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Bleeding Complications of Percutaneous Kidney Biopsy: Does Gender Matter?

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Key Points

- The incidence of bleeding complications after percutaneous kidney biopsies is low.
- Female sex may be associated with a greater risk for bleeding complications after percutaneous kidney biopsies.
- This association and the plausible mechanisms require further evaluation in prospective study

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Introduction

Percutaneous kidney biopsies (PKBs) are the gold standard for investigating renal parenchymal diseases. Although PKBs are generally considered low-risk procedures, particularly with the advances in real-time ultrasonography and automated spring-loaded biopsy devices, they still carry risks of bleeding of a severity that prolongs hospital stay and increases treatment costs. Management of postbiopsy bleeding may include transfusion of blood products, which represents an additional burden of sensitization, subsequently increasing the immunologic risk for future kidney transplant in individuals with kidney diseases (1,2).

A large and growing body of literature has investigated the incidence and the potential predictors of bleeding complications after PKB with significant variability in the results between these studies. Impaired renal function, lower prebiopsy hemoglobin, higher activated partial thromboplastin time/prothrombin time, larger gauge needles (14G versus 16G), a higher number of needle passes, and—more recently—female sex have all been reported as risk factors for bleeding (3–10). However, there is a paucity of studies in the Australian context. Therefore, we conducted a retrospective cohort analysis of our experience in a tertiary referral center in Australia of the incidence and predictors of bleeding complications.

Materials and Methods

This study was conducted at the Royal Brisbane and Women's Hospital (RBWH), Brisbane, Australia and included patients who underwent PKBs for clinical indications during the period of January 2017 to March 2020. Biopsies were performed by either nephrologists or advanced trainees who were supervised by a nephrologist. Minor bleeding complications were defined as either macroscopic hematuria or hematoma not requiring blood products. Major bleeding complications were the need for either blood products, radiologic or surgical invention, or admission to the intensive care unit.

PKBs were performed in accordance with the RBWH kidney biopsy protocol. Anticoagulants, antiplatelets, and other medications affecting coagulation were withheld according to Supplemental Table 1. Pre-PKB tests included full blood count, biochemistry panel, coagulation profile, and urine microscopy and sediment. If a previous ultrasound of the kidneys and urinary tract was not available, the proceduralist performed a point-of-care ultrasound (POCUS). If anatomic abnormalities of the kidneys were suspected, a formal ultrasound of the kidneys and urinary tract was requested before PKB. Patients who underwent elective PKBs recovered in the internal medicine day therapy unit and were discharged 6 hours after an uneventful PKB, whereas inpatients were observed in the renal ward and discharged at the discretion of the treating nephrologist. PKBs were performed using a 16- or 18-gauge automated spring-loaded biopsy needle under real-time ultrasound after obtaining written informed consent. For patients with an eGFR of <30 ml/min per 1.73 m^2, desmopressin (1 μg/kg body wt to a maximum dose of 20 μg) was administered half an hour before the procedure. The kidney was imaged immediately postbiopsy to assess for hemorrhage. Additional postbiopsy ultrasounds were requested if needed, *i.e.*, in case of tachycardia, hypotension, significant pain, prolonged macroscopic hematuria, or a drop in hemoglobin. After PKB, patients were asked to lie flat for 6 hours.

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Table 1. Characteristics of patients according to postbiopsy bleeding events (N=285)

