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Percutaneous Ultrasound-Guided Kidney Transplant Biopsy Outcomes: from the nephrologist perspective to the radiologist standpoint

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Adela Mattiazzi, Camilo Cortesi, Rhea Patil, Karla Carías Martínez, Mai Sedki, Franco Cabeza Rivera, Phillip Ruiz, Jason Salsamendi, and Giselle Guerra

Key Points:
* Ultrasound guided kidney transplant biopsy is considered safe with similar complications rates regardless of the performing team.
* Besides well-known risk factors for complications we found that sex and race are also predictors.
* The performance of kidney transplant biopsy remains an integral part of the nephrology training.

Abstract:
Background: Kidney transplant biopsies are the gold standard for evaluating allograft dysfunction. These biopsies are performed by nephrologists and radiologists under real-time ultrasound guidance. A few studies have examined the outcomes of ultrasound-guided kidney transplant biopsy in transplant recipients; however, none have compared these outcomes between both specialties. Methods: We retrospectively analyzed a cohort of 678 biopsies performed in a single center during a 44-month study period. Biopsies were stratified into two groups based upon the specialist performing the procedure, Interventional Radiology (IR) (n=447) and Transplant Nephrology (TN) (n=231). Results: There were 55 (8.1%) complications related to biopsies in the entire cohort: 37 cases (8.2%) in the IR group and 18 cases (7.7%) in the TN group, without statistical difference between the groups (p=0.94). Blood pressure control and prior use of anticoagulation were significant predictors of complicated biopsies (p=0.004, p=0.02, respectively). Female gender and prior use of anticoagulation were significant predictors of transfusion of blood products (p=0.01, p=0.01, respectively). Female gender and blood pressure control were significant predictors of overall perinephric hematoma (p=0.01, p=0.01, respectively) and black race was a significant predictor of perinephric hematoma without worsening of renal function (p=0.005). The specialist team performing the procedure was not a statistically significant predictor of biopsy complications, transfusion of blood products, or perinephric hematoma with comparable sample yield. Conclusions: Percutaneous ultrasound-guided kidney transplant biopsy performed by transplant nephrologists have similar complication rates when compared to interventional radiologists in an academic center.

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Author Contributions: Adela Mattiazzi: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Visualization; Writing - original draft; Writing - review and editing Camilo Cortesi: Data curation; Formal analysis; Investigation; Methodology; Writing - original draft Rhea Patil: Data curation; Formal analysis; Methodology; Software; Writing - review and editing Karla Carías Martínez: Data curation; Investigation; Methodology Mai Sedki: Data curation; Formal analysis; Investigation; Methodology; Software; Validation; Writing - original draft Franco Cabeza Rivera: Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing - original draft; Writing - review and editing Phillip Ruiz: Data curation; Resources Jason Salsamendi: Data curation; Resources Giselle Guerra: Formal analysis; Methodology; Supervision; Writing - review and editing

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Percutaneous Ultrasound-Guided Kidney Transplant Biopsy Outcomes: from the nephrologist to the radiologist standpoint

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KEY POINT

- Ultrasound guided kidney transplant biopsy is considered safe with similar complication rates regardless of the performing team.
- Besides well-known risk factors for complications we found that sex and race are also predictors.
- The performance of kidney transplant biopsy remains an integral part of the nephrology training.

ABSTRACT

Background: Kidney transplant biopsies are the gold standard for evaluating allograft dysfunction. These biopsies are performed by nephrologists and radiologists under real-time ultrasound guidance. A few studies have examined the outcomes of ultrasound-guided kidney transplant biopsy in transplant recipients; however, none have compared these outcomes between both specialties.

Methods: We retrospectively analyzed a cohort of 678 biopsies performed in a single center during a 44-month study period. Biopsies were stratified into two groups based upon the specialist performing the procedure, Interventional Radiology (IR) (n=447) and Transplant Nephrology (TN) (n= 231).

Results: There were 55 (8.1%) complications related to biopsies in the entire cohort: 37 cases (8.2%) in the IR group and 18 cases (7.7%) in the TN group, without statistical difference between the groups (p=0.94). Blood pressure control and prior use of anticoagulation were significant predictors of complicated biopsies (p=0.004, p=0.02, respectively). Female gender and prior use of anticoagulation were significant predictors of transfusion of blood products.
Female gender and blood pressure control were significant predictors of overall perinephric hematoma (p=0.01, p=0.01, respectively) and black race was a significant predictor of perinephric hematoma without worsening of renal function (p=0.005). The specialist team performing the procedure was not a statistically significant predictor of biopsy complications, transfusion of blood products, or perinephric hematoma with comparable sample yield.

Conclusions: Percutaneous ultrasound-guided kidney transplant biopsy performed by transplant nephrologists have similar complication rates when compared to interventional radiologists in an academic center.

