Timing of Complications in Percutaneous Renal Biopsy

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Abstract. Percutaneous renal biopsy (PRB) is a safe and effective tool in the diagnosis and management of renal disease; however, the optimal timing of observation after biopsy is not clearly established. With the use of real-time ultrasound guidance, PRB of native kidneys was performed in 750 adult patients at an academic institution by an attending nephrologist or fellow between June 1983 and June 2002. All patients were observed for 23 to 24 h after biopsy for the presence, severity, and timing of complications. Biopsy-related complications occurred in 98 (13%) patients; minor complications occurred in 50 (6.6%) patients, and major complications occurred in 48 (6.4%) patients. One (0.1%) patient died as a result of the biopsy. Multivariate analysis using logistic regression found only serum creatinine at baseline predictive of a complication. Patients with a serum creatinine ≥5.0 mg/dl were 2.3 times as likely to have a complication (odds ratio, 2.3; 95% confidence interval, 1.3 to 4.1; $P < 0.005$). Complications were identified in 38 (42%) patients by ≤4 h, in 61 (67%) patients by ≤8 h, in 77 (85%) patients by ≤12 h, and in 81 (89%) patients at ≤24 h. The PRB remains a safe procedure, but the risk of complication is higher in patients with advanced renal insufficiency. After biopsy, an observation time of up to 24 h remains optimal as an observation period of ≤8 h risks missing ≥33% of complications.

The percutaneous renal biopsy (PRB) of native kidneys has become an essential tool in the diagnosis and treatment of patients with renal disease. Since the introduction of PRB in the 1950s, technical advances in imaging and biopsy needles have simplified and improved the success of the procedure. With the use of real-time ultrasound and automated biopsy needles, ≥99% of biopsies are diagnostic (1). Nonetheless, the success of the procedure is defined not only by the ability to obtain adequate tissue for diagnosis but equally, if not more importantly, by the safety profile. Overall, the PRB has become a relatively safe procedure with life-threatening complications occurring in <0.1% of biopsies in recent reports (1–4).

The standard of care after renal biopsy has included bed rest with close observation for 24 h. However, because of the current safety profile of the procedure and an ongoing desire for cost containment, it has been proposed that PRB be performed as an "outpatient procedure," discharging patients after only 6 to 8 h of observation (5–7). Whether this is an adequate period of observation to ensure patient stability before discharge is not clear as experience with this practice has been limited and based on a very select group of patients, biopsied by highly experienced nephrologists (5–7). Thus, the safety of generalizing this practice is unknown, as information on the ideal timing for observation after a PRB has been extremely limited.

In 1996, we reported our experience on the timing of complications after PRB in 394 adults who underwent PRB of native kidneys (3). We found that only 77% of complications were apparent by 8 h of observation and that an observation period of 23 to 24 h was optimal, capturing 98% of complications overall and 100% of serious complications. Despite these findings, ongoing interest in early discharge persists as a result of ever-increasing demands for cost containment (5–7). As a result, we extended our observations by examining the timing and severity of complications in 750 adult patients who underwent PRB of native kidneys in an academic nephrology program.

Materials and Methods

PRB of native kidneys were performed in 750 adult (≥15 yr) patients consecutively from June 1983 through June 2002 at Rush-Presbyterian-St. Luke's Medical Center. Renal biopsies were performed by an attending nephrologist (18%, 136 of 750) or a fellow (82%, 614 of 750) under the supervision of an attending nephrologist. Imaging was performed by an experienced radiologist using real-time ultrasound as described previously (1,8). The lower pole of the kidney was identified for biopsy. A 14-gauge Tru-cut needle (Travenol Laboratories, Deerfield, IL) was used in the first 227 biopsies (June 1983 to October 1990), and a 14-gauge automated biopsy needle (Bard Biopty gun, CR Bard Inc., Covington, GA) was used for the subsequent 523 biopsies (November 1990 to June 2002). Adequate material for diagnosis was obtained in 99% (741 of 750) of biopsies.

Information collected at the time of biopsy included age, gender, race, systolic and diastolic BP, serum creatinine, bleeding time, prothrombin time (PT), activated partial thromboplastin time (PTT), and hemoglobin concentration. It is our practice to perform percutaneous biopsies in patients with a normal bleeding time, no evidence of a coagulopathy as determined by PT and PTT, and stable BP.