Characteristics	Total (*N*=285)	No Bleeding Complications (*N*=259)	Minor Bleeding Events (hematuria, hematoma) (*N*=15)	Major Bleeding Events (blood products, admission to ICU or intervention) (*N*=11)	P Value
Age (yr), mean (SD)	51.8 (17.8)	51.6 (17.7)	46.2 (17.1)	63.2 (18.0)	0.05[a]
Sex					0.001
Male	145 (51)	141 (54)	3 (20)	1 (9)	
Female	140 (49)	118 (46)	12 (80)	10 (91)	
Native/transplant					0.21
Native	231 (81)	207 (80)	13 (87)	11 (100)	
Transplant	54 (19)	52 (20)	2 (13)	0	
If native, which side					0.25
Left	200 (88)	180 (89)	12 (92)	8 (73)	
Right	27 (12)	23 (11)	1 (8)	3 (27)	
Inpatient/outpatient					0.92
Inpatient	190 (67)	172 (67)	10 (67)	8 (73)	
Outpatient	94 (33)	86 (33)	5 (33)	3 (27)	
Systolic BP					0.13
<140 (mmHg)	182 (66)	167 (67)	8 (57)	7 (64)	
140–150 (mmHg)	71 (26)	66 (27)	4 (29)	1 (9)	
151–160 (mmHg)	15 (6)	11 (4)	2 (14)	2 (18)	
>160 (mmHg)	6 (2)	5 (2)	0	1 (9)	
Diastolic BP					0.77
<80 (mmHg)	133 (56)	120 (55)	5 (50)	8 (80)	
80–90 (mmHg)	95 (40)	88 (40)	5 (50)	2 (20)	
91–100 (mmHg)	9 (4)	9 (4)	0	0	
>100 (mmHg)	1 (0.4)	1 (0.5)	0	0	
Creatinine (μmol/L) , median (IQR)	159 (108–253)	156 (108–250)	162 (88–272)	242 (128–369)	0.11
Urea (mmol/L), median (IQR)	10.9 (7.1–16.6)	10.8 (7.1–16.6)	11.2 (6.2–14.3)	12.6 (10.5–19.1)	0.28
Hemoglobin (g/L), mean (SD)	117.3 (22.7)	118.6 (22.3)	111.2 (21.1)	95.9 (22.4)	0.003
Platelets(x10^9), mean (SD)	272.4 (97.9)	272.5 (91.5)	245.6 (80.1)	306.5 (210.8)	0.29
INR, median (IQR)	1 (1–1.1)	1 (1–1.1)	1 (0.9–1.1)	1.1 (1–1.2)	0.11
aPTT (s), median (IQR)	27 (25–30)	27 (25–30)	26 (25–29)	30 (24–33)	0.33
Median uACR (g/mol), median (IQR)	48.8 (5.2–233)	34.7 (4.9–214)	132 (21.6–234)	168 (14.3–234)	0.31
RRT					0.03
No	265 (93)	243 (94)	14 (93)	8 (73)	
Yes	20 (7)	16 (6)	1 (7)	3 (27)	
Desmopressin					0.06
No	197 (69)	182 (70)	11 (73)	4 (36)	
Yes	88 (31)	77 (30)	4 (27)	7 (64)	
Needle gauge					0.31
16	243 (85)	219 (86)	14 (93)	10 (100)	
18	38 (13)	37 (15)	1 (7)	0	
Number of passes, median (IQR)	2 (2–3)	2 (2–3)	2 (2–3)	2 (2–3)	0.64

Except where otherwise indicated, all values are provided as *n* (%). ICU, intensive care unit; IQR, interquartile range; INR, international normalized ratio; aPTT, activated partial thromboplastin time; uACR, urine albumin-creatinine ratio.
[a]P≤0.05.

Observations (*i.e.*, pulse rate and BP) were recorded every 15 minutes for 2 hours, every 30 minutes for 2 hours, and hourly for 2 hours. All urine samples were examined for macroscopic hematuria during the 6-hour period. Pain relief was prescribed at the discretion of the treating medical officer. Patients were reviewed by the renal team before mobilization.

Data were extracted by review of medical records and laboratory database. The median urinary albumin-creatinine ratio was calculated from the protein-creatinine ratio using a formulated calculation (11). The study was approved by the RBWH Research Ethics Committee (HREC/18/QRBW/258).

We evaluated the association between the explanatory variables and post-PKB bleeding using a logistic regression. In the multivariate analysis, we adjusted for those variables that were significant in the univariate analysis. A two tailed $P<0.05$ indicated statistical significance. A *post hoc* analysis was undertaken to compare the presence of medullary tissue in histology between males and females.

Table 2. Odds ratios and 95% confidence intervals for the association between potential predictors and bleeding complications

Characteristics	Minor Bleeding Events	Major Bleeding Events	
	Unadjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age	0.98 (0.95 to 1.01)	1.04 (1.00 to 1.08)	1.04 (0.99 to 1.08)
Sex			
Male	Reference	Reference	Reference
Female	4.78 (1.32 to 17.34)	11.94 (1.51 to 94.71)	8.71 (1.06 to 71.58)
Systolic BP			
<140 (mmHg)	Reference	Reference	
140–150 (mmHg)	1.27 (0.37 to 4.34)	0.36 (0.04 to 3.00)	—
151–160 (mmHg)	3.80 (0.72 to 20.1)	4.34 (0.80 to 23.41)	—
>160 (mmHg)	—	4.77 (0.49 to 46.48)	—
Diastolic BP			
<80 (mmHg)	Reference	Reference	
80–90 (mmHg)	1.36 (0.38 to 4.85)	0.34 (0.07 to 1.64)	—
91–100 (mmHg)	—	—	—
>100 (mmHg)	—	—	—
Needle gauge			
16	Reference	Reference	
18	0.42 (0.05 to 3.31)	—	—
Number of passes	1.17 (0.66 to 2.07)	1.04 (0.51 to 2.08)	—
Creatinine (μmol/L)	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)	—
Hemoglobin (g/L)	0.98 (0.96 to 1.01)	0.95 (0.92 to 0.98)	0.97 (0.93 to 1.01)
Median uACR (g/mol)	0.99 (0.99 to 1.00)	0.99 (0.97 to 1.00)	—
RRT			
No	Reference	Reference	Reference
Yes	1.08 (0.13 to 8.78)	5.70 (1.38 to 23.56)	2.30 (0.37 to 14.15)
Desmopressin			
No	Reference	Reference	Reference
Yes	0.86 (0.27 to 2.78)	4.14 (1.18 to 14.53)	1.49 (0.33 to 6.82)