Abbreviations: AVF: arteriovenous fistula; BMI: body mass index; BP: Blood pressure; BUN: blood urea nitrogen; CBC: complete cell count; CT: computerized tomography scan; G: Gauge; Hct: hematocrit; Hgb: hemoglobin; INR: international normalized ratio; IR: interventional radiology; SLE: systemic lupus erythematos; TN: transplant nephrology; US-KTB: percutaneous ultrasound-guided kidney transplant biopsy; WRF: worsening renal function
INTRODUCTION

Percutaneous kidney biopsy was described in 1951 by Iversen and Brun\(^1\) and it remains the gold standard for diagnosis in native and transplanted kidneys. Since then, the procedure has evolved as complications have declined\(^{1-6}\). Nowadays, percutaneous ultrasound-guided kidney transplant biopsy (US-KTB) is performed by transplant nephrologists (TN) and interventional radiologists (IR). Although it is a relatively safe procedure, it is not exempt from complications. Complications such as hematuria, arteriovenous fistula (AVF), and small hematoma occur in up to 17\% of kidney biopsies between day 1 and 14 post procedure\(^{4-10}\). Severe complications such as Page kidney; or either hydronephrosis, AVF or perinephric hematoma associated with worsening renal function (WRF) range between 0.33– 2.7\%\(^{7,8}\) and can result in significant morbidity.

Similar complication rates have been described on native kidneys biopsies by both subspecialties\(^{11,12}\), but no studies have described outcomes in US-KTB performed by IR vs. TN in kidney transplant recipients. The aim of this study is to evaluate the incidence of non-severe and severe complications related to US-KTB, compare the rates of biopsy complications between specialists performing the procedure, and identify risk factors of post US-KTB complications in a single academic center.

MATERIALS AND METHODS

We retrospectively identified 573 kidney transplant recipients undergoing US-KTB between January 2013 and August 2016 in our center. Demographics, laboratory, pathology report based on Banff’s classification, and imaging were reviewed using electronic medical records. Patients under 18 years of age, computerized tomography scan (CT) guided or intraoperative kidney biopsy were excluded. The groups were stratified based on specialty
performing the procedure (IR vs. TN). As transplant nephrology literature differs on the
definition of severity of complications, for the purpose of our study we divided them based on
the need for non-surgical interventions vs. surgical intervention according to the absence or
presence of WRF as recently described. Non-severe complications were defined as perinephric
hematoma, hydronephrosis, AVF, hemoglobin (Hgb) drop >2 g/dL, and transfusion of blood
products; and severe complications were defined as Page kidney; or either hydronephrosis, AVF
or perinephric hematoma associated with WRF.
Anemia was defined as Hgb lower than the normal inferior value at our center (< 11.1 and < 13.3
g/dL for females and males, respectively).

Pre-biopsy protocol

Biopsies were done per protocol (surveillance) and per-cause (elevated creatinine from
baseline, new onset or worsening proteinuria or donor specific antibodies). The patients were
instructed to stop antiplatelets or anticoagulant medications at least 7 days prior to biopsy.
Desmopressin (0.3 mcg/kg/IV) was administered when platelet dysfunction was suspected and
there were no contraindications. Patient were nil per os after midnight prior to the procedure.
Complete blood count (CBC), basic metabolic panel, coagulation parameters, type and screen,
and vital signs were obtained prior to the procedure. US-KTB were cancelled if international
normalized ratio (INR) was >1.5, platelet counts < 50.000/mm3; or if blood pressure (BP) ≥
160/90 mmHg (uncontrolled) was noted after treatment with oral clonidine or intravenous
hydralazine.

Biopsy technique

TN performed biopsies at bedside, using real-time portable ultrasound Sonosite M-Turbo,
C60 x Convex Probe [2-5 MHz] with a 16-gauge (G) automated biopsy needle and performed ultrasound immediately after each pass to identify any signs of bleeding. TN are trained to visualize glomeruli in samples at the bedside. IR performed biopsies in their suite, using a Sonosite edge portable ultrasound C60 x Convex Probe [2-5 MHz] and HFL38x Linear Probe [6-13 MHz] for real-time guidance of all biopsies with a 18-G automated biopsy needle. Pathology residents evaluated their samples for the presence of glomeruli. Both specialties performed immediate post-biopsy ultrasound to diagnose immediate complications and used a cortical tangential approach. Biopsy were done by TN or IR based on first come, first serve approach.

Post-biopsy protocol

All patients were closely monitored for gross hematuria, flank pain, and/or hypotension. TN patients remained in supine position in the transplant unit with a 5 pound “sandbag” applied to the biopsy site for 6-hours. Vital signs were monitored every 15 minutes for the first 2 hours, then hourly for the next 4 hours along with macroscopic evaluation of the urine and pain assessment by the nursing staff. CBC was obtained 3 hours after the procedure. IR patients remained in their recovery room for 2-4 hours and were transferred to the transplant unit to continue with post biopsy monitoring. If any complication was suspected, an emergent ultrasound (US) of the transplant kidney or/and CT scan of the abdomen and pelvis was obtained.

