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ORIGINAL ARTICLE

Risk factors for bleeding complications after nephrologist-performed native renal biopsy

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Abstract

Background: Bleeding is a recognized complication of native percutaneous renal biopsy. This study aimed to describe the incidence of major bleeding after biopsy in a single centre over a 15-year period and examine factors associated with major bleeding.

Methods: We identified consecutive adult patients undergoing ultrasound-guided native renal biopsy in the Glasgow Renal and Transplant Unit from 2000 to 2014. From the electronic patient record, we collected data pertaining to biopsy indication, pre- and post-biopsy laboratory measurements, prescribed medication and diagnosis. Aspirin was routinely continued. We defined major bleeding post-biopsy as the need for blood transfusion, surgical or radiological intervention or death. Binary logistic regression analysis was used to assess factors associated with increased risk of major bleeding.

Results: There were 2563 patients who underwent native renal biopsy (1499 elective, 1064 emergency). The average age of patients was 57 (SD 17) years and 57.4% were male. Overall, the rate of major bleeding was 2.2%. In all, 46 patients required transfusion (1.8%), 9 patients underwent embolization (0.4%), no patient required nephrectomy and 1 patient died as a result of a significant late retroperitoneal bleed. Major bleeding was more common in those undergoing emergency compared with elective renal biopsy (3.4 versus 1.1%; $P < 0.001$). Aspirin was being taken at the time of biopsy in 327 of 1509 patients, with no significant increase in the risk of major bleeding ($P = 0.93$). Body mass index (BMI) data were available for 546 patients, with no increased risk of major bleeding in 207 patients classified as obese (BMI >30).

Conclusions: The risk of major bleeding following native renal biopsy in the modern era is low. Complications are more common when biopsy is conducted as an emergency, which has implications for obtaining informed consent. Our data support the strategy of not stopping aspirin before renal biopsy.

Key words: body mass index; chronic kidney disease; epidemiology; kidney biopsy; renal biopsy

Introduction

Native renal biopsy is the definitive diagnostic test for renal parenchymal disease and is generally considered a safe procedure. The reported complication rates are low [1–3], particularly since the move away from manual biopsy needles in favour of spring-loaded biopsy guns [4]. However, published data relating to the

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risk of native renal biopsy are often derived from small single centres or utilize historic cohorts covering several decades, during which the case mix and biopsy method have changed. Available data are lacking relating to risks in the modern era.

Bleeding remains the greatest risk after percutaneous renal biopsy and can be severe or even life-threatening. Efforts are made in most modern renal units to minimize the risk of bleeding by checking markers of blood coagulation, avoiding renal biopsy in uncontrolled hypertension and being vigilant of the prevalent prescription of antiplatelet and anticoagulant medications.

There is no consensus on whether it is safe to perform renal biopsy while a patient is taking aspirin. There are limited data available, and concern about a major iatrogenic bleed means that most units routinely withhold aspirin for up to 7 days in advance of elective renal biopsy. Many patients with chronic kidney disease have significant documented cardiovascular morbidity. A meta-analysis of 50 279 patients at risk for coronary artery disease demonstrated a 3-fold increase in major adverse cardiac events after discontinuation of aspirin [5]. The median time to infarction was 10.0 ± 1.9 days. Routine suspension of aspirin for a week or more around the time of biopsy is not a benign intervention. Some centres take this concern further and administer procoagulants to patients with prolonged bleeding times or those perceived to be at greatest risk, again a practice without evidence.

Furthermore, other factors associated with an increased risk of bleeding may include being older, having a higher serum creatinine, higher systolic blood pressure or use of a larger needle gauge [4]. We observed that we were undertaking renal biopsy in a greater proportion of patients who were obese and we had concerns over whether these patients were at increased risk.

The Glasgow Renal and Transplant Unit provides tertiary nephrology services for a population of 1.6 million people. Routine practice in our centre has been for renal biopsy to be performed on the ward by the attending nephrologist. As such, we have multiple operators but a single method of biopsy led by protocol. We previously studied the impact of discontinuing aspirin prior to native biopsy and found no reduction in events [6] and therefore our practice is to continue aspirin.

