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Predictors of hemorrhagic complications after ultrasound-guided nonfocal renal biopsy

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Abstract

Introduction: Ultrasound-guided non-focal renal biopsy (USNFRB) is a well-accepted procedure performed in the renal cortex to investigate medical renal disease or renal transplant rejection.
Objectives: The purpose of this study was to identify the hemorrhagic complication rate for a large cohort of patients after radiologist-performed USNFRB and to identify risk factors.
Patients and Methods: For this Institutional Review Board-approved retrospective review, all patients who underwent USNFRB from January 2001 to September 2012 were identified using a departmental database, and reviewed the electronic chart for demographics, laboratory workup, medications, procedural details, and complications. The impact of these variables on the likelihood of having a bleeding complication that either did (major) or did not (minor) require further intervention was assessed, using Fisher exact and Student's *t* tests, and multiple logistic regression.
Results: Of 570 USNFRBs performed by radiologists, 26 (4.6%) resulted in hemorrhagic complications, 15 of which were major and 11 minor. Neither age, gender, race, nor size of biopsy needle differed among patients with and without bleeding complications ($P>0.05$). When assessing the impact of coagulation and renal function laboratory measures, low estimated glomerular filtration rate (eGFR) was the strongest predictor of bleeding complication ($P=0.03$).
Conclusion: USNFRB is a relatively safe procedure, with less than 5% resulting in bleeding complications. Low eGFR is the strongest predictor of hemorrhagic complication, and is likely the most helpful variable in triaging patients during pre-procedure workup.

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Introduction

Ultrasound-guided non-focal renal biopsy (USNFRB) is a well-accepted procedure performed in the renal cortex to investigate medical renal disease or renal transplant rejection (1). Described risk factors for major complications include abnormal coagulation factors, steroid use, age, creatinine, hypertension, bleeding diathesis, anemia, gender, and renal dysfunction (2-6). The number of high-risk patients undergoing image-guided renal biopsies will likely increase in the future due to an aging population, increased use of anticoagulants, and combined liver and kidney disease caused by hepatitis C (7). Despite the importance and widespread usage of USNFRB, there remains a lack of comprehensive data defining the most reliable risk factors for procedure complications.

Objectives

The study objective was to identify the hemorrhagic complication rate for a large cohort of patients after USNFRB, and to identify associated risk factors.

Core tip

Ultrasound-guided nonfocal renal biopsy is associated with a risk of bleeding <5%, half of which are major hemorrhages. Patients at greatest risk are those with pre-existing severe renal impairment, suggesting that careful consideration of the relative benefits and risks of biopsy are warranted for this patient population.

Patients and Methods

Patients

This Institutional Review Board-approved and Health Insurance Portability and Accountability Act-compliant study was limited to the retrospective use of electronic medical records. For this type of study formal consent is not required. A radiology database search identified all consecutive patients

who underwent radiologist-performed USNFRB between January 2001 and September 2012 at a single institution, yielding 570 USNFRBs in 542 patients. Each procedure was taken as an independent event, assuming that clinical and laboratory variables at the time of each procedure determined the risk of bleeding complications, and prior biopsies did not impact the risk of a future biopsy in the same patient. Baseline characteristics are shown in Table 1.

Procedure and data collection

Anti-coagulant and anti-platelet medications were held 2-5 days per division protocol. USNFRB was performed as previously described (1), with prone position for native and supine for transplant kidneys. Per an institutional protocol initiated in May 2009, patients with eGFR<30 received desmopressin (DDAVP; Ferring Pharmaceuticals, Inc.) based on prior reports showing DDAVP may reduce bleeding time and hemorrhagic complications after biopsy (8,9). Using 14–18-gauge core biopsy devices (chosen by preference of the operator), 1–3 samples were collected under ultrasound guidance and checked intraprocedurally by an immunopathology technologist. Hemorrhagic complications included post-procedural perinephric, intraabdominal, and collecting system hemorrhage, seen on cross-sectional imaging prompted by patient pain or change in vital signs. Minor complications were those not requiring invasive intervention or blood transfusion (Foley catheterization and IV fluid administration were not considered invasive interventions) per SIR classification (10). Major complications (10) were those requiring additional intervention including blood transfusion, endovascular embolization or surgical exploration.

Table 1. Baseline characteristics

Number of procedures (n = 570)	Values[a]
Mean age	48.4 ± 19.1
Male gender (%)	350 (61.4)
Type of biopsy	
Transplant kidney (%)	141 (24.7)
Native kidney (%)	429 (75.3)
Side of biopsy	
Right kidney (%)	192 (44.8)
Left kidney (%)	237 (55.2)
Size of biopsy needle	
18 Gauge (%)	167 (29.3)
17 Gauge (%)	16 (2.8)
16 Gauge (%)	220 (38.6)
15 Gauge (%)	140 (24.5)
14 Gauge (%)	3 (0.5)
Unknown (%)	24 (4.3)
Mean platelet count (×10^3/μl)	249 ± 111
Mean INR	1.1 ± 0.2
Mean activated prothrombin time (s)	27.4 ± 7.4
Mean creatinine (mg/dl)	2.7 ± 2.1

Abbreviation: INR, international normalized ratio.
[a]Values are expressed in mean with standard deviation and percentages where applicable.