The study was approved by our institutional IRB: 20170575
Statistical Analysis

All statistical analysis was performed by using R Studio 1.4.1106. Differences in categorical measures between IR and TN groups were assessed using Pearson's Chi-squared test with Yates' continuity correction. Differences in quantitative measures between the groups were assessed using the Welch Two Sample t-test. Multivariable logistic regression was conducted to predict the incidence of the all outcomes. The logistic regression included the following variables: age, gender, specialty team, race, BP control, BMI, co-morbidities, prior renal transplant, transplant type and location, antiplatelet therapy, anticoagulation therapy, desmopressin use, steroid use, creatinine, BUN, platelets, INR, Hgb level, biopsy indication, needle G, degree of kidney fibrosis, and simian virus 40 positivity. The statistically significant variables found in the regression analyses were identified as the predictors of transfusion of blood products and perinephric hematoma outcomes respectively. These predictors were then put into a simplified multivariable regression model to report the adjusted odds ratio (AOR) and 95% confidence intervals (CI). The fit of these models were evaluated by the significance of the overall model and the coefficient of multiple determination ($R^2$). P value of less than 0.05 indicated statistical significance.

RESULTS

Demographics

A total of 678 US-KTB were performed in 573 patients in a 44-month period. 447 were done by IR and 231 by TN. Median patient’s age at the time of the biopsy was 53 years. 60% of the biopsies were performed in males and 40% in females. The most common comorbidities were hypertension (88%), diabetes mellitus (36%), coronary artery disease (15%), systemic
lupus erythematosus (SLE) (8%), hepatitis (7%) and HIV (3%). 74% received a transplant from a deceased donor and 26% from a living donor. 41% were on antiplatelet therapy and 6% were on anticoagulation therapy, held a week prior the biopsy. 19% of the patients had a BMI between 30 to 34.9 and 10% greater than 35. BP at the time of the biopsy was uncontrolled in 24% and controlled 76% of the cases. Mean serum creatinine at biopsy was 2.7 mg/dL (2.0 ± SD), BUN 38 mg/dL (22 ± SD), platelets 216 K/uL (79± SD), INR of 0.99 (0.1± SD), and Hgb 10.7 g/dL (1.8 ± SD). Desmopressin was administered in 120 cases. Steroids were initiated prior to biopsy in 232 cases. Patient’s BP control, diabetes mellitus, and transplant location were among the demographic variables that showed a statistical difference between the IR and TN group. 82% of the biopsies were per-cause. The median number of core biopsies were 3 for IR and 2 for TN. The median glomeruli were 14 (0-56) in the IR group and 13 (0-51) in the TN group. The only statistical difference found between the groups were the level of Hgb, hematocrit (Hct) and Needle size (p=<0.001) (Table 1).

*Post Kidney Transplant Biopsy Complications*

Overall complications were found in a total of 55 biopsies (8%) with 37 cases in the IR group and 18 cases in the TN group (p=0.94). The median number of days for post-biopsy complications for the IR group was 2 (0-30) with 70% during the first 15 days: 13% of the complications on the day of biopsy, 26% 24 hs post biopsy and 11% of the cases > 15 days post biopsy. For the TN group, the median number of days for post biopsy complications was 1 (0-32) with 46% during the 0-15 days period: 21% of the complications on the day of biopsy, 26 % 24 hs post biopsy and 14% after 15 days post procedure. There was no significant difference in the rate and type of complications for recipients up to 3 months posttransplant between the
groups (p=0.24). There was no significant difference in the rate of non-severe or severe complications between the IR and TN group (9%, 2% vs. 10%, 2%; p=0.50, p=1.0, respectively) (Table 2). IR intervention was required to coiled one case of AVF with WRF and another case of AVF with WRF that was associated with Page kidney that also needed surgical intervention. No graft or patient losses were associated directly with complications of the kidney biopsies.

Multivariable logistic regression analyses

*Risk Factors for Complications*

The test of the full model against a constant only model was statistically significant, indicating that the predictors as a set did reliably distinguish between whether or not a complication post biopsy occurred (chi square = 12.05, p < 0.05 (0.007) with df = 3). The Nagelkerke R² was 0.04, indicating a weak relationship between prediction and grouping. The Wald criterion demonstrated that uncontrolled BP and use of anticoagulants prior to biopsy made a significant contribution to the prediction of post-biopsy complications (p=0.004, p=0.023, respectively). Exp(B) values indicate that the risk of post-biopsy complications was higher in patients with uncontrolled BP (AOR 2.31, 95% CI 1.29-4.09) and patients who used anticoagulants prior to biopsy (AOR 2.77, 95% CI 1.06-6.37).

The model was applied on each individual complication and we only found significant risk factors in the following complications:

*Risk Factors for Transfusion of Blood Products*

The test of the full model against a constant only model was statistically significant for the prediction of transfusion of blood products (chi square= 12.56, p < 0.05 (0.004) with df = 2). The Nagelkerke R² was 0.06, indicating a weak relationship between prediction and grouping.
The Wald criterion demonstrated that female gender and use of anticoagulants prior to biopsy made a significant contribution to the prediction of the transfusion of blood products (p=0.01, p=0.01, respectively). Exp(B) values indicate that the risk of transfusion of blood products was higher in female patients (AOR 3.10, 95% CI 1.31-7.90) and patients who used anticoagulants prior to biopsy (AOR 4.29, 95% CI 1.17-12.56).

_Risk Factors of Perinephric Hematoma_

The test of the full model against a constant only model was statistically significant for the prediction of perinephric hematoma with and without worsening renal function (chi square= 16.92, p < 0.05 (0.001) with df = 4). The Nagelkerke $R^2$ was 0.089, indicating a weak relationship between prediction and grouping. The risk of perinephric hematoma was higher in female patients (AOR 2.92, 95% CI 1.29-7.04, p=0.01) and patients with uncontrolled BP (AOR 2.79, 95% CI 1.21-6.30, p=0.01). We identify black race as a stronger predictor of hematoma without WRF (AOR 12.90, 95% CI 2.5-100, p=0.005).

