Predictors of Complication after Percutaneous Ultrasound-Guided Kidney Biopsy in HIV-Infected Individuals: Possible Role of Hepatitis C and HIV Co-infection

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Background and objectives: HIV-infected patients often undergo kidney biopsy. The risks of percutaneous ultrasound-guided kidney biopsy in this population are not well established.

Design, setting, participants, & measurements: This was a case-control, single-center study of 1116 (243 with HIV infection and 873 without) consecutive ultrasound-guided biopsies from 1024 patients. The primary outcome was any major or minor complication. Major complications included biopsy-associated bleeding that required transfusion, angiography, or surgery; hypotension that required intervention; and death. Minor complications included development of a hematoma or gross hematuria. The odds of complication was assessed with logistic regression.

Results: Overall complication rates (8.6 *versus* 7.2%) did not significantly differ between HIV-infected and noninfected individuals. HIV-positive status did not predict complication. In the entire cohort, hepatitis C infection was associated with a 2.08 (95% confidence interval [CI] 1.47 to 2.93) increased odds of complication, and each 10,000-cells/mm^3 decrease in prebiopsy platelet count a 1.05 (95% CI 1.02 to 1.08) increased odds of complication. In addition, prebiopsy hematocrit <30% and estimated GFR <30 ml/min per 1.73 m^2 were associated with major complication. Whereas the association of prebiopsy platelet count was not modified by HIV infection, hepatitis C/HIV co-infection was associated with a 5.71 (95% CI 1.89 to 17.2) increased odds of complication as compared with 1.27 (95% CI 0.73 to 2.19) in hepatitis C–positive/HIV-negative individuals.

Conclusions: Ultrasound-guided percutaneous kidney biopsy is a relatively safe, well-tolerated procedure in the HIV-infected population. HIV-infected individuals who are co-infected with hepatitis C seem to be at greatest risk.

Clin J Am Soc Nephrol 4: 1766–1773, 2009. doi: 10.2215/CJN.03880609

HIV-infected patients with kidney disease often require percutaneous kidney biopsy to aid in diagnosis and management of the underlying kidney disease (1). Although relatively simple to perform, ultrasound-guided biopsies do entail known risks. The risks of percutaneous ultrasound-guided kidney biopsy have been well-described in the general population (2,3), but the specific risks in the HIV-infected population are relatively unknown.

Bleeding is the most common and serious of biopsy-related complications, which also include infection, pain, inadvertent injury to other organs, and rarely death. Several studies have assessed predictors of bleeding complications of ultrasound-guided biopsy in the general population (4,5), but, to date, the HIV-infected population has not been examined separately. Coagulopathies, thrombocytopenia, and endothelial dysfunction have been reported to exist at a higher frequency in HIV-infected patients (6–8) and may modify bleeding risk. As such, accurate data on the rate of biopsy complications in this population are important for the informed consent process; therefore, in this study, we assessed the risk for complication in HIV-positive patients as compared with HIV-negative patients who were undergoing real-time ultrasound-guided percutaneous kidney biopsy at a single tertiary care academic center.

Materials and Methods

Study Design and Population

A single-center, retrospective, case-control study of 1116 ultrasound-guided percutaneous native kidney biopsies that were performed on 1024 adult patients at the Johns Hopkins Hospital between February 1, 1995, and December 31, 2007, was performed. All patients who were ≥18 yr of age and underwent ultrasound-guided percutaneous kidney biopsy during this time frame were included. Patients did not undergo biopsy when they had uncontrolled hypertension (systolic BP >160 mmHg or diastolic BP >90 mmHg), international normalized ratio ≥1.3 s or partial thromboplastin time ≥42.1 s, platelet count <50,000 cells/mm^3, aspirin or clopidogrel use in the preceding 5 d, or evidence of hemodynamic instability at the time of the procedure. All patients had preprocedure coagulation studies. Bleeding times were not measured

Received June 12, 2009. Accepted August 26, 2009.

Published online ahead of print. Publication date available at www.cjasn.org.

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ISSN: 1555-9041/411–1766

for any patient. This study was approved by the institutional review board of the Johns Hopkins University School of Medicine.