OR, odds ratio; uACR, urine albumin-creatinine ratio.

Results

Our study included 285 biopsies in 273 patients (mean age 51.5 [SD, 17.8] years; males 51%). In total, 231 (81%) were native kidney and 54 (19%) were transplant biopsies. Out of the total, 20 (7%) biopsies were performed on patients on RRT, and 88 (31%) patients received desmopressin before their biopsy. The incidence of minor and major bleeding was 15 (5%) and 11 (3.8%), respectively. Seven patients (2%) developed macroscopic hematuria, four (1%) developed hematoma alone, four (4%) developed both macroscopic hematuria and hematoma, 10 (4%) required blood products, and one patient (0.35%) required both blood products and angiographic intervention. None of the transplant biopsies had major complications, but two patients had minor bleeding events.

Six patients had a small perinephric hematoma identified on POCUS performed immediately postbiopsy. A formal ultrasound confirmed the presence of hematoma in four of these patients. One patient with a small perinephric hematoma on POCUS did not have a formal ultrasound requested. Presence of hematoma on POCUS increased the length of admission by one night in two of these six patients who were meant to have a day procedure. There were four patients who had a hematoma on the formal ultrasound that was not detected on POCUS.

The baseline characteristics of our cohort can be seen in Table 1. Patients who presented with major bleeding complications were significantly older, more likely to be female, had a lower prebiopsy hemoglobin, received desmopressin prior, and/or were on RRT at the time of biopsy. Although not statistically significant, major bleeding complications were also more frequent among individuals with a higher serum creatinine, higher urinary albumin-creatinine ratio, and a systolic BP ≥160 mm Hg.

In the univariate analysis, minor bleeding complications were only associated with female sex, whereas major bleeding complications were significantly associated with female sex, older age, lower prebiopsy hemoglobin, desmopressin use, and receiving RRT at the time of biopsy (Table 2). After adjustment for desmopressin, age, hemoglobin, and KRT, females had higher odds of major bleeding events compared with males (adjusted odds ratio, 8.71; 95% CI, 1.06 to 71.58; Table 2). The results were found to be similar when the analysis was repeated after excluding transplant biopsies (Supplemental Table 2). A *post hoc* analysis was also undertaken to determine the variables that had a significant association with bleeding complications in females. The results showed no significant association with any demographic or clinical variables (the baseline characteristics of the females and the results of the *post hoc* analysis are shown in Supplemental Tables 3 and 4, respectively). Moreover, we found no significant difference in the kidney compartments sampled (cortical, medullary, or other nonrenal tissue) between males and females (Supplemental Table 5).

Discussion

Recent studies have yielded inconclusive evidence of female sex as a risk factor for bleeding complications post-PKB. In a large, retrospective cohort of 2204 native kidney biopsies, Monahan *et al.* (5) found that females were at higher risk for bleeding complications in the final adjusted analysis (odds ratio, 5.14; 95% CI, 1.47 to 18; $P=0.05$), although the association was not significant in either the unadjusted analysis or the general estimating equations. A meta-analysis reported studies that included more female participants had higher rates of erythrocyte transfusion, but no difference was found in the incidence of macroscopic hematuria (8). In our cohort, we found a significant association of female sex with both minor and major bleeding complications. It has been postulated that the increased bleeding risk in females may be due to their smaller kidney size, resulting in the biopsy needle penetrating deeper into the renal parenchyma, potentially causing more tissue and blood vessel damage (8). However, to our knowledge, this hypothesis has not been proven. Our analysis comparing the presence of medullary tissue in the histology between males and females did not support the theory, because the presence of medullary tissue was equal in the samples of both sexes. However, we acknowledge that the presence of medullary tissue is only a crude surrogate of the depth of needle penetration.

The incidence of bleeding complications, both major and minor, in our study is broadly consistent with the lower end of the range of incidence reported in the literature. The incidence of bleeding complications reported in the literature varied between 8%–57% and 0%–7% for minor and major bleeding complications, respectively (6). The potential reasons for variance in incidence may include variance of definitions and methods for defining and assessing bleeding complications across studies. For instance, studies that used routine postbiopsy renal ultrasound scans reported a higher incidence of asymptomatic hematoma (5).