_Gender analysis: (supplement table and figures)_

Females were statistically significantly younger, with lower BMI, lower Hgb and Hct, more SLE diagnosis, higher platelets, with less uncontrolled hypertension and required less biopsy cores than males. Of the 23 patients who received blood transfusions post procedure, 81% females vs. 91% males were anemic pre-biopsy. Females had a lower baseline Hgb vs male and also had a greater change on Hgb and Hct post biopsy than male (Delta Hgb: -28% ± -9% vs. -20% ± -6%, p= 0.0195 and Delta Hct: -27% ± -10% vs, -10% ± -7%, p= 0.0001) with a higher number of blood transfusions ( 81% vs. 33% p=0.036).
The specialty team that performed the biopsy was not a significant predictor for complications (AOR 1.69, 95% CI 0.02-20.48, p=0.64), the transfusion of blood productions (AOR 0.77, 95% CI 0.05-20.19, p=0.86), or perinephric hematoma (AOR 1.71, 95% CI 0.15-35.23, p=0.69).

DISCUSSION

Percutaneous ultrasound-guided kidney transplant biopsy is known as a safe procedure and the gold standard for obtaining tissue for histopathological diagnosis, but complications can occur. Complications and their risk factors have been extensively studied in native kidneys. According to a meta-analysis done by Corapi et al. the rate of perinephric hematoma post biopsy was 17% when post biopsy ultrasonography was regularly implemented\(^{(13)}\). Some series describe complications as high as in one-third of the biopsies with an average of 1% of severe complications\(^{(14)}\). For transplanted kidney, the number of studies describing outcomes and complications post biopsy under ultrasound (US) guidance are limited. There are two studies that have retrospectively evaluated a significant cohort of patients that underwent US-KTB showing rate of major complication close to 0.4 -1.8 %\(^{(7,8)}\). Minor complications such as hematuria, pain requiring analgesia, AVF were reported in 15-20 % in protocol biopsy from stable kidney grafts\(^{(10)}\). A prospective study by Whittier et al. compared US-KTB done by nephrologist in native and transplanted kidneys found the kidney transplant biopsies (KTB) patients (n=938) to be more hypertensive, with a higher serum creatinine and PTT, and lower baseline Hgb than the native kidney biopsy (NKB) patients( n=767). The NKB group had a greater drop in Hgb after the biopsy (0.97 ± 1.1 vs.0.73 ± 1.3 g/dL, P < 0.0001), a higher complication rate (6.5 vs.3.9%, P = 0.02) and higher transfusion rate (5.2 vs. 3.3%, P = 0.045). There was one death in each group attributed to the biopsy. The authors concluded that although death is equally rare the
complication rate is higher in NKB compared with KTB despite KTB having more of the traditional risk factors for bleeding\textsuperscript{(15)}. A retrospective analysis by Reschen et al. confirmed that kidney transplant biopsies were safe when performed by adequately trained nephrologists\textsuperscript{(16)}. There is no consensus about how to classify the severity of complications after kidney transplant biopsy. We use the presence of renal dysfunction and the need for surgical intervention as described in the literature\textsuperscript{(6-7)}. In our cohort we observed significantly lower rates of bleeding complications than those described for native kidneys\textsuperscript{(13)}. Our overall rate of severe complications was 1.6 % which is similar to the rate described by Morgan et al\textsuperscript{(7)} with perinephric hematoma with WRF being the most frequent severe complication. The overall rate for non-severe complication was 9.1% with transfusion of blood products being the most frequent complication.

The majority of the severe complications described in the literature occurred during the first 24 hs post procedure\textsuperscript{(7-15)}. We described 40 % of the total complications during the first 24 hs post procedure including 3 severe complications. 48 % occurred between 2-15 days post biopsy and 12 % occurred after 15 days post biopsy. Of note, only one severe complication of AVF with WRF occurred in this late group, including one as far as 32 days post procedure. Our finding of complications as high as 60% beyond the first 24 hs post US-KTB could be explained by the continuing awareness and high suspicion for potential post biopsy complications beyond the immediate post procedure period, that had led us to obtain or repeat images along with laboratory test as part of the differential diagnosis of kidney transplant dysfunction post biopsy.

As it has been described in the literature, we confirmed that uncontrolled BP \( \geq 160/90 \) mmHg at the time of biopsy and prior use of anticoagulation were statistically significant predictors of all
post-biopsy complications ($p=0.004$, $p=0.02$, respectively). Uncontrolled BP was also and additional predictor for overall perinephric hematoma ($p=0.013$) and the use of anticoagulation was a predictor on the need of transfusion of blood products ($p=0.010$).

We were able to correlate that female gender was also a significant predictor for the transfusion of blood products ($p=0.017$) and overall perinephric hematoma ($p=0.011$).