Outcomes

The primary outcome was any minor or major complication. Minor complication was defined as (*1*) hematoma ≥4 cm in size or described as "moderate" or "large" on imaging reports, (*2*) voiding difficulty that required temporary urethral catheterization, or (*3*) gross hematuria. Routine postbiopsy imaging was not performed on all patients. Imaging was performed only in the context of clinical symptoms (abdominal or flank pain) or drop in hematocrit that was worrisome for bleeding. Major complication was defined as biopsy-associated bleeding that required (*1*) packed red blood cell transfusion, angiography, or surgery; (*2*) hypotension that required transfer to a higher level of nursing care or need for intravenous fluid or vasopressor support; or (*3*) death. Secondary outcomes were the subgroups of minor and major complications.

Exposure Variables

Clinical, demographic, and laboratory data were abstracted from the electronic patient record. Data on prebiopsy blood urea nitrogen (BUN), creatinine, platelet count, and hematocrit were missing for 25, 19, 22, and 29 patients, respectively. For those with major complications, there were no missing hematocrit or platelet data and only one patient lacked a BUN and creatinine value. The primary predictor of interest was HIV infection, and the remaining predefined predictors of interest included age, prebiopsy mean arterial pressure, prebiopsy hematocrit <30%, prebiopsy platelet count (per 10,000-cells/mm^3 decrease), and estimated GFR (eGFR) <30 ml/min per 1.73 m^2. Hepatitis C infection emerged as a predictor of interest after data analysis. All HIV-infected patients had serologic evidence of HIV infection by ELISA and Western blotting. eGFR was calculated by the four-variable Modification of Diet in Renal Disease (MDRD) equation (9). An eGFR >60 ml/min per 1.73 m^2 by the MDRD equation was reassigned the value of 60 for statistical purposes. A history of hypertension was defined as BP ≥140/90 mmHg or a diagnosis of hypertension in the record. Similarly, a history of diabetes was defined as a diagnosis of diabetes in the record. Histopathologic diagnoses were obtained from pathology reports.

Biopsy Technique

Informed written consent was obtained before kidney biopsy. The biopsy technique remained essentially unchanged during the period of this study. Biopsies were performed by attending nephrologists or by nephrology fellows under direct attending supervision. Semiautomated 18-G needles were used for all biopsies, and experienced radiology technicians provided real-time ultrasound guidance. A needle-guide device attached to the ultrasound probe was used in 931 (83.4%) of the biopsies. Typically, two or three cores were obtained per biopsy. After biopsy, patients were monitored for signs of complication for at least 23 h, with frequent vital sign assessment, repeat hemoglobin measurement the next morning in most cases, and follow-up imaging when concern for a bleeding complication existed. Patients remained on bed rest for at least 6 h. Follow-up care was determined by the attending nephrologist, on the basis of the patient's clinical status and final renal pathologic diagnosis.

Statistical Analysis

Baseline characteristics between biopsies with and without a complication, as well as between biopsies from HIV-infected and non–HIV-infected patients, were compared by *t*, χ^2, and Wilcoxon rank-sum tests, as appropriate. Univariate logistic regression was used to determine the risk for a biopsy-related complication associated with a predefined predictor of interest. To account for missing hepatitis C status in HIV-negative individuals, hepatitis C status was imputed by univariate imputation sampling using characteristics of the HIV-negative participants with known hepatitis C status (10). Imputed hepatitis C data were used in regression analyses. Sensitivity analyses for the association of hepatitis C were also performed by analyzing the association with postbiopsy complication after assigning all missing data to either infected or noninfected. Because of the small sample size, multivariable adjustment was limited to five covariates (HIV infection, hepatitis C, prebiopsy hematocrit <30%, prebiopsy platelet count, and eGFR <30 ml/min per 1.73 m^2) identified as potential confounders in the univariate analysis. The presence of effect modification was assessed in variables of interest identified from the primary analysis. Robust variances were calculated to account for clustering that may occur on the basis of the biopsy attending of record. This study had 90% power for a detectable odds ratio (OR) of 2.0 for any complication in HIV-infected *versus* non–HIV-infected patients. In the primary analysis, the *P* value of the association was Bonferroni-corrected for seven comparisons, with an unadjusted $P \leq 0.003$ considered statistically significant to permit a Bonferroni-corrected $P \leq 0.05$ after adjustment for multiple comparisons. Unadjusted *P* values are reported except where indicated. Statistical analyses were performed using the Stata 9.2 statistical package (Stata Corp., College Station, TX).