There is little published data on the use of desmopressin to prevent bleeding complications in PKBs. A recent systematic review found insufficient high-quality evidence, from only two studies, and these supported the routine use of desmopressin before PKB (11). The increased incidence of bleeding complications associated with desmopressin use in this study is clinically counterintuitive, but is likely due to selection bias because desmopressin was administered only to those at higher risk of bleeding.

Our findings are limited by the modest sample size and retrospective study design. The effect size of major bleeding complications was small, and this may have limited the power of the study to demonstrate any significant association between other plausible predictors and post-PKB bleeding complications. Additionally, the study did not assess certain clinically relevant complications, such as the need for bladder catheterization due to clot retention, nor certain patient-related variables, such as body mass index. Given the retrospective nature of the study, we could not ascertain some of these variables. For example, body mass index could not be obtained because patients' weights and heights were not consistently documented in their charts.

In spite of these limitations, this study provides useful information on the incidence and risk factors of post-PKB bleeding complications from a real-world dataset in one of the largest biopsy series in Australia. The independent association between female sex and bleeding events warrants further evaluation in larger, prospective studies before changing our clinical practice. Future studies should also focus on determining the plausible reasons for this risk association.

Disclosures

P.H.F. Gois reports having consultancy agreements with, and receiving honoraria from Alexion Pharmaceuticals (for serving on a board committee for atypical hemolytic syndrome), and serving as a reviewer editor for *Frontiers in Physiology – Renal and Epithelial Physiology* and as a section editor for *International Journal of Environmental Research and Public Health*. H.G. Healy reports receiving honoraria from Amgen Australia; receiving the research funding from Amgen Australia, Bristol-Myers Squibb Pharmaceuticals, Genzyme International, and Novartis Pharmaceuticals Ltd. Australia; serving as the chief investigator of Chronic Kidney Disease Centre of Research Excellence, cochair of Chronic Kidney Disease Queensland, subeditor of *Frontiers in Physiology – Renal and Epithelial Physiology*, and director for Kidney Research Foundation. A. Mallett reports serving as the local site trial investigator for Achillion, Dicerna, Novotech, Reata, and Sanofi-Genzyme; having a Metro North Hospital and Health Service Clinical Research Fellowship and Royal Australasian College of Physicians Jacquot Research Establishment Fellowship; serving as a scientific advisor for, or member of, Otsuka; and receiving research funding from Otsuka and Sanofi-Genzyme. All remaining authors have nothing to disclose.

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Author Contributions

A. Anpalahan and P.H.F. Gois were responsible for investigation and methodology, and wrote the original draft; A. Anpalahan, P.H.F. Gois, and E. Malacova were responsible for formal analysis; A. Anpalahan and E. Malacova were responsible for data curation; P.H.F. Gois conceptualized the study, was responsible for resources, and provided supervision; P.H.F. Gois and H.G. Healy were responsible for funding acquisition; E. Malacova was responsible for software; and all authors reviewed and edited the manuscript.

Supplemental Material

This article contains the following supplemental material online at http://kidney360.asnjournals.org/lookup/suppl/doi:10.34067/KID.0002432021/-/DCSupplemental.

Supplemental Table 1. Guidance on anticoagulants, antiplatelets and other medications affecting coagulation prior to percutaneous kidney biopsy .

Supplemental Table 2. Odds ratios (OR) and 95% confidence intervals (CIs) for the association between potential predictors and bleeding complications in native kidney biopsies.

Supplemental Table 3. Descriptive characteristics of female patients according to minor and major bleeding events (N=140).

Supplemental Table 4. Odds ratios (OR) and 95% confidence intervals for the association between potential predictors and bleeding complications in females.

Supplemental Table 5. Break down of the type of kidney tissue present in the histology between males and females.

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Supplementary tables:

Supplementary Table 1: Guidance on anticoagulants, antiplatelets and other medications affecting coagulation prior to percutaneous kidney biopsy

7 days prior to percutaneous kidney biopsy*	5 days prior to percutaneous renal biopsy+	72 hours prior to percutaneous kidney biopsy+	24 hours prior to percutaneous kidney biopsy	6 hours prior to percutaneous kidney biopsy
Withhold aspirin, clopidogrel, ticagrelor, omega-3-fatty acids (e.g. krill oil, fish oil)	Withhold warfarin	Withhold direct oral anticoagulants (e.g. apixaban, rivaroxaban, dabigatran)	Withhold low molecular weight heparin (e.g. enoxaparin), No non-steroidal anti-inflammatories	Withhold unfractioned heparin infusion

* Decision regarding continuation of aspirin in patients at high risk for a cardiovascular event (i.e. within 3 months of bare metal coronary stent or 12 months of drug eluted stent, symptomatic myocardial ischemia, previous ischaemic stroke and peripheral vascular disease including peripheral stent) were individualised (risks vs. benefits). Non-urgent biopsies within 3 months of bare metal coronary stent or 12 months of drug eluted stent were delayed whenever appropriate.

