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Predictors of perirenal haematoma post-percutaneous ultrasound-guided renal biopsy

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Abstract

Objective: To perform a prospective study to determine the risk factors associated with perirenal haematoma development after percutaneous renal biopsy (PRB).

Methods: This multivariate prospective study collected demographic and clinical data from all consecutive adult patients that underwent real-time ultrasound-guided PRB of native kidneys. All biopsies were performed by two well-trained ultrasound physicians using 16G biopsy needles. Routine renal ultrasounds were performed within 12–24 h after biopsies in order to observe post-biopsy perirenal haematoma formation. Patients were stratified based on the occurrence of post-biopsy haematoma development.

Results: This prospective study enrolled 218 patients and stratified them into a haematoma group ($n = 126$) and a non-haematoma group ($n = 92$). Binary logistic regression analysis identified female patients (odds ratio [OR] 1.990; 95% confidence interval [CI] 1.125, 3.521), patients with a body mass index (BMI) $\geq$28 kg/m^2 (OR 2.660; 95% CI 1.097, 6.449) and patients with immediate post-biopsy active bleeding (IPAB) (OR 2.572; 95% CI 1.422, 4.655) as being more likely to have perirenal haematoma after real-time ultrasound guided PRB of native kidneys.

Conclusion: Female sex, a BMI $\geq$28 kg/m^2 and IPAB were risk factors for perirenal haematoma after real-time ultrasound-guided PRB of native kidneys.

Keywords

Percutaneous renal biopsy, perirenal haematoma, immediate post-biopsy active bleeding, body mass index, sex

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Introduction

Iversen and Brun were the first to report a successful renal biopsy in 1951.[1] At present, percutaneous renal biopsy (PRB) is considered a low-risk procedure and an essential technique that can provide important information to nephrologists during patient evaluation, research and clinical practice.[2] Development of ultrasound imaging technology and the application of automatic biopsy needles have resulted in a low occurrence of complications after renal biopsy.[3–10] In particular, the rate of serious complications, such as a need for angiographic intervention, nephrectomy or death, is $<1\%$.[2] However, bleeding complications do occur and the incidence was up to 30% or more in some research.[11–18] With improving social awareness, patients expect reduced procedure-related complications and costs, without compromising the results. Therefore, a successful PRB should not only ensure that sufficient material for an adequate diagnosis is obtained, but it should also minimize possible complications. Factors contributing to perirenal haematoma after PRB need to be identified. It is very important to determine which patients will develop a perirenal haematoma after performing PRB of native kidneys.

Many factors are related to the formation of haematoma after PRB. Previous studies have reached different conclusions.[19–21] One study reported that elevated creatinine and baseline blood pressure were associated with bleeding after PRB.[19] Another study found that inpatient status and thrombocytopaenia were the only significant risk factors for complications.[20] In another large retrospective study, low platelet count was reported to be the most important single risk factor in predicting bleeding post PRB.[21] Currently, which factors are related to the occurrence of perirenal haematoma after PRB remains controversial.

The objective of this research was to assess the factors that have a relationship with the incidence of perirenal haematoma after PRB in a prospective cohort of patients that underwent real-time ultrasound-guided automated PRB of native kidneys in a single ultrasonography centre.

Patients and methods

Patient population

This prospective study enrolled all consecutive adult patients that underwent real-time ultrasound-guided percutaneous native renal biopsy at the Department of Ultrasonography, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang Province, China, between August 2016 and April 2017. All patient details have been de-identified. All biopsies were taken by two well-trained ultrasound physicians that conduct >1000 biopsies each year (S.X. & Q.L.). In this current study, the nephrologists decided the indications for PRB and it was indicated due to the need for diagnosis in the following situations: nephrotic syndrome, nephritic syndrome, renal failure of unknown aetiology, asymptomatic urinary abnormalities. Paediatric patients, transplant kidney biopsies, kidney neoplasms biopsies, solitary kidney, abnormal kidney anatomy and patients with abnormal coagulation parameters were all excluded. The reporting of this study conforms with STROBE guidelines.[22]

This study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University (no. YJ2016-061-01; 2016.6.6). All patients provided written informed consent.