Ethical issues

1) The research followed the tenets of the Declaration of Helsinki; 2) informed consent was obtained, and they were free to leave the study at any time and 3) the research was approved by the ethical committee of department of radiology, Massachusetts General Hospital, Boston, Massachusetts.

Data analysis

Estimated glomerular filtration rate (eGFR) was calculated for all patients 20 years of age and older using the Modification of Diet in Renal Disease formula (11): eGFR = 175 × Cr $^{-1.154}$ × Age $^{-0.203}$ × 1.212 (if black) × 0.742 (if female). eGFR was not calculated for patients ≤19 years old, as height, needed for estimation in pediatric patients, was not documented reliably in the medical chart (12,13). Patients developing any hemorrhagic complication (major and minor) and those who did not were compared using Fisher exact, and Mann-Whitney U, and *t* tests. Binary logistic regression was used to analyze if pre-biopsy platelet count, international normalized ratio (INR), activated partial thromboplastin time (aPTT), serum creatinine, and eGFR were associated with increased complications. Fisher exact tests were used to compare complication rates between patients with an eGFR >30 cc/min versus eGFR <30 cc/min, a threshold chosen prospectively given that this determines patients at greater risk of bleeding due to uremia, and to compare complication rates between patients with eGFR<30 who did or did not receive DDAVP. Statistical analysis was performed with Prism 4 (GraphPad software, La Jolla, CA); logistic regressions were performed using http://statpages.org/logistic.html.

Results

Twenty-six patients (4.6%) had hemorrhagic complications after renal biopsy (Figure 1). No single patient experienced multiple complications after repeat biopsy. Fifteen complications were major, and 11 were minor. Details of the complications and subsequent interventions are summarized in Table 2. Among the 26 patients with complications, 4 were renal transplant patients being evaluated for renal failure and rejection. Indications for the 22 native kidney biopsies included acute renal failure/abnormal renal function tests (15), proteinuria (5), malignant hypertension (1), and vasculitis (1).

Univariate analysis revealed no effect of age, gender, biopsy side, or needle size on complication rate, but significantly higher creatinine and INR, longer aPTT, and lower platelet counts (Table 3). More patients who were on aspirin, clopidogrel, heparin, or Coumadin prior to the procedure had a hemorrhagic complication (11 of 162 patients, 7%) compared with those not on these medications (15 of 408 patients, 4%), despite the medications being withheld, though this was not significant by Fisher exact test ($P = 0.086$). Similar percentages of patients who received DDAVP before the biopsy had bleeding complications (4 of 66 patients, 6%) compared to those that did not (22 of 504 patients, 5%) ($P = 0.5$).

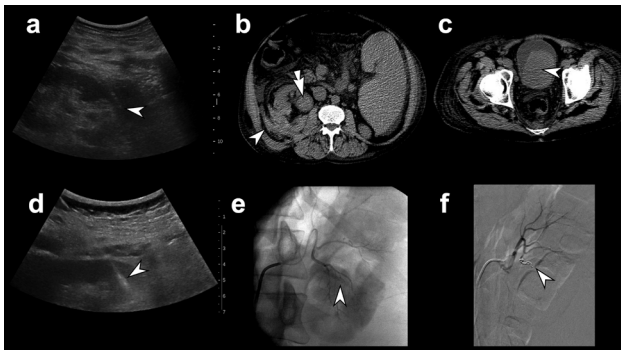

Figure 1. Examples of post-renal biopsy hemorrhagic complications. a–c. A 47-year-old man with estimated glomerular filtration rate (eGFR) 22.5 underwent USNFRB (arrowhead) for renal failure (a), and (b) subsequently developed a perinephric hematoma (arrowhead), with blood in the renal collecting system (arrow) and (c) bladder (arrowhead) on CT. The patient subsequently became bacteremic and developed multi-organ failure, did not respond to transfusions, and ultimately died. d–f. A 52-year-old woman with eGFR 11.7 underwent USNFRB (arrowhead) for proteinuria and renal failure (d), developed a perinephric and peritoneal hemorrhage, and subsequently underwent renal arteriography (e) demonstrating an arteriovenous fistula in the lower pole (arrowhead), successfully treated (f) with coil embolization (arrowhead).

Multivariate analysis using binary logistic regression was performed to assess the contribution of creatinine, eGFR, INR, PTT, and platelets on the likelihood of bleeding complication, with 386 patients with complete data sets available for analysis (18 patients with bleeding and 368 patients without bleeding). Two regressions were performed to determine which variables best predicted bleeding complication. When performed with creatinine, platelets, INR and aPTT but not eGFR, the regression was statistically significant ($P=0.04$), but no single variable, including creatinine, was an independent predictor of bleeding complication ($P>0.05$). When performed with eGFR, platelets, INR and aPTT but not creatinine, the regression was statistically significant ($P=0.005$), and only eGFR was a statistically significant independent predictor of bleeding complication ($P=0.03$), whereas platelets, INR and aPTT were not ($P>0.10$). Therefore, eGFR is an independent predictor of bleeding complication, independent of INR, aPTT and platelets; the same cannot be shown for creatinine.