+ Bridging anticoagulation was indicated in patients with mechanical mitral valve, mechanical aortic valve and additional stroke risk factors such as antiphospholipid syndrome, an embolic event within 3 months or a previous thromboembolic event with interruption of anticoagulation.

Supplementary Table 2: Odds ratios (OR) and 95% confidence intervals (CIs) for the association between potential predictors and bleeding complications in native kidney biopsies

Characteristics	**Minor Bleeding Events**	**Major Bleeding Events**	
	Unadjusted OR (95% CI)	**Unadjusted (95% CI)**	**Adjusted OR (95% CI)**
Age	0.97 (0.94-1.00)	1.04 (1.00-1.08)	1.03 (0.99-1.07)
Gender			
Male	Ref	Ref	Ref
Female	7.29 (1.58-33.73)	13.26 (1.67-105.49)	9.52 (1.15-78.60)
Systolic BP			
<140	Ref	Ref	
140-150	1.17 (0.30-4.58)	0.44 (0.05-3.71)	-
151-160	2.55 (0.28-23.35)	5.84 (1.02-33.42)	-
>160	-	5.11 (0.50-51.91)	-
Diastolic BP			
<80	Ref	Ref	
80-90	1.43 (0.34-5.90)	0.36 (0.07-1.73)	-
91-100	-	-	-

>100	-	-	-
Needle gauge			
16	Ref	Ref	
18	0.69 (0.09-5.56)	-	-
Number of passes	0.91 (0.47-1.78)	0.94 (0.45-1.93)	-
Creatinine	1.00 (0.99-1.00)	1.00 (0.99-1.00)	-
Hemoglobin	0.98 (0.96-1.01)	0.95 (0.91-0.98)	0.96 (0.92-1.00)
Median uACR	0.99 (0.99-1.00)	0.99 (0.99-1.00)	-
KRT			
No	Ref	Ref	Ref
Yes	1.48 (0.18-12.48)	6.68 (1.55-28.75)	2.04 (0.31-13.47)
DDAVP			
No	Ref	Ref	Ref
Yes	1.06 (0.32-3.59)	4.19 (1.18-14.83)	1.41 (0.30-6.54)

uACR: urine albumin:creatinine ratio; KRT: Kidney replacement therapy

Supplementary Table 3: Descriptive characteristics of female patients according to minor and major bleeding events (N=140)

Characteristics	**Total** N=140 N (%)	**No bleeding complications** N=118 N (%)	**Minor bleeding events (hematuria, hematoma)** N=12 N (%)	**Major bleeding events (blood products, admission to ICU or intervention)** N=10 N (%)	**P-value**
Age (Mean, SD)	51.1 (17.7)	51.2 (17.6)	41.4 (13.9)	61.8 (18.4)	0.0258
Native/Transplant					
Native	137 (40.4)	115 (97.5)	12 (100.0)	10 (100.0)	0.751
Transplant	3 (0.9)	2 (2.5)	0	0	
If Native, which side					0.281
Left	94 (86.2)	77 (87.5)	10 (90.9)	7 (70.0)	
Right	15 (13.8)	11 (12.5)	1 (9.1)	3 (30.0)	
Inpatient/Outpatient					0.632
Inpatient	129 (92.1)	108 (91.5)	11 (91.7)	10 (100.0)	
Outpatient	11 (7.9)	10 (8.5)	1 (8.3)	0	
Systolic BP					0.068
<140	90 (67.2)	77 (68.1)	7 (63.6)	6 (60.0)	