Results

Baseline Characteristics

A total of 1116 (HIV-infected = 243 [21.8%]; non–HIV-infected = 873 [78.2%]) ultrasound-guided percutaneous kidney biopsies were performed on 1024 individuals. Baseline characteristics of the cohort are presented in Table 1. Of the 1116 biopsies, 77 (6.9%) individuals had two biopsies, 13 (1.2%) had three biopsies, and two (0.2%) had four biopsies. Of these 92 repeat biopsies, 12 (13.0%) were from HIV-infected individuals. Because none of the individuals who underwent repeat biopsy experienced more than one complication, the data are based on a denominator of 1116. HIV-infected patients were more likely to be black (89.3 *versus* 48.6%; $P < 0.001$), male (63.8 *versus* 38.1%; $P < 0.001$), and hepatitis C positive (54.3 *versus* 5.6%; $P < 0.001$) and to have a lower median eGFR (29.2 *versus* 45.7 ml/min per 1.73 m^2; $P < 0.001$) at the time of biopsy. HIV-infected patients were also more likely to have baseline hypertension (56.4 *versus* 19.9%; $P < 0.001$) and to have a slightly lower prebiopsy hematocrit (32.4 *versus* 33.6%; $P = 0.006$) and median platelet count (207,500 *versus* 259,900 cells/mm^3; $P < 0.001$). Hepatitis C status was known for 100% of the HIV-positive individuals and 86.7% of HIV-negative individuals. After imputation of the missing hepatitis C values, a status was assigned to 98.6% of HIV-negative individuals, with 5.0% ($n = 44$) being hepatitis C positive as compared with 4.8% ($n = 42$) before imputation. Nonimputed data are presented in Table 1.

Postbiopsy Complications

The proportion of patients who experienced any complication (8.6 *versus* 7.2%; $P = 0.5$), a minor (5.4 *versus* 4.6%; $P = 0.6$), or a major complication (3.3 *versus* 2.6%; $P = 0.7$) did not differ significantly between the HIV-infected and non–HIV-infected patients, respectively. Of those who had multiple biopsies,

Table 1. Demographic data of 1024 individuals who underwent 1116 percutaneous ultrasound-guided native kidney biopsies

Parameter	Complication (n = 84; 7.5%)	No Complication (n = 1032; 92.5%)	P	HIV Positive (n = 243; 21.8%)	HIV Negative (n = 873; 78.2%)	P
Age (yr; mean ± SD)	46.0 ± 14.3	45.0 ± 15.0	0.6	45.0 ± 8.2	45.1 ± 16.4	0.8
Women (n [%])	49 (58.3)	579 (56.1)	0.7	88 (36.2)	540 (61.9)	<0.001
Black (n [%])	45 (53.6)	593 (57.9)	0.4	217 (89.3)	421 (48.6)	<0.001
Hypertension (n [%])	26 (31.0)	285 (27.6)	0.5	137 (56.4)	174 (19.9)	<0.001
Diabetes (n [%])	13 (15.5)	111 (10.8)	0.2	26 (10.7)	98 (11.2)	0.8
Hepatitis C (n [%])	22 (28.6)	152 (16.5)	0.007	132 (54.3)	42 (5.6)	<0.001
HIV positive (n [%])	21 (25.0)	222 (21.5)	0.5	NA	NA	NA
Prebiopsy hematocrit (%; mean ± SD)	32.5 ± 5.7	33.5 ± 5.9	0.2	32.4 ± 6.0	33.6 ± 5.9	0.006
Pre-biopsy hematocrit <30% (n [%])	29 (35.4)	299 (29.8)	0.3	87 (37.5)	241 (28.2)	0.006
Prebiopsy platelet count (1000 cells/mm^3; mean ± SD	213.1 ± 75.6	251.6 ± 101.7	<0.001	207.5 ± 92.7	259.9 ± 99.5	<0.001
Prebiopsy platelet count <100,000 cells/mm^3 (n [%])	8 (9.5)	41 (4.1)	0.05	17 (7.2)	32 (3.7)	0.02
Prebiopsy serum creatinine (mg/dl; median [IQR])	1.8 (1.0 to 3.8)	1.9 (1.0 to 3.8)	0.7	2.7 (1.7 to 4.9)	1.7 (0.9 to 3.4)	<0.001
Prebiopsy BUN (mg/dl; median [IQR])	28.5 (17.0 to 49.0)	29.0 (18.0 to 47.0)	0.9	34.0 (21.0 to 45.0)	28.0 (17.0 to 47.0)	0.01
Prebiopsy eGFR (ml/min per 1.73 m^2; median [IQR])[a]	43.6 (16.7 to 60.0)	41.1 (18.0 to 60.0)	0.7	29.2 (14.4 to 49.8)	45.7 (18.9 to 60.0)	<0.001
Prebiopsy eGFR <30 ml/min per 1.73 m^2 (n [%])	29 (34.9)	426 (42.0)	0.2	126 (51.9)	329 (38.5)	<0.001