After the procedure, patients lay in bed flat on their back for 4 to 6 h and then remained in bed for 23 to 24 h of observation. Patients were monitored closely after biopsy for signs or symptoms of complications, such as gross hematuria, flank pain, or 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. Each urine void was checked for

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hematuria visually, and the results were recorded. Hemoglobin levels were checked at approximately 5 to 8 h, 10 to 13 h, and 18 to 20 h after the procedure. The lowest hemoglobin level after biopsy was recorded. Additional follow-up studies and treatment were determined by each nephrologist on the basis of his or her assessment of the severity of the clinical signs and symptoms or laboratory results. Patients were reevaluated in the outpatient setting approximately 1 wk after discharge.

The timing of a complication was defined by the first indication (gross hematuria, severe flank pain, hypotension, or decrease in hemoglobin requiring a transfusion) that a clinically relevant problem existed. The severity of the complication was categorized as minor or major. Minor complications were defined as those resulting in gross hematuria and/or perinephric hematoma but spontaneously resolving without the need for further intervention. Major complications were those resulting in the need for an intervention, such as a transfusion of blood products or invasive procedure (radiographic or surgical), and those resulting in acute renal obstruction or failure, septicemia, or death.

Biopsies performed after November 1990 (523 biopsies) were evaluated prospectively for the development and timing of a post-biopsy complication. Biopsies performed before this date (227 biopsies) were evaluated retrospectively and based on review of hospital charts. Complications occurred in 98 biopsies. The time interval from the biopsy to recognition of the complication was determined in 24 (77%) of 31 biopsies evaluated retrospectively and in all 67 biopsies with complications that were evaluated prospectively.

Statistical Analyses

Statistical analysis was performed using the unpaired and paired *t* test for continuous data or the Fisher exact test for categorical data. Multivariate analysis using logistic regression was performed to determine which feature at baseline was predictive of a complication after renal biopsy. The baseline variables examined included race, gender, age, bleeding time, systolic and diastolic BP, serum creatinine, hemoglobin concentration, type of needle used (automated or manual), and who performed the biopsy (attending or fellow). For each continuous variable, the optimal cut point to dichotomize the variable was determined. Variables with a $P < 0.05$ were retained in the final model. Data are reported as mean ± SD, and $P < 0.05$ was considered significant.

Results

Complications related to renal biopsy occurred in 13% (98) of all biopsies (Table 1). There was no significant difference in age, gender, BP, or coagulation studies before the biopsy between patients with or without complications. Before biopsy, 50% (277 of 554) of patients had a hemoglobin concentration of ≤12 g/dl and 53% (399 of 750) of patients had a serum creatinine >1.3 mg/dl. Patients with a complication had a lower pre-biopsy hemoglobin concentration (11 ± 2 g/dl *versus* 12 ± 2 g/dl; $P < 0.05$) and a higher pre-biopsy serum creatinine (2.9 ± 2.7 mg/dl *versus* 2.2 ± 2.5 mg/dl; $P < 0.05$) than patients with uncomplicated biopsies. A multivariate analysis of features at baseline was performed to determine which, if any, variable was predictive of a complication after renal biopsy. The only variable predictive of a complication was the level of serum creatinine. Biopsies in patients with a serum creatinine ≥5.0 mg/dl were 2.3 times more likely to have a complication after renal biopsy (odds ratio, 2.3; 95% confidence interval, 1.3 to 4.1; $P < 0.005$). The final renal histology was not predictive of a complication. There was no significant difference in complication rate between the biopsies that were performed by an attending nephrologist compared with those that were performed by a fellow.

Table 1. Patient characteristics at biopsy

	With Complication	Without Complication	*P*
n	98 (13%)	652 (87%)	
Age (yr)	48 ± 19	45 ± 17	NS
Male	30%	39%	NS
Creatinine (mg/dl)	2.9 ± 2.7	2.2 ± 2.5	0.0177
Systolic BP (mmHg)[c]	137 ± 18	134 ± 19	NS
Diastolic BP (mmHg)[c]	81 ± 11	80 ± 13	NS
Bleeding time (min)[d]	6 ± 2	6 ± 2	NS
Pre-Hgb (g/dl)[c]	11 ± 2	12 ± 2	0.0175
Post-Hgb (g/dl)[e]	9 ± 2[a]	11 ± 2[b]	<0.0001
Δ Hemoglobin (g/dl)[e]	2.1 ± 1.6	0.9 ± 0.8	<0.0001

[a] Change in Hgb (g/dl) in with complication: 11 ± 2 to 9 ± 2; $P < 0.0001$.
[b] Change in Hgb (g/dl) in without complication: 12 ± 2 to 11 ± 2; $P < 0.0001$.
[c] Data available in 71 patients with complication and 483 without complication.
[d] Data available in 98 patients with complication and 626 without complication.
[e] Data available in 71 patients with complication and 478 without complication.