140-150	35 (26.1)	30 (26.6)	4 (36.4)	1 (10.0)	
151-160	7 (5.2)	5 (4.4)	0	2 (20.0)	
>160	2 (1.5)	1 (0.9)	0	1 (10.0)	
Diastolic BP					0.747
<80	70 (59.3)	59 (57.8)	4 (57.1)	7 (77.8)	
80-90	43 (36.4)	38 (37.3)	3 (42.9)	2 (22.2)	
91-100	5 (4.2)	5 (4.9)	0	0	
Creatinine (Median, IQR)	146.5 (94-219.5)	141 (95-214)	139 (87-294.5)	230.5 (128-369)	0.663
Urea (Median, IQR)	10.5 (6.9-14.3)	10.4 (6.9-14.0)	9.1 (5.8-13.3)	12.6 (10.5-19.1)	0.131
Hemoglobin (Mean, SD)	111.2 (20.1)	112.1 (19.4)	113.6 (21.7)	97 (23.3)	0.066
Platelets (Mean, SD)	293.4 (105.1)	295.1 (92.4)	256.7 (85.9)	318 (218.5)	0.363
INR (Median, IQR)	1 (0.9-1.1)	1 (0.9-1.1)	1 (0.9-1.1)	1.1 (1-1.2)	0.354
aPTT (Mean, SD)	27.6 (4.0)	27.5 (4.0)	27.4 (2.5)	29 (5.2)	0.526
Median uACR (Median, IQR)	68.4 (5.1-231.5)	48.8 (4.9-224)	121.5 (18.5-211)	200 (31.6-234)	0.455
Kidney replacement therapy					0.013
No	130 (92.9)	112 (94.9)	11 (91.7)	7 (70.0)	
Yes	10 (7.1)	6 (5.1)	1 (8.3)	3 (30.0)	

DDAVP					0.123
No	96 (68.6)	83 (70.3)	9 (75.0)	4 (40.0)	
Yes	44 (31.4)	35 (29.7)	3 (25.0)	6 (60.0)	
Needle gauge					0.516
16	123 (36.3)	103 (88.0)	11 (91.7)	9 (100.0)	
18	15 (4.4)	14 (12.0)	1 (8.3)	0	
Number of passes (Median, IQR)	2 (2-3)	2 (2-3)	2 (2-3.5)	2.5 (2-3)	0.801
Number of cores (Mean, SD)	2.0 (0.7)	1.9 (0.7)	2.1 (0.7)	1.9 (1.0)	0.811

p-values are based on chi-squared for categorical data, ANOVA for normally distributed variables when comparing three groups, K-sample equality of medians test for non-normally distributed variables.

Supplementary Table 4: Odds ratios (OR) and 95% confidence intervals for the association between potential predictors and bleeding complications in females.

Characteristics	**Minor bleeding events (hematuria, hematoma)**		**Major bleeding events (blood products, admission to ICU or intervention)**	
	Unadjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Unadjusted (95% CI)**	**Adjusted OR (95% CI)**
DDAVP				
No	Ref		Ref	
Yes	0.79 (0.20-3.10)	-	3.56 (0.65-13.39)	-
Age	0.97 (0.93-1.00)	-	1.04 (0.99-1.08)	-

Systolic BP				
<140	Ref		Ref	
140-150	1.47 (0.40-5.38)	-	0.43 (0.05-3.70)	-
151-160	-	-	5.13 (0.82-32.27)	-
>160	-	-	12.83 (0.71-231.75)	-
Diastolic BP				
<80	Ref		Ref	
80-90	1.16 (0.25-5.49)	-	0.44 (0.09-2.25)	-
91-100	-	-	-	-
Needle gauge				
16	Ref		Ref	
18	0.67 (0.08-5.58)	-	-	-
Number of passes	1.26 (0.68-2.34)	-	1.20 (0.59-2.42)	-
Creatinine	1.00 (1.00-1.00)	-	1.00 (1.00-1.00)	-
Hemoglobin	1.00 (0.97-1.04)	-	0.96 (0.92-0.99)	0.97 (0.93-1.01)
Median uACR	1.00 (1.00-1.00)	-	1.00 (1.00-1.00)	-
Kidney replacement therapy				
No	Ref		Ref	Ref

Yes	1.70 (0.19-15.40)	-	8 (1.64-38.93)	3.83 (0.62-23.56)
Number of Aspirin taken	-	-	**-**	-
Taken Aspirin				
No	Ref			
Yes	1.71 (0.21-14.08)	-	**-**	-

Supplementary Table 5: Break down of the type of kidney tissue present in the histology between males and females

Kidney tissue samples*	**Male N (%)**	**Females N (%)**
Medulla	3 (2)	1 (0.7)
Cortex	69 (47.5)	66 (47.1)
Medulla and Cortex	72 (49.1)	72 (51.4)
Non kidney tissue	1 (0.7)	1 (0.7)

*Fisher's exact test p-value=0.862

Supplementary tables:

Supplementary Table 1: Guidance on anticoagulants, antiplatelets and other medications affecting coagulation prior to percutaneous kidney biopsy