Columns may not sum to total due to missing data. IQR, interquartile range.
[a]eGFR >60 ml/min per 1.73 m^2 expressed as 60.

none experienced a complication twice. The overall complication rate in the entire population did not differ by the use of a guide (8.1% with a guide *versus* 4.9% without a guide; $P = 0.2$). Table 2 details the individual major complications that occurred in the HIV-infected group. Only one patient required angiography, and three patients who required blood transfusion also experienced hemodynamic instability. Of the eight patients with major complications, three were discharged within 24 h and four in <1 wk. Seven (88%) of these eight patients were hepatitis C positive. Eleven (84.6%) of 13 HIV-infected patients with minor complications were hepatitis C positive. Among non–HIV-infected patients, two (8.7%) of 23 patients with major complications and two (5%) of 40 with minor complications were hepatitis C infected. A comparison of the types of major complication stratified by HIV status are reported in Table 3. Of note, there were no deaths as a result of kidney biopsy in this cohort.

The associations of *a priori* selected predictors of complication are reported in Table 4. HIV positivity was associated with a nonstatistically significant OR of 1.28 (95% confidence interval [CI] 0.95 to 1.73; $P = 0.1$) for any complication. In the entire cohort, biopsies from individuals who were positive for hepatitis C infection had a 2.08 (95% CI 1.47 to 2.93) increased odds of any complication relative to individuals who were not infected with hepatitis C. This association remained statistically significant ($P < 0.001$) after Bonferroni correction. A consistent, statistically significant relationship was also seen for the associations of hepatitis C infection with the subgroups of minor and major complications. Each decrease of 10,000 cells/mm^3 in the prebiopsy platelet count was also associated with a statistically significant OR of 1.05 (95% CI 1.02 to 1.08) for any complication, and this remained statistically significant after Bonferroni correction ($P = 0.01$). No other robust associations were seen between the predefined covariates and any compli-

Table 2. Individual biopsy-related major complications in 243 biopsies from 231 HIV-infected patients