When we further explore the potential risk factors of these findings in our population beside being significantly younger, with SLE diagnosis, lower BMI, higher platelet count, less uncontrolled BP and requiring less core number of biopsies, similarly to the general population, females had lower Hgb and Hct at the time of biopsy. In patients that were transfused, Hgb and Hct pre-biopsy did not differ between gender. However, females had a greater decline on it post biopsy than males leading to a higher requirement of blood transfusions. It would be interesting whether this gender effect recently described also in native renal biopsies\(^{(17)}\) persists in a larger prospective trial, as currently gender is not a relevant factor to trigger indication for blood transfusions\(^{(18-19)}\). As we also found that female gender is a risk factor for overall perinephric hematoma, one could only hypothesize the presence of a technical factor leading to potential deeper tissue sample that will increase the risk for bleeding with the concomitant need for blood transfusions. It remains unclear why black race was found to be a risk factor for perinephric hematoma without WRF and further research is needed.

It is necessary to highlight that biopsies were performed at an academic institution where in both cases, the TN and IR group, are performed mainly by fellows under direct attending supervision.

The significant transition overtime in the performance of US-KTB by nephrologist to IR is not unique since it follows the same trend as native kidney biopsies. US-KTB outcomes and risk
complications have been evaluated in limited large cohorts but without mentioning which team did the biopsies. Here we described outcomes based on the specialty team at an academic institution in order to evaluate the implications of using different techniques, equipment and protocols, and the impact of the increasing reduced exposure to this procedure in the transplant nephrology field given the tendency of interventional radiologists to perform most of the procedures.

The advantages of the transplant nephrologist doing this procedure is that theoretically they are more capable of making real-time decisions about the adequacy of sample size for a given suspected diagnosis, based on better understanding of indications, contraindications and the patient condition. On the other side, interventional radiologists have had greater exposure to this type of procedure acquiring major expertise especially in challenging cases, with a better understanding of how to manage some severe complications.

Similarities and differences found in both groups are that at our institution procedures are mainly done by physicians on training under close supervision, there was no difference in the number of glomeruli obtained between the groups, IR mainly uses 18 G needle and TN 16 G needle, as that has been described in the literature to results in better histological quality and lower frequency of complications compared to 18G(20-23).

As part of the TN protocol a sandbag is applied on the biopsy site during 6 hours with strict bed rest; the interventional radiology department’s ultrasound machine is technically superior than the one used by the TN department; procedure done by the IR group are done in the interventional radiology suite room as opposed to the TN group that performs the procedure at the bedside.
Our study has several limitations. To begin, this is a retrospective, observational study; therefore, conclusions cannot be directly extrapolated because unmeasurable variables not accounted for by multivariable analysis may have affected the results. In addition, because the majority of data was gathered from the electronic medical records there is likely selection bias due to missing data. Another major limitation is the operator dependent factor since IR has many different fellows performing the procedures whereas in TN the procedure is performed by the nephrology fellow who is consistent for the year. Last, this is a center specific study from a high-volume academic institution where meticulous training is required during transplant nephrology and interventional radiology fellowships, and the results cannot be generalized.

CONCLUSION
Percutaneous ultrasound-guided kidney transplant biopsy is the gold standard in the clinical practice of transplant nephrologists to determine diagnosis, prognosis and treatment of graft dysfunction. This procedure is considered safe if it is performed in centers where competent training is provided. In our center they have similar complication rates and comparable glomerular tissue samples beside using different needle sizes when performed either by TN or IR. Blood pressure control and management of anticoagulation are fundamental to decrease the risk of complications. Prospective studies are needed to further understand why gender and race were predictors for complications such as blood transfusion need and perinephric hematoma development.
DISCLOSURES: A. Mattiazzi reports the following: Honoraria: CareDx; and Speakers Bureau: CareDx. J. Salsamendi reports the following: Honoraria: Trisalis. The remaining authors have nothing to disclose.

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AUTHOR CONTRIBUTIONS: Adela Mattiazzi: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Visualization; Writing - original draft; Writing - review and editing. Camilo Cortesi: Data curation; Formal analysis; Investigation; Methodology; Writing - original draft. Rhea Patil: Data curation; Formal analysis; Methodology; Software; Writing - review and editing. Karla Carias Martinez: Data curation; Investigation; Methodology. Mai Sedki: Data curation; Formal analysis; Investigation; Methodology; Software; Validation; Writing - original draft. Franco Cabeza Rivera: Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing - original draft; Writing - review and editing. Phillip Ruiz: Data curation; Resources. Jason Salsamendi: Data curation; Resources. Giselle Guerra: Formal analysis; Methodology; Supervision; Writing - review and editing.

DATA SHARING STATEMENT: All data is included in the manuscript and/or supporting information.
SUPPLEMENTAL MATERIAL: This article contains the following supplemental material.

Supplemental Table 1: Demographics by gender.

Supplemental Figure 1: Pre-Biopsy Mean Hgb and Hct by gender.

Supplemental Figure 2: Mean Hgb change by gender.

Supplemental Figure 3: Delta Hgb and Hct pre and post biopsy.

Supplemental Figure 4: Post biopsy transfusions by gender.

