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# A Color Flow Tract in Ultrasound-Guided Random Renal Core Biopsy Predicts Complications

Marie-Helene Gagnon, MD, Michael F. Lin, MD, Samantha Lancia, MS, Amber Salter, PhD, Motoyo Yano, MD, PhD <sup>(1)</sup>

*Objectives*—To determine patient and procedural risk factors for major complications in ultrasound (US)-guided random renal core biopsy.

**Methods**—Random renal biopsies performed by radiologists in the US department at a single institution between 2014 and 2018 were retrospectively reviewed. The patient's age, sex, race, and estimated glomerular filtration rate (eGFR) were recorded. The biopsy approach, needle gauge, length of cores, number of throws, and presence of a color flow tract were recorded. Outcome data included minor and major complications. Associations between variables were tested with  $\chi^2$  analyses and univariable/multivariable logistic regression models.

**Results**—A total of 231 biopsies (167 native and 64 allografts) were reviewed. There was no significant difference in the sex, age, race, or eGFR between native and allograft groups. The overall rate for any complication was 18.2%, with a 4.3% rate of major complications, which was significantly greater in native compared to allograft biopsies (6% versus 0%; P = .045). A risk analysis in native biopsies only showed that major complications were significantly associated with a low eGFR such that patients with stage 4 or 5 kidney disease had higher odds of complications (odds ratio [95% confidence interval]: stage 4, 9.405 [1.995–44.338]; P = .0393; stage 5, 10.749 [2.218–52.080]; P = .0203) than patients with normal function (eGFR >60 mL/min). The presence of a color flow tract portended a 10.7 times greater risk of having any complication (95% confidence interval, 4.595–24.994; P < .001). Other procedural factors were not significantly associated with complications.

*Conclusions*—There is an increased risk of major complications in US-guided random native kidney biopsy in patients with a low eGFR (<30 mL/min) and a patent color flow tract in the immediate postbiopsy setting.

Key Words-complication; Doppler; renal biopsy; ultrasound guided

S ince the first renal biopsy was performed in the 1950s, percutaneous renal biopsies have become an important tool in the diagnosis and management of renal disease. These biopsies allow for histologic diagnosis of renal disease not obtainable by any other means.<sup>1,2</sup> The introduction of the spring-loaded core biopsy needle in the 1980s led to an increase in the safety and yield of renal biopsy,<sup>1</sup> but bleeding remains a substantial complication.<sup>3-6</sup> Bleeding is considered a minor complication when a small hematoma requires no or nominal therapy but is considered a major complication when the patient requires hospitalization, transfusion, vascular embolization, or nephrectomy to control the bleeding or if the bleeding leads to permanent damage or death.<sup>7</sup>

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#### Abbreviations

AVF, arteriovenous fistula; eGFR, estimated glomerular filtration rate; US, ultrasound

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There are several established risk factors for bleeding complications in the setting of renal biopsy. Absolute contraindications to percutaneous renal biopsy include uncontrolled severe hypertension, inability to cooperate with the biopsy, and uncontrollable bleeding diathesis. Relative contraindications may include severe azotemia, renal anatomic abnormalities, anticoagulation, pregnancy, and urinary tract infections.<sup>4,8</sup> There are scattered reports of female sex,<sup>6</sup> obesity,<sup>6,8</sup> and laboratory factors such as anemia and thrombocytopenia<sup>6,9,10</sup> as risk factors for complications. However, hypertension<sup>5,11,12</sup> and renal failure<sup>3,6,9,11,13,14</sup> are more consistently reported risk factors for complications. Technical factors related to biopsy may also affect the complication risk. A recent meta-analysis showed that larger-gauge needles (14 gauge) were associated with more transfusion events compared to 16- and 18-gauge needles.<sup>3</sup> Other technical factors, such as the axis of biopsy, length of throw, and number of passes, have not been studied extensively. Although patent tracts have been shown to occur with renal biopsies,<sup>15</sup> to our knowledge, the prognostic importance of a patent color flow tract after renal biopsy has not been investigated.

#### Materials and Methods

This study and its reporting were performed as a quality improvement project and was deemed "not human subject research" by the Institutional Review Board (ID number 201904188), and the requirement for informed consent was therefore waived.

#### **Study Population**

Patients were identified from a database of all patients who underwent ultrasound (US)-guided random renal core biopsies by the radiology department at our institution between November 2014 and August 2018. If a single patient received more than a single biopsy during that time frame, data from each biopsy event was collected and considered independently.