Patient	Age (yr)	Race	Gender	Complication	Outcome
1[a]	52	Black	F	9.0 × 7.5 × 16.0-cm retroperitoneal hematoma that required transfusion of 2 U of PRBC	Full recovery from biopsy complication but had prolonged hospitalization for medical reasons unrelated to biopsy
2[a]	42	Black	F	5 × 2-cm perinephric hematoma and gross hematuria that required transfusion of 2 U of PRBC	Full recovery overnight; discharged home next day
3[a]	59	Black	M	Hematocrit drop that required transfusion of 2 U of PRBC; small hematoma seen on ultrasound	Full recovery overnight; discharged home next day
4[a]	42	Black	M	Developed hypotension with hematocrit drop and responded to transfusion of 2 U of PRBC and 2 U of fresh-frozen plasma	Full recovery from biopsy complication; discharged home after clearance by primary medical team for other conditions
5[a]	41	Black	F	9.4 × 6.3 × 6.4-cm retroperitoneal hematoma associated with hypotension; stabilized after transfusion of 4 U of PRBC	Hospitalized for 3 d before full recovery and discharge home
6[a]	43	Black	M	Retroperitoneal hemorrhage that required transfusion of 1 U of PRBC and angiography with embolization of a branch vessel	Hospitalized for 3 d before full recovery and discharge home
7	39	White	M	Developed hypotension 10 h after biopsy in association with retroperitoneal hemorrhage described as "large"; transfusion of 6 U of PRBC was required	Hospitalized for 4 d before full recovery and discharge home
8[a]	52	Black	M	Developed 5.6 × 4.0-cm retroperitoneal hematoma that required transfusion of 2 U of PRBC	Full recovery overnight; discharged home next day

PRBC, packed red blood cells.
[a]Hepatitis C positive.

Table 3. Major bleeding complications after 1116 percutaneous ultrasound-guided kidney biopsy, by HIV-infection status

Bleeding Complication[a]	HIV Positive (n = 243)	HIV Negative (n = 873)
Transfusion	4	15
Angiography	0	4
Transfusion and angiography	1	1
Hemodynamic instability alone	0	1
Transfusion and hemodynamic instability	3	0
Hemodynamic instability that required angiography	0	2
Total	8 (3.3%)	23 (2.6%)

[a]No biopsy-related deaths.

Table 4. Unadjusted and multivariable adjusted ORs of biopsy-related complications in 1116 ultrasound-guided native kidney biopsies

Variable	Complication			
	Any (OR [95% CI])	P (P')[a]	Minor (OR [95% CI])	Major (OR [95% CI])
Unadjusted				
HIV positive	1.28 (0.95 to 1.73)	0.1 (0.6)	1.24 (0.93 to 1.64)	1.32 (0.64 to 2.73)
hepatitis C positive	2.08 (1.47 to 2.93)	<0.001 (<0.001)	1.81 (1.31 to 2.50)	2.37 (1.18 to 4.78)
age (yr)	1.00 (0.99 to 1.01)	0.6 (1.0)	1.00 (0.99 to 1.01)	1.01 (0.99 to 1.03)
MAP (mmHg)	0.99 (0.98 to 1.00)	0.1 (0.6)	0.99 (0.97 to 1.00)	1.00 (0.98 to 1.02)
hematocrit <30%	1.39 (0.93 to 2.08)	0.1 (0.5)	0.59 (0.20 to 1.70)	4.12 (2.14 to 7.94)
prebiopsy platelet count[b]	1.05 (1.02 to 1.08)	0.002 (0.01)	1.04 (1.01 to 1.06)	1.06 (0.99 to 1.14)
eGFR <30 ml/min per 1.73 m^2	0.79 (0.62 to 1.02)	0.08 (0.4)	0.42 (0.33 to 0.55)	2.01 (1.39 to 2.91)
Adjusted[c]				
HIV positive	0.72 (0.48 to 1.09)	0.1	0.83 (0.60 to 1.14)	0.59 (0.22 to 1.58)
hepatitis C positive	2.06 (1.43 to 2.97)	<0.001	1.64 (1.18 to 2.28)	2.57 (1.23 to 5.36)
prebiopsy hematocrit <30%	1.40 (0.90 to 2.18)	0.1	0.64 (0.20 to 2.07)	3.74 (1.80 to 7.78)
prebiopsy platelet count	1.04 (1.01 to 1.07)	0.003	1.04 (1.02 to 1.07)	1.04 (0.99 to 1.10)
eGFR <30 ml/min/1.73m^2	0.67 (0.53 to 0.86)	0.001	0.44 (0.30 to 0.64)	1.29 (0.80 to 2.07)

MAP, mean arterial pressure.
[a]P' represents Bonferroni-corrected P value adjusted for seven comparisons.
[b]OR of complication for each 10,000-cells/mm^3 decrease in platelets.
[c]Multivariable adjusted for HIV infection, hepatitis C, pr-biopsy hematocrit <30%, prebiopsy platelet count, and eGFR <30 ml/min per 1.73 m^2.