The hemorrhagic complication rate in patients with eGFR<30 (7.5%) differed significantly from patients with eGFR > 30 cc/min (1.7%) by Fisher exact test ($P=0.004$). With an eGFR threshold of 30, sensitivity and specificity were 82.6% (95% CI: 61.2–95.1%) and 48.5% (95% CI: 43.9–53.2%) respectively. Relative risk of hemorrhagic complication was 4.3 (95% CI: 1.5–12.4) while the odds ratio was 4.5 (95% CI 1.5–13.5). Of the 255 patients with eGFR<30, 54 were given pre-procedure DDAVP and 201 were not. Bleeding complication rate was not significantly different by Fisher exact test ($P=1$), with 7.4% of patients treated with DDAVP and 7.5% of patients not treated with DDAVP with subsequent hemorrhagic complications.

Discussion

USNFRB is an important minimally invasive image-guided technique used to evaluate renal disease. The present study reports an overall hemorrhagic complication rate of 4.6%, with a 2.6% major complication rate, within an acceptable standard of <5% (14,15). Comparing patients who did and did not have bleeding complications, there were significant differences in creatinine, eGFR, platelet levels, INR, and aPTT on univariate analysis, similar to reported data (6,14). However, multiple logistic regression suggests that eGFR was the only independent predictor of bleeding complication, compatible with the fact that eGFR offers a better characterization of renal impairment than serum creatinine (16). Whereas others have pointed to female gender and younger or older age as risk factors (6,14,17), here there was no significant impact of these factors. Similar to prior studies (6,18), there was no effect of needle size or side of biopsy on the rate of complication. There was no impact of DDAVP administration on bleeding complication rate, either in the entire study population or in patients with eGFR<30 cc/min, a finding at odds with prior studies demonstrating reduction in post-biopsy hemorrhage (9) and the suggestion that DDAVP decreases the bleeding time (8). Our findings suggest more work on the impact of DDAVP in this population undergoing renal biopsy is warranted.

Table 2. Classification of hemorrhagic complications and treatment

	No. of patients (n = 570)
Overall complication rate (%)	26/570 (4.6)
Major bleeding complication rate (%)	15/570 (2.6)
Types of intervention	
Blood transfusion only (%)	9 (1.5)
Endovascular coil embolization (%)	4 (0.7)
Surgical exploration (%)	2 (0.4)
Minor bleeding complication rate (%)	11/570 (1.9)
Intravenous fluids (%)	2 (0.4)
Observation only (%)	7 (1.2)
Foley catheterization (%)	1 (0.1)

Table 3. Univariate analysis of bleeding complication risk factors

	With complication	Without complication	*P* value
n	26	544	
Age (years)	49	46	0.4
% Male	62%	61%	1
% Right	54%	53%	1
% Large bore[a]	65%	67%	1
Creatinine (mg/dl)	3.57	2.68	0.04
INR	1.2	1.1	0.04
aPTT (s)	28.4	27.4	0.04
Platelets ($\times 10^3$/μl)	197.0	252.0	0.005
eGFR[b] (cc/min)	24.8	37.7	0.04

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio; eGFR, estimated glomerular filtration rate.

[a] Large bore: 14-, 15- and 16-gauge needles.

[b] For patients 20 years and older.

Conclusion

In summary, USNFRB carries a risk of bleeding <5%, half of which are major complications. Patients with lower eGFRs

are at highest risk of bleeding; eGFR is a better predictor of hemorrhage than creatinine. As DDAVP administration did not decrease bleeding risk, careful evaluation of the relative risks and benefits of biopsy is warranted when considering procedure requests for patients with eGFR<30 cc/min.

Limitations of the study

The primary study limitation is its retrospective design, which introduces potential bias. For example, though administration of DDAVP did not alter the risk of hemorrhagic complication in our cohort, this finding would require testing in a prospective setting. Most significantly, the eGFR in pediatric patients could not be assessed, who were therefore excluded from our regression analyses. However, only 3 patients with a bleeding complication were under 20 years old. Future work could focus on this patient population and ascertain whether eGFR or creatinine is a better predictor of bleeding risk, and would require greater numbers of pediatric patients.

Authors' contribution

AD; data collection, statistical analysis, manuscript writing. FL and CST; data collection, statistical analysis, manuscript writing. PH; research initiation and approval, study design, statistical analysis, review of scientific content, manuscript preparation. AT and PM; review of scientific content, manuscript preparation. EH; statistical analysis, review of scientific content, manuscript preparation. SG; research initiation and approval, study design, statistical analysis, review of scientific content, manuscript preparation and guarantor of study.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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