#### Demographic Data Points

For each biopsy, the patient's age at the time of biopsy, sex, race, and status as inpatient or outpatient were collected. The patient's serum creatinine level at the time of biopsy was recorded to calculate an estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease equation as follows: eGFR =  $175 \times (\text{serum creatinine}) - 1.154 \times (\text{age}) - 0.203 \times 0.742$  (if female)  $\times 1.212$ (if African American). The patient's height and weight were used to unadjust the calculation for the ideal body surface area.<sup>16</sup>

#### **Biopsy Data**

Real-time US-guided biopsies were performed with a 16- or 18-gauge spring-loaded core biopsy needle (BioPince; Argon Medical Devices, Inc, Frisco, TX) under local anesthesia only with onsite evaluation of specimens by a cytotechnologist to assess specimen adequacy. Generally, at least 2 cores were favored, but ultimately, the radiologist performing the biopsy determined the total number of cores obtained on the basis of the specimens obtained and the patient's status.

An immediate postbiopsy US examination was performed to evaluate for hemorrhage or hematoma and to assess for the presence or absence of a color flow tract. Postbiopsy images were obtained for all cases. During the time frame for these biopsies, regardless of the site of biopsy, the departmental practice was to return inpatients to their hospital units for observation. Outpatients were observed for 2 hours after biopsy, at which time outpatients were discharged if asymptomatic and vital signs were stable. The radiology report was used to determine the location of the biopsied kidney (right or left native or allograft), needle gauge, number of throws, and throw length. To determine the approach for biopsy (transverse versus longitudinal relative to the axis of the kidney), the images from the biopsy were reviewed by a fellowship-trained abdominal radiologist with greater than 10 years of experience. If the approach was ambiguous based on the images, it was recorded as indeterminate. The presence of a patent color flow tract (Figure 1) documented either in the radiology report or on the immediate postbiopsy images was also recorded and categorized as indeterminate if there was no statement regarding a color flow tract in the report or not documented on the images. The report was reviewed for the use of Gelfoam (Pfizer, New York, NY) or thrombin injection into the biopsy tract. Cases were excluded if the approach to biopsy

or the presence of a color flow tract was indeterminate or if a hemostatic agent was used (Figure 2).

The electronic medical record was interrogated for descriptions of complications in radiology reports and progress notes, any subsequent imaging examinations, drops in the hemoglobin level, the need for transfusion, or the need for additional procedures. For outpatients, the medical record was reviewed to determine whether the patient returned to the

Figure 1. Example of a color flow tract after core biopsy of the kidney.



Figure 2. Schema for the study population.

emergency department or required admission in the 48 hours after the biopsy.

Major and minor complications were classified according to the Society of Interventional Radiology Standards of Practice Committee.<sup>7</sup> Briefly, for the purposes of this study, minor complications consisted of nominal therapy and overnight admission for observation only; examples included a perinephric hematoma requiring only observation. Major complications consisted of bleeding requiring therapy with hospitalization, such as transfusion or intervention such as vascular embolization, permanent adverse sequelae, or death.

#### **Statistical Analyses**

Categorical variables were summarized as frequencies (percentages). Continuous variables were summarized as medians (interquartile ranges). Differences for each of the measures between groups were determined by the  $\chi^2$  or Fisher exact test as appropriate for categorical data or the Kruskall-Wallis test for continuous measures. Univariate logistic regression models were used to determine predictors of any, minor, and major complications in the native kidney biopsy population only. Stepwise multivariate logistic regression with the Bayesian information criterion for selection was used to determine factors associated



with postbiopsy complications. All tests were 2 sided, and a significance level of .05 was used. SAS version 9.4 software (SAS Institute Inc, Cary, NC) was used to conduct data analyses.

**Table 1.** Demographic Data for the Native Kidney and Allograft

 Biopsy Populations Examined in this Study

Characteristic	Native Kidney (n = 167)	Allograft (n = 64)	Р
Sex			.36
Female	80 (48)	35 (55)	
Male	87 (52)	29 (45)	
Race			.62
African American	66 (40)	23 (36)	
Non–African American	101 (60)	41 (64)	
Age, y			.76
Median	54	53	
Interquartile range	38–64	41–64	
Range	18–88	21–80	
Admission status			<.001
Inpatient	70 (42)	59 (92)	
Outpatient	97 (58)	5 (8)	
eGFR, mL/min	26.4	29.9	.09
	(14.9–46.7)	(15.4–58.5)	

Data are presented as number (percent) and median (interquartile range) where applicable.