cation. On subgroup analysis, a prebiopsy hematocrit <30% was statistically significantly associated with a 4.12 (95% CI 2.14 to 7.94) increased odds of major complication but had a trend toward a decreased odds of minor complication (OR 0.59; 95% CI 0.20 to 1.70). Likewise, an eGFR <30 ml/min per 1.73 m^2 was statistically significantly associated with a 2.01 (95% CI 1.39 to 2.91) increased odds of a major complication and a 0.42 (95% CI 0.33 to 0.55) decreased odds of a minor complication. The association with any complication was not statistically significant for either prebiopsy hematocrit <30% or eGFR <30 ml/min per 1.73 m^2. Multivariable adjustment of the entire cohort did not meaningfully alter the univariate relationships.

Given the possibility for biologic interplay between hepatitis C and HIV co-infection, the association of hepatitis C with postbiopsy complication was examined after stratification by HIV status (Figure 1). Hepatitis C/HIV co-infection was associated with a 5.71 (95% CI 1.89 to 17.2; P = 0.002) increased odds of any complication as compared with 1.27 (95% CI 0.73 to 2.19; P = 0.4) in hepatitis C–positive/HIV-negative individuals (P = 0.006 for interaction). Similarly, prebiopsy hematocrit <30% in HIV-infected individuals was associated with a 2.69 (95% CI 1.57 to 4.62; P < 0.001) increased odds of any complication as compared with a 1.08 (95% CI 0.68 to 1.71; P = 0.7) increased odds in HIV-negative individuals (P = 0.02 for interaction). When the outcome of major complication was examined, prebiopsy hematocrit <30% in HIV-infected individuals was associated with a 2.97 (95% CI 1.56 to 5.65; P = 0.001) increased odds of complication as compared with a 15.3 (95%

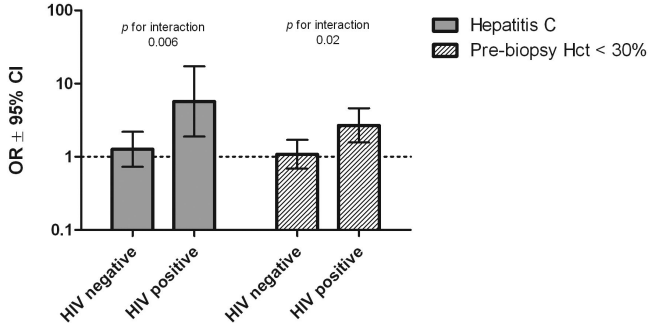

Figure 1. Risk for any complication associated with hepatitis C or prebiopsy hematocrit <30%, stratified by HIV status. Hct, hematocrit.

CI 2.06 to 114.2; $P = 0.008$) increased odds in HIV-negative individuals ($P = 0.2$ for interaction). The association of prebiopsy platelet count was not significantly modified by the presence (OR 1.03) or absence (OR 1.05) of HIV infection. Multivariable adjustment after stratification by HIV status was not performed because of the resulting small sample sizes.

To confirm the validity of the association between imputed hepatitis C data and the risk for complication, we performed sensitivity analyses using the original data, as well as after assigning all missing values to either a hepatitis C–positive or –negative status. Using the original, nonimputed data, the OR of any complication for a hepatitis C–positive individual was 2.07 (95% CI 1.42 to 3.02; $P < 0.001$) relative to a hepatitis C–negative individual. After assigning all missing data as hepatitis C positive, the OR of any complication was 1.56 (95% CI 1.19 to 2.06; $P = 0.001$), and after assigning all missing data as hepatitis C negative, the OR for any complication was 2.11 (95% CI 1.50 to 2.96; $P < 0.001$). Imputation for missing BUN, creatinine, hematocrit, and platelet count data did not change the results of the analysis (data not shown).