REFERENCES


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<td>7 (1)</td>
<td>3 (1)</td>
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<tr>
<td>18-24.9</td>
<td>205 (30)</td>
<td>129 (29)</td>
<td>76 (33)</td>
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<tr>
<td>25-29.9</td>
<td>270 (40)</td>
<td>178 (40)</td>
<td>92 (40)</td>
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<tr>
<td>&gt;30-34.9</td>
<td>126 (19)</td>
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<td>43 (19)</td>
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<tr>
<td>&gt;35</td>
<td>67 (10)</td>
<td>50 (11)</td>
<td>17 (7)</td>
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<tr>
<td><strong>Comorbidities (%)</strong></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>598 (88)</td>
<td>387 (87)</td>
<td>211 (91)</td>
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<td>Diabetes Mellitus</td>
<td>241 (36)</td>
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<td>23 (3)</td>
<td>20 (4)</td>
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<td>71 (14)</td>
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<td>15 (6)</td>
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<td>8 (2)</td>
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<td>39 (6)</td>
<td>26 (6)</td>
<td>13 (6)</td>
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<td>SLE</td>
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<td>30 (7)</td>
<td>26 (11)</td>
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<td><strong>Prior Renal Transplant (%)</strong></td>
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<td>416 (93)</td>
<td>205 (89)</td>
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<td>46 (7)</td>
<td>27 (6)</td>
<td>19 (8)</td>
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<tr>
<td>2</td>
<td>9 (1)</td>
<td>4 (0.8)</td>
<td>5 (2)</td>
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<td>3</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
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<tr>
<td>≥ 4</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
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<td><strong>Transplant type (%)</strong></td>
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<td>500 (74)</td>
<td>335 (75)</td>
<td>165 (71)</td>
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<td>Living donor</td>
<td>178 (26)</td>
<td>112 (25)</td>
<td>66 (29)</td>
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<td><strong>Transplant location (%)</strong></td>
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<td>0.027</td>
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<td>Right iliac fossa</td>
<td>558 (82)</td>
<td>357 (80)</td>
<td>201 (87)</td>
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<tr>
<td>Left iliac fossa</td>
<td>120 (18)</td>
<td>90 (20)</td>
<td>30 (13)</td>
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<td><strong>Pre-biopsy medications (%)</strong></td>
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<tr>
<td>Antiplatelet therapy</td>
<td>275 (41)</td>
<td>181 (40)</td>
<td>94 (40)</td>
<td>1.00</td>
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<td>Anticoagulation therapy</td>
<td>39 (6)</td>
<td>29 (6)</td>
<td>10 (4)</td>
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<td>Desmopressin</td>
<td>120 (18)</td>
<td>66 (15)</td>
<td>54 (23)</td>
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<td>Steroids</td>
<td>232 (35)</td>
<td>151 (34)</td>
<td>81 (35)</td>
<td>0.806</td>
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<td><strong>Pre-biopsy laboratory test (mean ± SD)</strong></td>
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</tr>
<tr>
<td>Creatinine - mg/dL</td>
<td>2.71 ± 2.03</td>
<td>2.78 ± 1.90</td>
<td>2.57 ± 2.25</td>
<td>0.241</td>
</tr>
<tr>
<td>BUN - mg/dL</td>
<td>38.14 ± 21.77</td>
<td>39.09 ± 21.70</td>
<td>36.30 ± 21.84</td>
<td>0.117</td>
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<td>Platelets - K/uL</td>
<td>215.79 ± 78.97</td>
<td>214.80 ± 80.61</td>
<td>217.72 ± 85.74</td>
<td>0.669</td>
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<tr>
<td>INR</td>
<td>0.99 ± 0.11</td>
<td>0.99 ± 0.12</td>
<td>0.97 ± 0.10</td>
<td>0.039</td>
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<tr>
<td>Hemoglobin - g/dL</td>
<td>10.7 ± 1.84</td>
<td>10.48 ± 1.83</td>
<td>11.09 ± 1.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit - %</td>
<td>33.2 ± 6.13</td>
<td>32.56 ± 6.26</td>
<td>34.42 ± 5.71</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Biopsy Indication (%)</strong></td>
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<td></td>
<td>0.45</td>
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<td>Protocol</td>
<td>123 (18)</td>
<td>77 (17)</td>
<td>46 (20)</td>
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<tr>
<td>Per cause</td>
<td>555 (82)</td>
<td>370 (83)</td>
<td>185 (80)</td>
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</tr>
<tr>
<td><strong>Number of core biopsies, median (range)</strong></td>
<td>3 (1-7)</td>
<td>3 (1-7)</td>
<td>2 (1-5)</td>
<td>0.916</td>
</tr>
<tr>
<td>&lt;0.001</td>
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<td></td>
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<tr>
<td><strong>Needle Gauge (%)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>16 G</td>
<td>238 (35)</td>
<td>15 (3)</td>
<td>227 (98)</td>
<td></td>
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<tr>
<td>18 G</td>
<td>421 (62)</td>
<td>417 (93)</td>
<td>4 (2)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>19 (3)</td>
<td>19 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Glomeruli, median (range)</strong></td>
<td>13 (0-56)</td>
<td>14 (0-56)</td>
<td>12 (0-51)</td>
<td>0.660</td>
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<tr>
<td>Degree of Fibrosis n=677</td>
<td></td>
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<td></td>
<td>0.866</td>
</tr>
<tr>
<td>Mild fibrosis (&lt;25%)</td>
<td>59 (9)</td>
<td>38 (8)</td>
<td>21 (9)</td>
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<tr>
<td>Moderate fibrosis (25-50%)</td>
<td>425 (62)</td>
<td>278 (62)</td>
<td>147 (64)</td>
<td></td>
</tr>
<tr>
<td>Severe fibrosis (&gt;50%)</td>
<td>193 (29)</td>
<td>130 (30)</td>
<td>63 (27)</td>
<td></td>
</tr>
<tr>
<td>BVK positive biopsy (%)</td>
<td>57 (8)</td>
<td>39 (9)</td>
<td>18 (8)</td>
<td>0.770</td>
</tr>
</tbody>
</table>