#### Results

#### **Patient Population**

The US biopsy database for random renal biopsies included 251 cases in the almost 4-year time frame of this study, with 185 biopsies of the native kidney and 66 of an allograft. In the native kidney group, 4 patients underwent 2 separate biopsy events during the study period. In the allograft group, 2 patients underwent 2 biopsy events, and 1 patient underwent 3 biopsy events. There were 18 exclusions in the native kidney group and 2 exclusions in the allograft group (Figure 2). There were no significant differences in the sex, race, or age between the groups. The admission status was significantly different between the groups, as patients with allograft biopsies were overwhelmingly of the inpatient rather than outpatient status (P < .001; Table 1). There was no significant difference in the eGFR between the groups.

#### Native Compared to Allograft Biopsy

Overall, the rate of developing any complication after kidney biopsy was 18.2%, and the rate of developing a major complication was 4.3%. Major complications were significantly associated with native rather than

Table 2	Comparison	of Bionsy	Data	Points	for Native	Kidnev	Versus	Allograft
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Factor	Native (n = 167)	Allograft (n = 64)	Total (n = 231)	Р
Any complication				.077
No	132 (79.0)	57 (89.1)	189 (81.8)	
Yes	35 (21.0)	7 (10.9)	42 (18.2)	
Minor complication				.43
No	142 (85.0)	57 (89.1)	191 (86.0)	
Yes	25 (15.0)	7 (10.9)	31 (14.0)	
Major complication				.045
No	157 (94.0)	64 (100.0)	212 (95.5)	
Yes	10 (6.0)	0 (0.0)	10 (4.5)	
Needle gauge				.19
16	16 (9.6)	10 (15.6)	23 (10.4)	
18	151 (90.4)	54 (84.4)	199 (89.6)	
Length of throw, cm	2.0 (2.0–3.0)	2.0 (2.0–3.0)	2.0 (2.0–3.0)	.49
Number of throws	2.0 (1.00–2.0)	2.0 (1.0–2.0)	2.0 (1.00–2.0)	.98
Biopsy approach				.94
Longitudinal	87 (52.1)	33 (51.6)	115 (51.8)	
Transverse	80 (47.9)	31 (48.4)	107 (48.2)	
Presence of color flow tract				.013
No	127 (76.0)	58 (90.6)	176 (79.3)	
Yes	40 (24.0)	6 (9.4)	46 (20.7)	
Number of glomeruli	25 (16.0–34.0)	23.0 (18.0–33.0)	25.0 (17.0–33.0)	.75

Data are presented as number (percent) and median (interquartile range) where applicable.

allograft biopsies; no major complications occurred with allograft biopsies (Table 2). There was no significant difference in technical factors between the native and allograft biopsies with respect to the needle gauge, length of throw, number of throws, or biopsy approach (Table 2). Color flow tracts were present in a significantly greater proportion of native kidneys than allografts (P = .013; Table 2).

#### Native Kidney Biopsy Risk Factors

To further interrogate the risk factors for complications in renal biopsies, the native kidney cohort was evaluated separately, as major complications only occurred in this group (Table 3). The risk of any complication increased by 0.02% for each 1-unit decrease in the unadjusted eGFR. Compared to renal biopsies in patients with stage 1 or 2 chronic kidney disease (eGFR >60 mL/min), patients with stage 4 and 5 kidney disease (eGFR <30 mL/min) had 9.405 (95% confidence interval, 1.995–44.338; P = .0393) and 10.749 (95% confidence interval, 2.218–52.080; P = .0203) increased odds of complications, respectively. Independent of eGFR, patients with a color flow tract were 10.7 times more likely to have any complication (95% confidence interval, 4.595-24.994; P < .001) than patients without a color flow tract. In the stepwise multivariate logistic regression analysis, only a color flow tract was predictive of any complication (P < .0001). A probability plot for complications plotted against the eGFR for patients with and without a color flow tract in shown in Figure 3. The positive predictive value of the color flow tract for any complication was 55%, and the negative predictive value was approximately 90%.