Comparing hepatitis C–co-infected HIV-positive patients with HIV-positive patients without hepatitis C revealed no significant difference in hematocrit, platelet count, BUN, creatinine, eGFR, CD4 count, HIV viral load, gender, race, or presence of diabetes or hypertension. Co-infected patients were older (mean age 46.0 *versus* 43.7 yr; $P = 0.04$). Not surprising, the key difference in these populations was the high proportion of illicit drug use in the co-infected group (86.8 *versus* 13.2%; $P < 0.001$).

Discussion

This study comprises the largest series of HIV-infected patients who underwent percutaneous ultrasound-guided kidney biopsy to date. No previous study has evaluated biopsy complication rates in this population. These data demonstrate that ultrasound-guided percutaneous kidney biopsy is well tolerated in this population, with complication rates in hepatitis C–negative/HIV-positive individuals comparable to those in the non–HIV-infected population. The major complication rates between 2.6 and 3.3% are consistent with those seen in previous studies. In a cohort study of 750 adult patients who underwent percutaneous kidney biopsy from 1983 to 2002, Whittier and Korbet (5) recorded a major complication rate of 6.4%. In 2004, Manno *et al.* (4) performed a prospective cohort study of 471 adult patients who underwent percutaneous ultrasound-guided native kidney biopsy and observed a major complication rate of 1.2%. More recently, Soares *et al.* (11) assessed bleeding complications in 101 patients with systemic amyloidosis as compared with 188 control patients who underwent percutaneous kidney biopsy. Major complication rates of 4 and 2.1%, respectively were observed. Definitions of major complications were similar across these previous studies, whereas definitions for minor complications varied widely. It is difficult to compare directly minor complication rates in the face of this variability in definition.

HIV infection alone was not associated with the development of postbiopsy complications. In the assessment of predictors, we found hepatitis C to be a positive predictor of increased bleeding complications, with hepatitis C/HIV co-infection being the strongest predictor. To our knowledge, this has not been previously described in studies of risk factors for complication in percutaneous kidney biopsy. Sterling *et al.* (12) evaluated percutaneous liver biopsy safety in 29 male adults with hemophilia with hepatitis C infection, 44% of whom had HIV co-infection. There were no complications in any patient, regardless of HIV status, although the sample size was small.

HIV co-infection is not known to increase independently the risk for bleeding in patients with hepatitis C, beyond accelerating the progression of underlying liver disease with resultant coagulopathy (13–15). Pineda *et al.* (16) did not find an increased risk for gastrointestinal bleeding as either the first cirrhotic decompensation or cause of death in patients who were co-infected with HIV and hepatitis C. Overt coagulopathy alone cannot explain the increased rate of complications that we observed in patients with hepatitis C/HIV co-infection, because biopsies were not performed on patients with abnormal international normalized ratio and partial thromboplastin times. The data, however, do suggest platelet count, and traditional measures of coagulation may not fully define the risk for bleeding in this patient group.

A possible explanation for our observations is that hepatitis C/HIV co-infection may result in subclinical liver disease, with impaired hemostasis that manifests only after the biopsy of an organ with high vascularity such as the kidney. Unfortunately, we do not have liver biopsy data to support this contention. Moreover, the mechanism of impaired hemostasis may not necessarily involve the liver. It is conceivable that hepatitis C/HIV co-infection may alter endothelial–platelet interactions, thereby limiting an effective response to vascular injury. Other factors that predispose to a greater biopsy complication rate may include greater illicit drug and alcohol exposure in the hepatitis C/HIV co-infected population (17). The limited number of complications and lack of biopsy data on the underlying severity of liver disease do not allow for adequate study of this issue in the current cohort. Comparison of HIV-infected with and without hepatitis C revealed only a difference in age and illicit drug use. These factors are unlikely to explain an in-

creased bleeding risk. Further studies are required to investigate the mechanism of increased bleeding risk.

Although the risk for complication in the entire cohort increased with every 10,000-cells/mm^3 decrease in the prebiopsy platelet count, inclusion of this variable in a multivariable adjustment model did not alter the association of hepatitis C. As such, the effect of hepatitis C positivity on the risk for bleeding complications likely cannot be explained by platelet count alone.