Controlled: defined as blood pressure <160/90 at the time of biopsy, Uncontrolled: defined as blood pressure ≥ 160/90 at the time of biopsy, BMI: body mass index, HIV: human immunodeficiency virus, CAD: coronary artery disease, SD: standard deviation
Table 2: Complications Post Kidney Transplant Biopsy

<table>
<thead>
<tr>
<th></th>
<th>Total (n=678)</th>
<th>Interventional Radiology (n=447)</th>
<th>Transplant Nephrology (n=231)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total complications related to biopsies (%)</td>
<td>55 (8.1)</td>
<td>37 (8.2)</td>
<td>18 (7.7)</td>
<td>0.943</td>
</tr>
<tr>
<td>Day of post-biopsy complication, median (range)</td>
<td>0 (0-32)</td>
<td>2 (0-30)</td>
<td>1 (0-32)</td>
<td>0.447</td>
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<tr>
<td>Total number of complications</td>
<td>73</td>
<td>45</td>
<td>28</td>
<td>0.492</td>
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<tr>
<td>Non-Severe Complications</td>
<td>62</td>
<td>38</td>
<td>24</td>
<td>0.504</td>
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<tr>
<td>Hydronephrosis</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0.523</td>
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<tr>
<td>Perinephric hematoma</td>
<td>19</td>
<td>10</td>
<td>9</td>
<td>0.319</td>
</tr>
<tr>
<td>Transfusion of blood products</td>
<td>23</td>
<td>15</td>
<td>8</td>
<td>1.000</td>
</tr>
<tr>
<td>Drop in hemoglobin &gt;2g/dL</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Severe Complications</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Page kidney</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Arteriovenous fistula with WRF</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Arteriovenous fistula</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Hydronephrosis with WRF</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>0.478</td>
</tr>
<tr>
<td>Perinephric hematoma with WRF</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Hemoperitoneum with WRF</td>
<td></td>
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</tbody>
</table>

WRF = worsening renal function; w/ = with

Table 3: Predictors of complications

<table>
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<tr>
<th>Predictor of all complications</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled blood pressure</td>
<td>2.318</td>
<td>1.290 - 4.098</td>
<td>0.004</td>
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<tr>
<td>Use of anticoagulants</td>
<td>2.771</td>
<td>1.065 - 6.379</td>
<td>0.023</td>
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</tbody>
</table>

Predictors of Transfusion of Blood Products

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>3.108</td>
<td>1.318 - 7.905</td>
<td>0.017</td>
</tr>
<tr>
<td>Use of anticoagulants</td>
<td>4.291</td>
<td>1.176 - 12.569</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Predictors of Perinephric Hematoma Without WRF

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black race</td>
<td>12.904</td>
<td>2.563 - 100.995</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Predictors of Perinephric Hematoma with and without worsening renal failure

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>2.928</td>
<td>1.299 - 7.041</td>
<td>0.011</td>
</tr>
<tr>
<td>Uncontrolled blood pressure</td>
<td>2.790</td>
<td>1.216 - 6.300</td>
<td>0.013</td>
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Uncontrolled blood pressure defined as blood pressure ≥ 160/90 mmHg at the time of biopsy
**Supplemental Table 1:** Demographics by Gender