Data collection

The following information was analysed for each patient before the procedure: age, sex, height, weight, serum creatinine (SCr), blood urea nitrogen (BUN), uric acid, haemoglobin (Hb), platelet count, history of

hypertension, history of diabetes mellitus, estimated glomerular filtration rate (eGFR; using the Modification of Diet in Renal Disease formula, kidney function was determined using an abbreviated equation developed using data from the Modification of Diet in Renal Disease study to estimate glomerular filtration rate), 24-h urinary protein, total cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C). The SCr, Bun, uric acid, 24-h urinary protein, total cholesterol, triglyceride, LDL-C and HDL-C were measured using an AU5800 Series Clinical Automatic Chemistry Analyzer (Beckman, Shanghai, China). The Hb and platelet count were measured using a BC6800 Series Automatic blood cell analyzer (Mindray, Shenzhen, China). Information collected at the time of biopsy included systolic and diastolic blood pressures, peak velocity of renal artery (PVRA), peak velocity of arcuate artery (PVAA) and renal parenchymal thickness (RPT).

Renal biopsy procedure

Patients stopped anticoagulation therapy appropriately and antiplatelets use at least 5 days prior to the biopsy. All patients had normal prothrombin time (PTT), prothrombin activity (PTA) and international normalized ratio (INR) prior to the procedure. The systolic and diastolic arterial pressures were below 160 mmHg and 90mmHg at the time of the procedure, respectively. When perirenal haematoma was found post-biopsy, coagulation drugs or vasoconstrictors were considered for use by nephrologists.

All renal biopsies were performed in an ultrasonography laboratory using a HI VISION Ascendus ultrasound system (Hitachi Aloka Medical Ltd., Tokyo, Japan) and a C715 convex probe (1–5 MHz; Hitachi Aloka Medical Ltd.). All data were collected with the same equipment. A Tru-Core^{TM} II Automatic Biopsy Instrument with an MCXS2016TY biopsy needle (16G; Disposable Automatic Argon Medical Devices Inc., Plano, TX, USA) was used. Patients were positioned in the prone position with their abdomen on a firm pillow. They were required to remain still during the procedure. The left kidney or right kidney was selected randomly by tossing coins. The lower lateral pole of the kidney was selected for biopsy. After location, the place of needle insertion was marked on the skin. Routine sterilization and draping were performed. The probe was covered with a sterile cover and sterile jelly applied. The operator conducted the procedure with the left hand holding the ultrasound probe and the right hand holding the biopsy gun. A solution of 2% lidocaine was injected under real-time ultrasound guidance from the target skin to the renal capsule. When the biopsy needle reached the lower pole of the kidney capsule, the patient was told to hold their breath. The biopsy gun was fired and the needle tip was confirmed in the kidney. Then the biopsy needle was removed quickly from the kidney. Two cores of renal tissue were obtained to ensure an adequate sample for diagnosis. After the procedure, Doppler ultrasonography was routinely performed immediately to observe any signs of active bleeding (Figure 1). The occurrence of bleeding was recorded for each patient.

Post-biopsy evaluation of complications

Following the PRB, a bandage was applied to the flank and the patient was required to lay in bed flat on their back for 6 h. They then remained in bed for 24 h in the nephrology ward. Routine renal ultrasounds were performed within 12–24 h after biopsies to observe any perirenal haematoma formation (Figure 2). Other outcomes due to the renal biopsy were recorded including embolization, surgery or death.

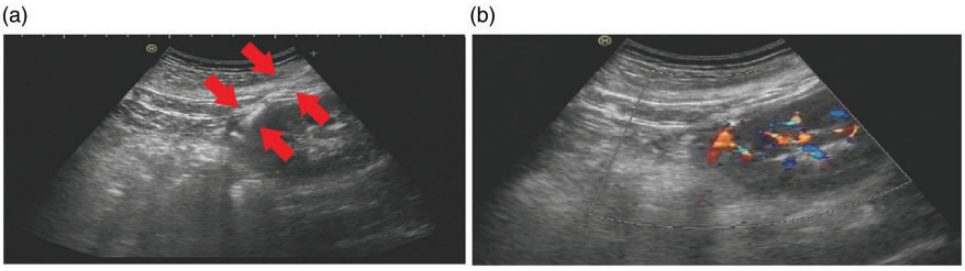

Figure 1. Representative Doppler ultrasonography images showing the puncture needle within the kidney (red arrows) (A) and active bleeding along the needle path toward the ultrasound probe after the puncture needle was withdrawn from the kidney during percutaneous renal biopsy (B). The colour version of this figure is available at: http://imr.sagepub.com.