After biopsy, a significant decrease in hemoglobin was seen in both groups of patients; however, the decrease in hemoglobin concentration was greater in patients with a complication (2.1 ± 1.6 g/dl [range, −1.2 to 8.6] *versus* 0.9 ± 0.8 g/dl [range, −1.1 to 4.8]; $P < 0.0001$). In uncomplicated biopsies, a post-biopsy decrease in hemoglobin of ≥1.0 g/dl was observed in 46% (222 of 478) of cases and a decrease of ≥2.0 g/dl was observed in 9.6% (46 of 478) of cases. In biopsies with a complication, a post-biopsy decrease in hemoglobin of ≥1.0 g/dl was observed in 89% (63 of 71) of cases (uncomplicated *versus* complicated, $P < 0.0001$) and a decrease of ≥2.0 g/dl was observed in 48% (34 of 71) of cases (uncomplicated *versus* complicated, $P < 0.0001$).

Minor complications were observed in 6.7% (50) of biopsies, and major complications were observed in 6.4% (48) of biopsies (Table 2). Gross hematuria was the most common complication observed overall, seen in 57% (56 of 98) of complicated biopsies (7.5% of all biopsies). In biopsies with major complications, the most frequent intervention was a blood transfusion, which occurred in 79% (38 of 48) of biopsies (5.0% of all biopsies). The median number of packed red blood cell (PRBC) transfusions was 2 units, with 8 biopsies requiring 1 unit, 20 biopsies requiring 2 units, and 10 biopsies requiring ≥3 units of PRBC. Invasive procedures were required in five patients (0.7% of all biopsies): two patients required cystoscopy, and three patients required angiography with subsequent gel-foam or coil embolization (two of these

Table 2. Type of complication[a]

	n	%	% of All Biopsies
Minor complication			
gross hematuria	23	46%	3.1%
hematoma	16	32%	2.1%
both	8	16%	1.1%
other	3	6%	0.4%
Total	50	100%	6.7%
Major complication			
gross hematuria	12	25%	1.6%
hematoma	14[b]	29%	1.9%
both	13	27%	1.7%
no. with AV fistula	3	6.3%	0.4%
no. with Obst/ARF	2	4.2%	0.3%
drop in Hgb	2	4.2%	0.3%
other	2[b]	4.2%	0.3%
Total	48	100%	6.4%

[a] AV, arteriovenous; Obst/ARF, obstruction and/or acute renal failure.
[b] Death.

patients also required PRBC transfusion). No patient required surgical nephrectomy. Two patients died; however, only one (0.1%) death could be attributed to the biopsy procedure. In the death attributed to the renal biopsy, evidence of bleeding was noted within 4 h of an otherwise uneventful procedure. The patient died 9 h after the biopsy and was found to have a massive perinephric hematoma at autopsy. The second death occurred suddenly, before discharge and 24 h after biopsy, in an elderly patient who had diabetes mellitus and had an uneventful biopsy with no signs or symptoms of complication or change in hemoglobin after biopsy. At autopsy, there was no evidence of a significant subcapsular or perinephric hematoma.

The timing of the complications is shown in Tables 3 and 4. Only 67% of complications were apparent within 8 h. Overall, the complication was identified within 12 h of the procedure in 85% of cases and within 24 h in 89% of biopsies. In patients with major complications, the complication was identified within 8 h of the procedure in 67% of cases, within 12 h in 89% of cases, and within 24 h in 91% of biopsies. In 10 (11%) patients, the complication was not evident until after 24 h, and 4 of these were patients with major complications. Two patients with major complications presented with gross hematuria and a drop in hemoglobin 48 and 72 h after biopsy. This resulted in the need for PRBC transfusion. The other two patients presented with severe flank pain and in one case gross hematuria 72 and 120 h after biopsy. Although these two patients did not require PRBC transfusion or an invasive procedure, both were found to have a large perinephric hematoma requiring readmission for prolonged bed rest and close observation.

Table 3. Cumulative timing of post-biopsy complication

	n	Hours Post-Biopsy				
		≤ 4	≤ 8	≤12	≤24	>24
Total	91	42%	67%	85%	89%	11%
Minor complication	46	46%	67%	80%	87%	13%
Major complication	45	38%	67%	89%	91%	9%

Patients with a major complication after biopsy were older (53 ± 17 yr *versus* 43 ± 18 yr; $P < 0.05$) and had a lower hemoglobin concentration before the PRB (10.7 ± 2.3 g/dl *versus* 12.3 ± 1.6 g/dl; $P = 0.0001$) compared with patients with minor complications (Table 5). The average change in hemoglobin after biopsy was ≥2 g/dl in patients with complications but was not significantly different between those with a major or a minor complication. Patients with a major complication tended to have a higher serum creatinine compared with those with a minor complication, but this did not reach statistical significance. There was no difference in the complication rate or in the proportion of patients with major or minor complications for patients who were evaluated retrospectively ($n = 227$, using the 14-gauge Tru-cut needle) compared with patients who were evaluated prospectively ($n = 523$, using the 14-gauge automated needle).

