related factors, such as operator, positioning, needle size and/or post-procedure management, contribute to this difference in safety.

CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this manuscript have not been published previously in whole or part except in abstract form.

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