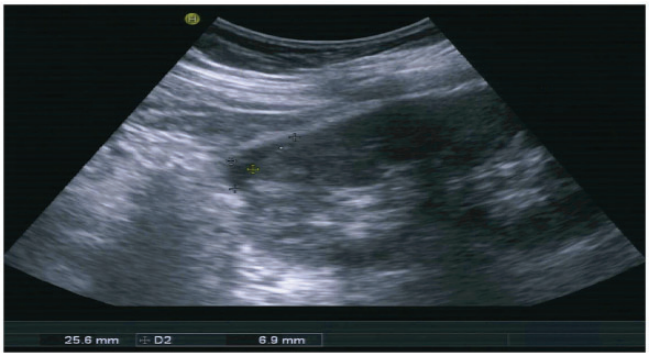

Figure 2. Representative routine ultrasonography image showing a perirenal haematoma within 12–24 h after percutaneous renal biopsy.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Data are presented as mean ± SD, median (interquartile range) or absolute frequency. χ^2-test was used to compare categorical data. Student's *t*-test was used to compare continuous data. Binary logistic regression analysis was used to determine the effect of various factors on the formation of haematoma. The factors included in this analysis were sex, age, body mass index (BMI), SCr, BUN, uric acid, Hb, platelet count, history of hypertension, history of diabetes mellitus, eGFR, 24-h urinary protein, total cholesterol, triglyceride, LDL-C, HDL-C, PVRA, PVAA, immediate post-biopsy active bleeding (IPAB) and RPT. A *P*-value <0.05 was considered statistically significant.

Results

This prospective study enrolled 218 patients that underwent real-time ultrasound-guided automated PRB of native kidneys. Demographic and clinical characteristics of the overall study cohort are shown in Table 1. The mean ± SD BMI of the patients was $24.30 \pm 3.71\,kg/m^2$ (range, 16.45–39.26 kg/m^2). There were 109 of 218 (50.0%) patients with a BMI $\geq 24\,kg/m^2$ and 31 of 218 (14.2%) patients had a BMI

Table 1. Baseline demographic and clinical data of patients ($n = 218$) that underwent real-time ultrasound-guided automated percutaneous renal biopsy of native kidney.

Characteristic	Study cohort $n = 218$
Haematoma:non-haematoma	126 (57.8):92 (42.2)
Left kidney:right kidney	94 (43.1):124 (56.9)
PTT, s	13.13 ± 0.81
PTA, %	103.03 ± 13.57
INR	0.99 ± 0.08
Sex, male:female	104 (47.7):114 (52.3)
Age, years	45.7 ± 14.2
SCr , μmol/l	81.5 (61.0–112.3)
BUN, mmol/l	7.1 ± 4.6
Uric acid, μmol/l	380.6 ± 92.3
Total cholesterol, mmol/l	6.3 ± 2.5
Triglyceride, mmol/l	2.6 ± 2.3
HDL-C, mmol/l	1.2 ± 0.4
LDL-C, mmol/l	3.6 ± 1.8
Hb, g/l	125.4 ± 23.7
History of hypertension, yes:no	102:116
History of diabetes mellitus, yes:no	28:190
IPAB, yes:no	85:133
PVRA, cm/s	78.5 ± 29.2
PVAA, cm/s	25.3 ± 10.6
eGFR, ml/min/1.73m^2	81.9 ± 33.6
RPT, mm	7.0 ± 1.5
24-h urinary protein, mg/dl	159.6 (74.3–289.5)
BMI, ≥ 28:< 28 kg/m^2	31:187
Platelet count, $\times 10^9$/l	243.3 ± 73.7

Data presented as mean $\pm$ SD, median (interquartile range) or n of patients (%).

No significant between-group differences ($P \geq 0.05$); categorical data compared using χ^2-test; continuous data compared using Student's t-test.

PTT, prothrombin time; PTA, prothrombin activity; INR, international normalized ratio; SCr, serum creatinine; BUN, blood urea nitrogen; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Hb, haemoglobin; IPAB, immediate post-biopsy active bleeding; PVRA, peak velocity of renal artery; PVAA, peak velocity of arcuate artery; eGFR, estimated glomerular filtration rate; RPT, renal parenchymal thickness; BMI, body mass index.