Discussion

In our experience, the PRB is safe with minimal risk of serious complication. During the course of 20 yr, only 5 (0.7%) biopsies resulted in the need for an invasive procedure, no patient required emergent surgery or nephrectomy, and a death attributed to the procedure occurred in only one (0.1%) patient. Nonetheless, complications did occur in 13% of biopsies, and 6.4% of complications were considered major, primarily because of the need for transfusion after biopsy. Major complications were apparent in only 67% of patients by 8 h, but >90% of these were evident by 24 h.

The PRB is safe and free of complications in the majority of cases. In a review of 9595 biopsies performed in the past 50 yr, only 0.3% of patients required major surgical or radiographic intervention, and death resulting from the procedure occurred in <0.1% of cases (1). With the use of newer biopsy techniques, only one death has been reported in the past 20 yr. Nonetheless, the potential for a serious complication still remains.

On average, clinically significant complications are seen in 7.4% of biopsies, but complication rates as high as 19.5% have been reported (1). Most complications are minor and resolve spontaneously; however, major complications have been reported in up to 7.3% of biopsies (1). Factors that have been found to predispose to complications after PRB include renal insufficiency (>1.2 mg/dl), poorly controlled hypertension (diastolic BP >90 to 110 mmHg), and a prolonged bleeding time (9,10). It has been shown that the risk of bleeding postoperatively increases with worsening levels of renal insufficiency, and this is a significant issue as >50% of the patients who are biopsied in our program have chronic renal insufficiency. Patients with advanced renal insufficiency (estimated GFR of <40 ml/min) have a sixfold increase in risk of severe

Table 4. Type and timing of post-biopsy complication[a]

	Hours Post-Biopsy				
	≤ 4	5–8	9–12	13–24	>24
Minor complication					
gross hematuria	12	5	2	1	1
hematoma	5	3	2	2	3
both	3	1	1	0	2
other	1	1	1	0	0
Total (n = 46)	21	10	6	3	6
Major complication					
gross hematuria	4	4	2	0	2
hematoma	4[b]	6	2	0	1
both	6	2	2	0	1
no. with AV fistula	2	0	1	0	0
no. with Obst/ARF	1	0	1	0	0
drop in Hgb	0	0	2	0	0
other	0	1	0	1[b]	0
Total (n = 45)	17	13	10	1	4

[a] AV, arteriovenous; Obst/ARF, obstruction and/or acute renal failure.
[b] Death.

Table 5. Patient characteristics with complications

	Major Complication	Minor Complication	P
n	48	50	
Age (yr)	53 ± 17	43 ± 18	0.0130
Male	29%	30%	NS
Creatinine (mg/dl)	3.1 ± 2.8	2.6 ± 2.6	NS
Systolic BP (mmHg)[c]	140 ± 18	134 ± 18	NS
Diastolic BP (mmHg)[c]	82 ± 12	81 ± 10	NS
Bleeding time (minutes)	7 ± 2	6 ± 2	NS
Pre-Hgb (g/dl)[c]	10.7 ± 2.3	12.3 ± 1.6	0.0001
Post-Hgb (g/dl)[c]	8.4 ± 1.8[a]	10.4 ± 1.5[b]	<0.0001
Δ Hemoglobin (g/dl)[c]	2.3 ± 1.8	2.0 ± 1.2	NS

[a] Change in Hgb (g/dl) in major complication: 10.7 ± 2.3 to 8.4 ± 1.8; $P < 0.0001$.
[b] Change in Hgb (g/dl) in minor complication: 12.3 ± 1.6 to 10.4 ± 1.5; $P < 0.0001$.
[c] Data available in 34 pts with minor complication and 37 pts with major complication.

bleeding postoperatively, and even those with mild levels of renal insufficiency (estimated GFR of 61 to 80 ml/min) have a twofold increase in the risk of serious postoperative bleeding compared with patients with normal renal function after adjusting for measures of coagulation status and platelet function (11). Consistent with this observation is our finding that serious complications were more than twice as common in patients with advanced renal insufficiency (serum creatinine ≥5.0 mg/dl). Despite the understanding of predisposing risk factors, there is no definitive way to predict which patients will develop a serious complication.