7 days prior to percutaneous kidney biopsy*	5 days prior to percutaneous renal biopsy+	72 hours prior to percutaneous kidney biopsy+	24 hours prior to percutaneous kidney biopsy	6 hours prior to percutaneous kidney biopsy
Withhold aspirin, clopidogrel, ticagrelor, omega-3-fatty acids (e.g. krill oil, fish oil)	Withhold warfarin	Withhold direct oral anticoagulants (e.g. apixaban, rivaroxaban, dabigatran)	Withhold low molecular weight heparin (e.g. enoxaparin), No non-steroidal anti-inflammatories	Withhold unfractioned heparin infusion

* Decision regarding continuation of aspirin in patients at high risk for a cardiovascular event (i.e. within 3 months of bare metal coronary stent or 12 months of drug eluted stent, symptomatic myocardial ischemia, previous ischaemic stroke and peripheral vascular disease including peripheral stent) were individualised (risks vs. benefits). Non-urgent biopsies within 3 months of bare metal coronary stent or 12 months of drug eluted stent were delayed whenever appropriate.

+ Bridging anticoagulation was indicated in patients with mechanical mitral valve, mechanical aortic valve and additional stroke risk factors such as antiphospholipid syndrome, an embolic event within 3 months or a previous thromboembolic event with interruption of anticoagulation.

Supplementary Table 2: Odds ratios (OR) and 95% confidence intervals (CIs) for the association between potential predictors and bleeding complications in native kidney biopsies

Characteristics	**Minor Bleeding Events**	**Major Bleeding Events**	
	Unadjusted OR (95% CI)	**Unadjusted (95% CI)**	**Adjusted OR (95% CI)**
Age	0.97 (0.94-1.00)	1.04 (1.00-1.08)	1.03 (0.99-1.07)
Gender			
Male	Ref	Ref	Ref
Female	7.29 (1.58-33.73)	13.26 (1.67-105.49)	9.52 (1.15-78.60)
Systolic BP (mmHg)			
<140	Ref	Ref	
140-150	1.17 (0.30-4.58)	0.44 (0.05-3.71)	-
151-160	2.55 (0.28-23.35)	5.84 (1.02-33.42)	-
>160	-	5.11 (0.50-51.91)	-
Diastolic BP (mmHg)			
<80	Ref	Ref	
80-90	1.43 (0.34-5.90)	0.36 (0.07-1.73)	-
91-100	-	-	-

>100	-	-	-
Needle gauge			
16	Ref	Ref	
18	0.69 (0.09-5.56)	-	-
Number of passes	0.91 (0.47-1.78)	0.94 (0.45-1.93)	-
Creatinine (µmol/L)	1.00 (0.99-1.00)	1.00 (0.99-1.00)	-
Hemoglobin (g/L)	0.98 (0.96-1.01)	0.95 (0.91-0.98)	0.96 (0.92-1.00)
Median uACR (g/mol)	0.99 (0.99-1.00)	0.99 (0.99-1.00)	-
KRT			
No	Ref	Ref	Ref
Yes	1.48 (0.18-12.48)	6.68 (1.55-28.75)	2.04 (0.31-13.47)
DDAVP			
No	Ref	Ref	Ref
Yes	1.06 (0.32-3.59)	4.19 (1.18-14.83)	1.41 (0.30-6.54)

uACR: urine albumin:creatinine ratio; KRT: Kidney replacement therapy

Supplementary Table 3: Descriptive characteristics of female patients according to minor and major bleeding events (N=140)

Characteristics	**Total** N=140 N (%)	**No bleeding complications** N=118 N (%)	**Minor bleeding events (hematuria, hematoma)** N=12 N (%)	**Major bleeding events (blood products, admission to ICU or intervention)** N=10 N (%)	**P-value**
Age (Mean, SD)	51.1 (17.7)	51.2 (17.6)	41.4 (13.9)	61.8 (18.4)	0.0258
Native/Transplant					
Native	137 (40.4)	115 (97.5)	12 (100.0)	10 (100.0)	0.751
Transplant	3 (0.9)	2 (2.5)	0	0	
If Native, which side					0.281
Left	94 (86.2)	77 (87.5)	10 (90.9)	7 (70.0)	
Right	15 (13.8)	11 (12.5)	1 (9.1)	3 (30.0)	
Inpatient/Outpatient					0.632
Inpatient	129 (92.1)	108 (91.5)	11 (91.7)	10 (100.0)	
Outpatient	11 (7.9)	10 (8.5)	1 (8.3)	0	
Systolic BP (mmHg)					0.068
<140	90 (67.2)	77 (68.1)	7 (63.6)	6 (60.0)	