$\geq 28\,\text{kg/m}^2$. The platelet counts of most patients were in the normal range (125–350 $\times 10^9$/l), while only nine patients had platelet counts $< 125 \times 10^9$/l.

The patients were stratified according to the occurrence of post-biopsy haematoma ($n = 126$) and the clinical and demographic data for the two groups are presented in Tables 2 and 3. There were no significant differences between the haematoma and non-haematoma groups in terms of age, SCr, BUN, uric acid, total cholesterol, triglyceride, HDL-C, LDL-C, Hb, PVRA, PVAA, eGFR, RPT, 24-h urinary protein and platelet count. There were no significant differences in history of hypertension or history of diabetes mellitus between the haematoma and non-haematoma groups. There were significant differences in IPAB ($P = 0.004$) and BMI ($P = 0.046$) between the haematoma and non-haematoma groups. In the sex comparison between the two groups, the non-significant P-value ($P = 0.069$) was close to 0.05 so sex was also included in the binary logistic regression analysis. The binary logistic regression analysis found that BMI, IPAB and sex had a statistical relationship with the occurrence of perirenal haematoma after PRB (Table 4).

Perirenal haematoma was the only complication observed. There were no occurrences of embolization, surgery or death due to the biopsy.

Discussion

Most of the published studies about bleeding complications after percutaneous ultrasound-guided renal biopsy were retrospective analyses,[2] while this current study was a multivariate prospective analysis. In this current study, all biopsies were performed by only two sonographers and all biopsy needles were 16G. This helped to avoid the impact of different operators (variable experience) or different types of biopsy needles when analysing the risk factors for post-biopsy

Table 2. Baseline continuous demographic and clinical data of patients ($n = 218$) that underwent real-time ultrasound-guided automated percutaneous renal biopsy of native kidney stratified according to the development of post-biopsy haematoma.

Characteristic	Non-haematoma group $n = 92$	Haematoma group $n = 126$
Age, years	46.66 ± 14.83	44.92 ± 13.74
SCr, μmol/l	109.86 ± 102.84	139.59 ± 190.87
BUN, mmol/l	6.84 ± 3.26	7.23 ± 5.45
Uric acid, μmol/l	387.47 ± 94.32	375.44 ± 90.74
Total cholesterol, mmol/l	6.09 ± 2.44	6.42 ± 2.47
Triglyceride, mmol/l	2.56 ± 2.53	2.62 ± 2.11
HDL-C, mmol/l	1.15 ± 0.35	1.23 ± 0.46
LDL-C, mmol/l	3.42 ± 1.59	3.75 ± 1.94
Hb, g/l	126.81 ± 24.08	124.38 ± 23.52
PVRA, cm/s	79.69 ± 29.17	77.70 ± 29.23
PVAA, cm/s	25.49 ± 10.66	25.12 ± 10.59
eGFR, ml/min/1.73 m^2	82.94 ± 31.27	81.10 ± 35.26
RPT, mm	6.92 ± 1.53	7.07 ± 1.51
24-h urinary protein, mg/dl	300.08 ± 482.20	296.95 ± 503.88
Platelet count, $\times 10^9$/l	246.43 ± 72.96	240.98 ± 74.41

Data presented as mean ± SD.

No significant between-group differences ($P \geq 0.05$); continuous data compared with Student's *t*-test.

SCr, serum creatinine; BUN, blood urea nitrogen; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Hb, haemoglobin; PVRA, peak velocity of renal artery; PVAA, peak velocity of arcuate artery; eGFR, estimated glomerular filtration rate; RPT, renal parenchymal thickness.

Table 3. Baseline categorical demographic and clinical data of patients ($n = 218$) that underwent real-time ultrasound-guided automated percutaneous renal biopsy of native kidney stratified according to the development of post-biopsy haematoma.

Characteristic		Non-haematoma group $n = 92$	Haematoma group $n = 126$	Statistical analyses[a]
History of hypertension	Yes	39	63	NS
	No	53	63	
History of diabetes mellitus	Yes	13	15	NS
	No	79	111	
BMI, kg/m^2	≥28	8	23	$P = 0.046$
	<28	84	103	
Sex	Female	41	73	NS
	Male	51	53	
IPAB	Yes	25	60	$P = 0.004$
	No	67	66	

Data presented as *n* of patients.