<table>
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<th>Age (median years)</th>
<th>Male (n=406)</th>
<th>Female (n=272)</th>
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<tbody>
<tr>
<td></td>
<td>54</td>
<td>51</td>
<td>0.010</td>
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<tr>
<td>Race (%)</td>
<td></td>
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<tr>
<td>White</td>
<td>231 (57)</td>
<td>137 (50)</td>
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</tr>
<tr>
<td>Black</td>
<td>169 (42)</td>
<td>129 (48)</td>
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</tr>
<tr>
<td>Other</td>
<td>6 (4)</td>
<td>6 (2)</td>
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</tr>
<tr>
<td>BP</td>
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<td>0.374</td>
</tr>
<tr>
<td>Controlled</td>
<td>302 (75)</td>
<td>213 (78)</td>
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</tr>
<tr>
<td>Uncontrolled</td>
<td>104 (25)</td>
<td>59 (22)</td>
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</tr>
<tr>
<td>BMI total (%)</td>
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<td>0.032</td>
</tr>
<tr>
<td>&lt;18</td>
<td>2 (0.5)</td>
<td>8 (3)</td>
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<tr>
<td>18-24.9</td>
<td>116 (28)</td>
<td>89 (33)</td>
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<tr>
<td>25-29.9</td>
<td>174 (43)</td>
<td>96 (35)</td>
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<tr>
<td>30-34.9</td>
<td>70 (17)</td>
<td>56 (21)</td>
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</tr>
<tr>
<td>&gt;35</td>
<td>45 (11)</td>
<td>22 (8)</td>
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</tr>
<tr>
<td>Comorbidities (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hypertension</td>
<td>368 (91)</td>
<td>230 (85)</td>
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<td>Diabetes mellitus</td>
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<td>87 (32)</td>
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<td>HIV</td>
<td>14 (3)</td>
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<tr>
<td>CAD</td>
<td>66 (16)</td>
<td>38 (14)</td>
<td>0.483</td>
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<td>Hepatitis B or C</td>
<td>31 (8)</td>
<td>18 (7)</td>
<td>0.726</td>
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<td>Hepatitis C</td>
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<td>Lupus</td>
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<td>Prior Renal Transplant (%)</td>
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<tr>
<td>0</td>
<td>375 (92)</td>
<td>246 (90)</td>
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<td>27 (7)</td>
<td>19 (7)</td>
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</tr>
<tr>
<td>2</td>
<td>2 (0.5)</td>
<td>7 (3)</td>
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</tr>
<tr>
<td>3</td>
<td>1 (0.25)</td>
<td>0 (0)</td>
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</tr>
<tr>
<td>&gt;4</td>
<td>1 (0.25)</td>
<td>0 (0)</td>
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<tr>
<td>Transplant type</td>
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<tr>
<td>Deceased donor</td>
<td>300 (73)</td>
<td>204 (75)</td>
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<tr>
<td>Living donor</td>
<td>106 (27)</td>
<td>68 (25)</td>
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<td>Transplant location</td>
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<tr>
<td>Right iliac fossa</td>
<td>336 (83)</td>
<td>222 (82)</td>
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<tr>
<td>Left iliac fossa</td>
<td>70 (17)</td>
<td>50 (18)</td>
<td></td>
</tr>
<tr>
<td>Pre-biopsy medications (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>158 (39)</td>
<td>117 (42)</td>
<td>0.305</td>
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<tr>
<td>Anticoagulant therapy</td>
<td>27 (7)</td>
<td>12 (4)</td>
<td>0.294</td>
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<td>Desmopressin</td>
<td>64 (16)</td>
<td>56 (20)</td>
<td>0.138</td>
</tr>
<tr>
<td>Steroids</td>
<td>132 (33)</td>
<td>100 (38)</td>
<td>0.308</td>
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<tr>
<td>Pre-biopsy laboratory test (mean ± SD)</td>
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</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>2.8 ± 2.7</td>
<td>2.5 ± 2.4</td>
<td>0.16</td>
</tr>
<tr>
<td>BUN</td>
<td>39.30 ± 21.5</td>
<td>36.41 ± 22</td>
<td>0.089</td>
</tr>
<tr>
<td>Platelets (k/uL)</td>
<td>209 ± 82</td>
<td>226 ± 84</td>
<td>0.009</td>
</tr>
<tr>
<td>INR</td>
<td>0.99 ± 0.11</td>
<td>0.99 ± 0.12</td>
<td>0.689</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.0 ± 1.16</td>
<td>10.13 ± 0.90</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>34.7 ± 5.13</td>
<td>31.1 ± 3.84</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Biopsy indication</td>
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<td>Protocol</td>
<td>69 (17)</td>
<td>54 (20)</td>
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</tr>
<tr>
<td>Per cause</td>
<td>337 (83)</td>
<td>218 (80)</td>
<td></td>
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<tr>
<td>Number of core biopsies, median (range)</td>
<td>0.098</td>
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<td></td>
</tr>
<tr>
<td>Needle gauge</td>
<td></td>
<td></td>
<td>0.397</td>
</tr>
<tr>
<td>16 G</td>
<td>134 (33)</td>
<td>104 (38)</td>
<td></td>
</tr>
<tr>
<td>18 G</td>
<td>259 (64)</td>
<td>162 (60)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>13 (3)</td>
<td>6 (2)</td>
<td></td>
</tr>
<tr>
<td>Degree of fibrosis (%)</td>
<td>n =677</td>
<td></td>
<td>0.491</td>
</tr>
<tr>
<td>Mild fibrosis</td>
<td>34 (8)</td>
<td>25 (9)</td>
<td></td>
</tr>
<tr>
<td>Moderate fibrosis</td>
<td>250 (62)</td>
<td>175 (65)</td>
<td></td>
</tr>
<tr>
<td>Severe fibrosis</td>
<td>122 (30)</td>
<td>71 (26)</td>
<td></td>
</tr>
<tr>
<td>BK positive biopsy</td>
<td>37 (9)</td>
<td>20 (7)</td>
<td>0.085</td>
</tr>
</tbody>
</table>
Supplemental Figure 1: Pre-Biopsy Mean Hgb and Hto by gender

Supplemental Figure 2: Mean Hgb change by gender
Supplemental Figure 3: Delta Hgb and Hto pre and post biopsy

Supplemental Figure 4: Post biopsy transfusions by gender

*One patient with CAD received blood transfusion without dropping Hgb> 2 g/dL.