140-150	35 (26.1)	30 (26.6)	4 (36.4)	1 (10.0)	
151-160	7 (5.2)	5 (4.4)	0	2 (20.0)	
>160	2 (1.5)	1 (0.9)	0	1 (10.0)	
Diastolic BP (mmHg)					0.747
<80	70 (59.3)	59 (57.8)	4 (57.1)	7 (77.8)	
80-90	43 (36.4)	38 (37.3)	3 (42.9)	2 (22.2)	
91-100	5 (4.2)	5 (4.9)	0	0	
Creatinine (µmol/L) (Median, IQR)	146.5 (94-219.5)	141 (95-214)	139 (87-294.5)	230.5 (128-369)	0.663
Urea (mmol/L) (Median, IQR)	10.5 (6.9-14.3)	10.4 (6.9-14.0)	9.1 (5.8-13.3)	12.6 (10.5-19.1)	0.131
Hemoglobin (g/L) (Mean, SD)	111.2 (20.1)	112.1 (19.4)	113.6 (21.7)	97 (23.3)	0.066
Platelets ($x10^9$) (Mean, SD)	293.4 (105.1)	295.1 (92.4)	256.7 (85.9)	318 (218.5)	0.363
INR (Median, IQR)	1 (0.9-1.1)	1 (0.9-1.1)	1 (0.9-1.1)	1.1 (1-1.2)	0.354
aPTT (s) (Mean, SD)	27.6 (4.0)	27.5 (4.0)	27.4 (2.5)	29 (5.2)	0.526
Median uACR (g/mol) (Median, IQR)	68.4 (5.1-231.5)	48.8 (4.9-224)	121.5 (18.5-211)	200 (31.6-234)	0.455
Kidney replacement therapy					0.013

No	130 (92.9)	112 (94.9)	11 (91.7)	7 (70.0)	
Yes	10 (7.1)	6 (5.1)	1 (8.3)	3 (30.0)	
DDAVP					0.123
No	96 (68.6)	83 (70.3)	9 (75.0)	4 (40.0)	
Yes	44 (31.4)	35 (29.7)	3 (25.0)	6 (60.0)	
Needle gauge					0.516
16	123 (36.3)	103 (88.0)	11 (91.7)	9 (100.0)	
18	15 (4.4)	14 (12.0)	1 (8.3)	0	
Number of passes (Median, IQR)	2 (2-3)	2 (2-3)	2 (2-3.5)	2.5 (2-3)	0.801
Number of cores (Mean, SD)	2.0 (0.7)	1.9 (0.7)	2.1 (0.7)	1.9 (1.0)	0.811

p-values are based on chi-squared for categorical data, ANOVA for normally distributed variables when comparing three groups, K-sample equality of medians test for non-normally distributed variables.

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	Unadjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Unadjusted (95% CI)**	**Adjusted OR (95% CI)**
DDAVP				
No	Ref		Ref	

Yes	0.79 (0.20-3.10)	-	3.56 (0.65-13.39)	-
Age	0.97 (0.93-1.00)	-	1.04 (0.99-1.08)	-
Systolic BP (mmHg)				
<140	Ref		Ref	
140-150	1.47 (0.40-5.38)	-	0.43 (0.05-3.70)	-
151-160	-	-	5.13 (0.82-32.27)	-
>160	-	-	12.83 (0.71-231.75)	-
Diastolic BP (mmHg)				
<80	Ref		Ref	
80-90	1.16 (0.25-5.49)	-	0.44 (0.09-2.25)	-
91-100	-	-	-	-
Needle gauge				
16	Ref		Ref	
18	0.67 (0.08-5.58)	-	-	-
Number of passes	1.26 (0.68-2.34)	-	1.20 (0.59-2.42)	-
Creatinine (µmol/L)	1.00 (1.00-1.00)	-	1.00 (1.00-1.00)	-
Hemoglobin (g/L)	1.00 (0.97-1.04)	-	0.96 (0.92-0.99)	0.97 (0.93-1.01)
Median uACR (g/mol)	1.00 (1.00-1.00)	-	1.00 (1.00-1.00)	-

Kidney replacement therapy				
No	Ref		Ref	Ref
Yes	1.70 (0.19-15.40)	-	8 (1.64-38.93)	3.83 (0.62-23.56)
Number of Aspirin taken	-	-	**-**	-
Taken Aspirin				
No	Ref			
Yes	1.71 (0.21-14.08)	-	**-**	-

Supplementary Table 5: Break down of the type of kidney tissue present in the histology between males and females

Kidney tissue samples*	**Male** **Number (%)**	**Females** **Number (%)**
Medulla	3 (2)	1 (0.7)
Cortex	69 (47.5)	66 (47.1)
Medulla and Cortex	72 (49.1)	72 (51.4)
Non kidney tissue	1 (0.7)	1 (0.7)

*Fisher's exact test p-value=0.862