Although it has been shown that complication rates have improved with the use of automated needles, it has been suggested that post-biopsy complications may be even less frequent with the use of smaller gauge needles (16- or 18-gauge needles compared with the 14-gauge needle) (1). Studies that have addressed this issue in native kidney biopsies have been flawed as they compared complications in patients who were biopsied with smaller gauge automated needles to those of patients who were biopsied with larger gauge manual needles; thus, their results may reflect the impact of biopsy technique rather than needle size (12–14). To date, the only prospective study to evaluate the impact of needle size using automated biopsy needles has been conducted in renal allograft biopsies; no significant difference in complication rate was found, but the sample was significantly greater with the 14-gauge needle biopsies (15). Thus, the 14-gauge needle offers the largest sample size without an increased risk of complications.

It must be recognized that although serious complications are infrequent, the potential for a serious complication after renal biopsy is significant. Although clinically significant perinephric hematomas occur in 6% or fewer of biopsies, perinephric hematomas have been demonstrated at 24 to 72 h after biopsy in >90% of cases evaluated prospectively (1,16). The majority of hematomas are asymptomatic and small in size, but in up to 50% of biopsies, they are moderate to large in size (17,18). As a result, the present practice of 24-h bed rest and observation after biopsy may be therapeutically important and contribute to the low incidence of clinically significant hematomas. Unfortunately, there are no reliable measures that can predict which patients will go on to have a clinically significant hematoma as radiographic evaluation immediately after biopsy detects <15% of hematomas (5,12).

A drop in hemoglobin by ≥1 g/dl after biopsy is common and has been reported to occur in almost 50% of cases (19–22). Although this might herald the development of a significant hemorrhagic complication, in the majority of cases, this is associated with an uneventful course. The cause of the "nonhemorrhagic" 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 routine infusion of saline after biopsy (19), or postural hemodilution (23) resulting from the resorption of interstitial fluid in severely edematous patients after prolonged bed rest after biopsy. We found that patients with hemorrhagic complications had a greater decrease in hemoglobin concentration after biopsy; however, even a large proportion (46%) of uncomplicated biopsies had a ≥1 g/dl decrease, and the degree of change was not predictive of the severity of complication. Khajehdehi *et al.* (22) found the overall correlation between the percentage change in post-biopsy hemoglobin at 6 h and the hemoglobin level at 24 h was poor, and this was particularly true in patients with the largest change in hemoglobin (>10%) at 24 h. 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.

As a result of the overall low complication rate observed with PRB, a number of reports have advocated the safety of "early" (6 to 8 h after biopsy) or "same day" discharge after PRB (5,7,24). These have often been based on evaluations of small numbers of select patients, and the biopsies are generally performed by a limited number of experienced nephrologists. In general, the rationale for this practice is strictly driven by the potential cost savings. In several reports, a post-biopsy ultrasound was done before discharge to screen for potential complications, a measure that would significantly reduce any real cost saving (6,25). In addition, some studies limit the practice of early discharge to patients who live or can make arrangements to stay close to the hospital on the post-biopsy night in case of emergency (7,24). Nonetheless, even though such a practice is intended for a "select" group of patients, once instituted, it often becomes mandated as the standard for all patients. Because the number of biopsies performed on a yearly basis (median, 10; range, 5 to 15), as well as the level of competence and complication rates, may vary significantly among nephrologists, it is not clear that the universal application of this practice is in the patient's best interest (26).

The appropriate amount of time that a patient should be observed after biopsy should be based on when most significant complications are likely to occur. The observation period should allow the nephrologist ample opportunity to identify and treat a potential complication in a timely manner to prevent a serious or catastrophic outcome. In our ongoing experience (3), we find that major complications were identified in >90% of cases by 24 h. Consistent with our findings, Jones *et al.* (6) found that 66% of complications were apparent within 6 h of observation and 100% within 12 h of post-biopsy observation. The cost savings at our institution for discharging a patient after 12 to 14 h compared with observing the patient for 23 h was <$25, hardly enough to justify such a practice (3). Unfortunately, there are no reliable measures that can absolutely predict which patients will go on to have a complication. As noted above, neither an assessment by ultrasound after biopsy nor initial change in hematocrit after biopsy can reliably distinguish patients who are at risk of a serious complication from patients who can safely be discharged home early after the procedure (1). Thus, for patients who undergo PRB of native kidneys, the standard period of observation of up to 24 h is recommended. The potential risk to our patients incurred by shorter periods of observation cannot be justified.

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