[a]Categorical data compared with χ^2-test; NS, no significant between-group difference ($P \geq 0.05$).

BMI, body mass index; IPAB, immediate post-biopsy active bleeding.

haematoma. Twenty potential risk factors were included in this current study, including haemodynamic factors that were analysed for the first time to the best of our knowledge.

Perirenal haematoma occurred in 126 of 218 (57.8%) patients after PRB in the current study. This would appear to be a high rate, but it was reasonable. First, a post-biopsy ultrasound examination was carried out for every patient that underwent PRB in this current study, whereas in other research, an ultrasound examination was only carried out for patients with symptoms.[23] Secondly, the rate of perirenal haematoma is highly associated with the timing of the post-biopsy ultrasound examination. For example, a previous study demonstrated that only 6% of biopsies had haematoma when an ultrasound examination was carried out immediately after the PRB.[24] Whereas, another study found that 32% of patients had a haematoma when the ultrasound examination was carried out 7–8 h after the PRB.[25] When the ultrasound examination was carried out 18 h after the PRB, 37.8% of patients had a haematoma.[13] If the ultrasound examination or a computerized tomography scan were undertaken at 24–72 h after the PRB, 70% to >90% of patients experienced a haematoma.[26,27] In this current study, the ultrasound examination was performed 12–24 h, so a rate of post-biopsy haematoma of 57.8% would appear to be acceptable. Thirdly, the mean ± SD BMI of the patients was $24.30 \pm 3.71\,kg/m^2$ in the current study (range, $16.45–39.26\,kg/m^2$). There were 109 of 218 (50.0%) patients with a BMI $\geq 24\,kg/m^2$ and 31 of 218 (14.2%) patients had a BMI $\geq 28\,kg/m^2$ in the current study. Previously, body weight was found to be associated with a higher risk of bleeding complications after PRB, which was similar to the current results based on BMI.[28] The probability of perirenal haematoma in obese patients (BMI $\geq 28\,kg/m^2$) was 2.66-times the nonobese patients after renal biopsy (Table 4).

Previous research has demonstrated that post-biopsy bleeding was related to sex and age.[15] The current study also found that post-biopsy bleeding was related to sex, but the findings did not support the view that post-biopsy bleeding was related to age. Female patients were 1.99-times more likely to develop post-biopsy haematoma after PRB than male patients (Table 4). Other research has found no statistical association between bleeding complications and age and sex.[21] The same study also found that the platelet count prior to the renal biopsy was highly predictive of symptomatic haematoma, but there were no statistical associations between bleeding complications and uncontrolled hypertension, Hb, INR and PTT.[21] In contrast, there was no statistical association between perirenal haematoma and platelet count in the current study, which might have been because the platelet count in the majority of patients was in the normal range (range, $125–350 \times 10^9$/l). Only nine patients had platelet counts $< 125 \times 10^9$/l. It should be noted that the objective of the current

Table 4. Binary logistic regression analysis of factors associated with the perirenal haematoma after percutaneous renal biopsy of native kidney.

Risk factor	OR	95% CI	*P*-value
BMI, ≥ 28 versus < 28 kg/m2	2.660	1.097, 6.449	P = 0.030
IPAB, yes versus no	2.572	1.422, 4.655	P = 0.002
Sex, female versus male	1.990	1.125, 3.521	P = 0.018

OR, odds ratio; CI, confidence interval; BMI, body mass index; IPAB, immediate post-biopsy active bleeding.

study was different to that of the previous study.[21] The current study focused on the relationship between all post-PRB haematomas and platelet counts, whereas the previous study focused on the relationship between symptomatic haematomas and platelet counts.[21] In consideration of the fact that coagulability as a major influencing factor for bleeding after invasive procedures, all patients in the current study had normal PTT, PTA and INR values prior to the PRB. Therefore, the relationship between INR, PTT and post-biopsy perirenal haematoma could not be investigated in the current study. Consistent with their findings,[21] the current study also found no statistical relationship between perirenal haematoma and Hb. However, some previous research demonstrated that a lower pre-biopsy Hb level was associated with a higher risk of complications.[10,29]