When multiple variables (needle gauge, length of throw, number of throws, >3 throws, biopsy approach, color flow tract, eGFR, and number of glomeruli) were entered separately into a predictive model, only the presence of a color flow tract (P < .0001) and eGFR (P = .0034) were predictive of any (minor or major) complication. When these variables were entered into a predictive model for major complications only, the presence of a color flow tract approached but does not reach significance (P = .0588), and the eGFR was not significantly predictive (P = .1959).

			eGFR (Unadjusted)			Management of
Patient	Age, y	Sex	mL/min	Description of Complication	Admission Status	Complication
1	64	Male	11.7	Large perinephric hematoma with dropping hemoglobin	Inpatient	Catheter angiography with renal artery embolization
2	64	Male	18.8	Hematuria with dropping hemoglobin	Inpatient	Blood transfusion
3	67	Male	18.3	Large perinephric hematoma, AVF	Inpatient	Blood transfusion
4	42	Female	20.4	Large perinephric hematoma with dropping hemoglobin	Inpatient	Catheter angiography but no intervention
5	62	Male	24.1	Large perinephric hematoma with pseudoaneurysm	Outpatient, admitted	Observation
6	56	Male	24.6	Small perinephric hematoma and AVF, hematuria followed by inability to void bladder	Outpatient, admitted	Observation, patient declined catheter angiography
7	66	Female	9.7	Large perinephric hematoma with pseudoaneurysm and AVF	Outpatient, admitted	Blood transfusion
8	55	Male	155.8	No perinephric hematoma but patent color flow tract at conclusion of biopsy	Outpatient, delayed admission	Delayed presentation of complication 4 d after biopsy, admitted for observation
9	40	Male	7.8	Large perinephric hematoma with dropping hemoglobin	Inpatient	Catheter angiography with renal artery embolization, transfusion
10	18	Female	12.9	Perinephric hematoma with patent color flow tract, hematuria	Inpatient	Blood transfusion

**Table 3.** Patients With Native Kidney Biopsy Who Had Major Complications



Figure 3. Probability plot for complications (minor or major) after core biopsy of the native kidney.

#### Discussion

The overall complication rate inclusive of minor and major complications was 18.2%, similar to the literature.<sup>17,18</sup> The overall major complication rate in all kidneys was 4.3% but 6% in native kidneys; no major complications occurred in allograft biopsies. The greater complication rate in native kidneys compared to allografts is consistent with the literature.<sup>13,19,20</sup> Our complication rates were within the range of 0% to 7.4% major complication rates reported in a 2012 meta-analysis of 34 studies by Corapi et al.<sup>3</sup> Our rates were also within the range of more recent studies.<sup>6,21-24</sup> Simard-Meilleur et al<sup>21</sup> published a retrospective single-institution study of 312 biopsies and showed a transfusion rate of 9%, with vascular embolization required in 1% of patients. A recent single-institution retrospective study showed a major complication rate of 1.64% in a cohort of more than 2200 patients.<sup>6</sup> Our complication rate was reflective of several factors, including the patient population. During the period of our study, 1 of 4 hospital service areas performed random renal biopsies at our institution: nephrology, US, computed tomography, and interventional radiology. Biopsies performed by the US service were generally referred by nephrology because of availability, a failed prior attempt at biopsy, a large patient body habitus, or otherwise higher risk. This practice may have resulted in the skewing of our population to those biopsies that were technically challenging. The phenomenon of referring patients with a

larger body habitus from nephrology to radiology is a known practice.<sup>24</sup> There were also other technical factors that may have affected the comparison of complication rates between our institution and others; for example, we primarily used the BioPince biopsy needle compared to the Monopty needle (Bard, Murray Hill, NJ) used by Monahan et al.<sup>6</sup>

Given the presence of major complications in only the native kidney biopsy population, our analysis of complications was performed in only the native kidney population. We found that procedural factors such as the needle gauge, length of throw, number of throws, and biopsy approach did not affect the complication rate. Ninety percent of our biopsies were performed with an 18-gauge needle. This number contrasts with approximately 80% of biopsies performed with a 16-gauge needle in the study by Simard-Meilleur et al,<sup>21</sup> which resulted in an approximately 10% major complication rate, and a combination of 14- and 16-gauge needles by Whittier et al,<sup>13</sup> which resulted in a 6.5% complication rate. Although Monahan et al<sup>6</sup> found that more than 4 throws were associated with complications, we did not find an association with the number of throws, similar to other studies.<sup>12,13,23,25</sup> We also found that the biopsy approach (transverse or longitudinal) did not affect the complication rate. Of the few studies that have examined the effects of technical factors on the complication risk,  $2^{26-28}$  none specifically compared the biopsy approach, although Li et al<sup>29</sup> found complications only with the sagittal approach.