Our study also found that a prebiopsy hematocrit <30% was associated with an increased risk for major complication in the cohort as a whole. On further analysis, the risk for any complication associated with hematocrit <30% was limited to the HIV-positive individuals, although both HIV-positive and -negative patients had an increased risk for major complication. Although a low hematocrit may simply reflect a lower clinical threshold for transfusing these patients, the observation is consistent with multiple previous studies that showed a low preprocedure hematocrit, particularly <30%, worsens bleeding in surgical patients with uremia and that blood transfusions can help correct that bleeding risk (18–21). Although most patients in this study did not have overt uremia, chronic kidney disease–related anemia may alter their hemostatic phenotype (22). In fact, the median eGFR of the HIV-infected patients was lower than that of the HIV-negative patients, and low hematocrit was associated with greater risk in the HIV-infected patients as compared with the uninfected.

Hematocrit <30% and eGFR <30 ml/min per 1.73 m^2 were associated with protection from minor complication but an increased risk for major complication. An explanation for these findings is that patients with a lower hematocrit or more advanced renal dysfunction tend to have greater comorbidities, and if such a patient has a complication, then it may have a tendency to be more severe. Conversely, patients with a hematocrit ≥30% or eGFR ≥30 ml/min per 1.73 m^2 may tend to have less severe complications, again reflecting their better overall health status.

Importantly, the diversity of pathologic diagnoses confirms that kidney biopsy remains an essential tool for accurately diagnosing the cause of renal disease in this population (Table 5). Only 29% of the group had HIV-associated nephropathy manifested as collapsing FSGS, with an additional 8% having HIV-related immune complex glomerulonephritis. It is interesting that interstitial nephritis was common at 11%. This high prevalence reflects the difficulty in making this diagnosis on clinical features alone, because consistent, "classical" findings of fever, rash, and eosinophilia are often absent (23).

This study has several limitations. First, the study population may not be generalizable to all HIV-infected patients. HIV-infected patients in this study were drawn from an urban inner-city population where the major route for HIV infection is injection drug use. Second, specific data on the exact number of needle passes and differences in operator technique were not readily available. Technical differences, however, were accounted for in part by the calculation of robust variances that were based on the attending of record. Third, rates of minor complication may be underreported because kidneys are not routinely reimaged after biopsy unless clinical circumstances warrant. Fourth, the relatively small number of complications in the subset of HIV-infected patients limits the power of this study to identify associations with specific predictors. Fifth, hepatitis C status was imputed for 11.9% of the HIV-negative patients, although sensitivity analyses demonstrated the results to be qualitatively similar. Finally, a definitive mechanism for the increased complication rate in hepatitis C/HIV co-infected patients cannot be answered with certainty from this study.

Table 5. Final histopathologic diagnoses of 243 biopsies in HIV-infected individuals at the Johns Hopkins Hospital from February 1995 to December 2007

Primary Diagnosis	*n* (%)
HIV-associated nephropathy (collapsing FSGS)	72 (29)[a]
Noncollapsing FSGS	46 (19)
Acute interstitial nephritis	26 (11)
HIV-associated immune complex GN	19 (8)[b]
Hypertensive nephropathy	14 (6)
Diabetic nephropathy	14 (6)
Postinfectious GN	12 (5)
Acute tubular necrosis	10 (4)
IgA nephropathy	6 (2)
Membranoproliferative GN (hepatitis C related)	5 (2)
Membranous GN	4 (2)
Amyloidosis (AA)	4 (2)
Other[c]	9 (4)
No diagnosis	2 (1)

GN, glomerulonephritis.
[a]Five with superimposed immune complex disease.
[b]Nine with lupus-like GN.
[c]One each of necrotizing GN, lymphoma, fibrillary GN, minimal change, thrombotic microangiopathy, nonspecific mesangial proliferation, glomerulosclerosis, reflux/chronic pyelonephritis, and xanthogranulomatous pyelonephritis.

Conclusions

This study demonstrates that ultrasound-guided percutaneous kidney biopsy remains a relatively safe, well-tolerated procedure in HIV-infected patients. Patients with hepatitis C/HIV co-infection are at greatest risk for biopsy-related complications.

Disclosures

None.

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