In terms of the relationship between blood pressure and post-biopsy perirenal haematoma, a range of different findings have been reported. For example, research has shown that the predictive characteristics of any complication (minor or major) were systolic blood pressure $\geq$170 mm Hg, bleeding time $>$7.5 min and SCr $>$3.5 mg/dl.[30] Arterial hypertension was found to double the bleeding risk in an analysis of 462 biopsies.[31] Similar results were published by the Norwegian registry on 8573 biopsies.[32] Nevertheless, there were studies that did not confirm this association,[33,34] emphasizing that the history of hypertension was a factor and not the present blood pressure. The risk of bleeding was increased in patients with a history of hypertension, irrespective of blood pressure at the time of biopsy.[19] It is possible that arteriolar hyalinosis associated with chronic hypertension limits the ability of vessels to contract following renal biopsy, regardless of the current blood pressure.[23] As blood pressure at the time of the renal biopsy could be related to a range of factors such as nervousness and apprehension, not having a good night's sleep the night before the biopsy, infusion quantity and environmental factors, the current study recorded the history of hypertension; and required that the systolic and diastolic arterial pressures were $<$160 and $<$90 mmHg at the time of the procedure, respectively. The current study found that a history of hypertension had no statistical relationship with post-biopsy renal haematoma.

Traditionally, a history of diabetes mellitus and hyperlipidaemia might have an impact on blood vessels, especially the arterial blood vessels. Therefore, they could be risk factors for the occurrence of haematoma after renal biopsy. To investigate this possibility, the current study collected data on a history of diabetes mellitus, total cholesterol, triglyceride, LDL-C and HDL-C from each study participant. The analyses demonstrated that a history of diabetes mellitus, total cholesterol, triglyceride, LDL-C and HDL-C had no relationship with the development of post-biopsy perirenal haematoma. It should be noted that only 28 of 218 patients (12.8%) had diabetes mellitus in the current study, which may have impacted on the results.

Higher SCr and acute renal insufficiency were significant confounding factors in biopsy complications in a large multicentre study on 2563 patients.[35] Data related to renal function were also collected in the current study including SCr, BUN, uric acid, 24-h urinary protein and eGFR. None of these factors were associated with the occurrence of post-biopsy perirenal haematoma. RPT was also recorded and it had no relationship with post-biopsy perirenal haematoma. It is inevitable that during the process of taking a kidney biopsy some blood vessels of the kidney will be damaged, especially the arterial vessels. It was surmised that renal haemodynamic parameters might have an impact on the formation of post-biopsy perirenal haematoma, so the

current study analysed the kidney-related haemodynamic parameters PVRA and PVAA. There was no relationship between PVRA, PVAA and the formation of perirenal haematoma after biopsy.

In some patients in the current study, colour Doppler ultrasonography identified a stream of blood flow along the needle path towards the ultrasound probe after the puncture needle was withdrawn from the kidney. This was defined it as IPAB and it was associated with the occurrence of post-biopsy perirenal haematoma. The risk of post-biopsy perirenal haematoma in patients with IPAB was 2.57-times that of patients without active bleeding after biopsy (Table 4).

This current study had several limitations. First, the sample size was not large enough to accurately reflect the overall situation in the general population. Secondly, although routine ultrasonography was performed 12–24 h for all patients after the PRB, a small proportion of haematomas might have been missed. Thirdly, this was a single-centre study, which is not as reliable as a multi-centre study. Fourthly, hypertension has been found to increase the bleeding risk after renal biopsy.[19,30,31] Some research has found that partial thromboplastin time and bleeding time predicted post-biopsy bleeding.[15,30] These factors were not included in this current study. Finally, only the possibility of post-biopsy perirenal haematoma development was studied and not the size of the haematomas. As a consequence of these limitations, the clinical significance of the current findings remains relatively limited. Larger, multi-centre studies with more patients are required to confirm the risk factors for the occurrence of perirenal haematoma after PRB.

In conclusion, this prospective study of 218 patients demonstrated that female patients, patients with a BMI $\geq 28\,kg/m^2$ and patients with IPAB were more likely to have perirenal haematoma after real-time ultrasound-guided PRB of native kidney.

Author contributions

Conceived and designed the experiments: Shihao Xu and Wenjie Zhao; performed the experiments and collected the data: Qiao Li, Saifeng Lin, Shihao Xu and Wenjie Zhao; analysed the data: Lei Wang, Bing Xiong and Wenjie Zhao; wrote the manuscript: Bing Xiong and Wenjie Zhao. All authors read and approved the final version of the manuscript.

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Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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