Although we did not examine laboratory factors linked to the complication risk,<sup>3,5</sup> biopsies are generally not performed by the US department unless minimum standards for laboratory values (platelet count >50,000/mm<sup>3</sup>, international normalized ratio <1.5, and partial thromboplastin time of 25-37 seconds) are satisfied and antiplatelet and anticoagulant medications are held for the appropriate period around the time of biopsy. Other patient factors such as female sex,<sup>30</sup> obesity,<sup>6,8</sup> and hypertension,<sup>3,19,23,25,30</sup> which have previously been linked to greater patient risk, were also not examined. Although we did not examine the acuity of renal failure, which has been shown to be a risk factor for biopsy complications, 23,25,30 we did assess the severity of renal failure by the eGFR. A low eGFR was predictive of postbiopsy complications, especially in patients with stage 4 or 5 chronic

kidney disease (unadjusted eGFR <30 mL/min). This finding was consistent with the increasing volume of literature linking poorer renal function with complications,  ${}^{3,6,11,19,23,24,28,30,31}$  especially an eGFR lower than 30 mL/min.<sup>6,23</sup>

We found that the presence of a color flow tract was a significant predictor of complications, such that patients with this finding were 10.7 times more likely to have a minor or major complication. Although prior studies investigated the prognostic significance of this tract in the liver,<sup>32</sup> especially its persistence after 5 minutes of manual compression, we are unaware of prior studies showing the significance of this finding in renal biopsies. In 2007, Werner et al<sup>15</sup> investigated color flow abnormalities in the kidney immediately after biopsy with the primary aim of determining the natural history of presumed postbiopsy arteriovenous fistulas (AVFs). In their cohort of 77 patients studied prospectively, 7 patients were found to have color flow abnormalities that did not meet criteria for an AVF. These color flow tracts were identified at the site of biopsy and presumably corresponded to postbiopsy bleeding, which resolved spontaneously for all 7 patients. In 2011, McGahan et al<sup>33</sup> showed an association between a color tract after lesion ablation and development of postprocedural hematoma, but there was no association with a major complication requiring intervention. These results, however, are difficult to interpret, as the tract was coagulated before electrode removal. Our results show that the presence of a color flow tract is associated with complications after biopsy. Due to the retrospective nature of this study, it was not possible to ascertain whether the color flow tract appeared with the first pass or whether it developed with subsequent passes. However, the presence of this color flow tract after the first pass may help inform the risk of additional passes, should they be required because of insufficient glomeruli. A larger prospective study would be necessary to evaluate the true prognostic nature of a color flow tract after renal biopsy.

There were several limitations to this study, most notably its retrospective design and the inherent limitation in discovering data points not clearly documented by images or in the report. Although we excluded such patients when there was ambiguity regarding the biopsy technique, a prospective design would have allowed for more confidence in biopsy data points. We also excluded cases (n = 5) in which the presence or absence of a color flow tract could not be ascertained from the images or the report. However, it is possible that some cases that were ultimately categorized as "no color flow tract" did have a color flow tract transiently. The radiologist may have held pressure after seeing a color flow tract and only saved an image after the color flow tract had resolved. It may therefore be more appropriate to consider our conclusions regarding the color flow tract for those tracts that are persistent after some reasonable time of holding pressure at the site of sampling. A prospective evaluation of the timing of this color flow tract may be helpful to further stratify patient risk, as has been shown in the liver.<sup>32</sup> Second, we excluded patients in whom a hemostatic agent was injected into the biopsy tract, as that would likely alter the natural history of any bleeding, potentially altering the classification of a complication from major to minor or minor to none. Including these patients who received hemostatic agents may have increased the overall complication rate, although that may have also been offset by those radiologists who chose to prophylactically inject hemostatic agents into the biopsy tract on completion of the biopsy. Third, we did not interrogate pathology and clinical reports to determine whether the core samples were adequate to answer the clinical question.

In conclusion, the presence of a color flow tract at random native kidney biopsy in patients with poor renal function as manifested by a low eGFR, especially less than 25 mL/min, should be surveilled closely, as this finding is associated with an increased risk of major complications.

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