Given the degree of uncertainty in the literature and lack of uniform practice, we extended our previous cohort of patients and aimed to study factors associated with an increased risk of significant bleeding in patients undergoing native renal biopsy.

Materials and methods

Adult patients undergoing native renal biopsy in the Glasgow Renal and Transplant Unit from 2000 to 2014 were identified. Biopsies were performed using real-time ultrasound (US) guidance (Titan, Sonosite, Herts, UK) and disposable 16-gauge spring-loaded biopsy guns (Bard Max Core, CR Bard, Covington, GA, USA) as described from our previous cohort [6]. Usual practice was to obtain between one and three cores of renal cortex; on no occasion were more than five passes attempted to obtain tissue. To minimize bleeding risk, we used the following pre-biopsy parameters as a guide: prothrombin time (PT) <15 s, platelet count $\geq 100 \times 10^9$/L and blood pressure controlled where possible, though our protocol does not call for a specific blood pressure target. Aspirin was routinely continued but clopidogrel and warfarin were stopped for 7 days or until PT was <15 s, respectively. Bleeding times were not checked and procoagulants were not administered. If there was any uncertainty in the decision to proceed, consultant opinion was sought. Patients undergoing native renal biopsy were expected to have a formal departmental US scan within 6 months before biopsy. Renal biopsy was not performed if there was evidence of active, untreated urinary infection.

Patients who underwent a day case procedure were routinely observed for 6 h and were discharged home if there was no evidence of bleeding and they did not live alone. In circumstances where the biopsy was deemed high risk, including frail patients or those travelling long distances from home, patients were kept overnight for monitoring. We performed repeat haemoglobin if bleeding was suspected or if patients had an overnight stay. We did not perform US scanning after a biopsy unless bleeding was suspected clinically.

Data were extracted from the prospectively completed electronic patient record for biopsy indication, pre-biopsy haemoglobin, platelet count, PT, estimated glomerular filtration rate (eGFR), serum creatinine, urinary protein:creatinine ratio, body mass index (BMI), use of antiplatelets or anticoagulants and diagnosis. BMI was calculated, with BMI <25 kg/m^2 being classified as healthy weight, 25–29.9 kg/m^2 as overweight and ≥ 30 kg/m^2 as obese. We defined major bleeding post-biopsy as the need for blood transfusion, surgical or radiological intervention or death. We have reported rates of minor bleeding as a haemoglobin drop >2 g/L or other morbidity, which includes visible haematuria, requirement for catheter/irrigation, haematoma not requiring transfusion, additional period of observation or loin pain. Patients who underwent renal biopsy during a non-elective admission to the renal unit for investigation and treatment of renal disease (usually acute kidney injury or nephrotic syndrome) were considered to have undergone biopsy as an emergency. Binary logistic regression analysis was used to assess factors associated with an increased risk of major bleeding (SPSS version 22, IBM, Armonk, NY, USA). Comparisons between groups used *t*-test, one-way analysis of variance, Mann–Whitney U test or chi-square test as appropriate.

Results

Baseline demographics

There were 2619 patients who underwent native renal biopsy during the 15-year period. We excluded 56 procedures conducted in the radiology department (by a consultant radiologist), which were US- or computed tomography–guided (no transjugular biopsies), leaving 2563 biopsies (1499 elective, 1064 emergency). There was a slight preponderance of male patients (57.4%) and the mean age was 57 (SD 17) years. In all, 497 (19.4%) were undertaken as day cases. Baseline demographics are shown in Table 1. There were >55 operators over the 15 years studied, of whom >90% were nephrology trainees.

The rate of major bleeding overall was 2.2%: transfusion 1.8%, embolization 0.4% and death 0.1%. During the study, one patient died as a direct result of renal biopsy. This patient had a history of recurrent pulmonary emboli and restarted warfarin 7 days after biopsy. He presented on day 12 after biopsy with severe abdominal pain, vomiting and shock. Post-mortem examination confirmed a late retroperitoneal haemorrhage directly related to the renal biopsy.

The rate of major bleeding in 56 radiologist-performed biopsies excluded from the main analysis was not statistically different from that in nephrologist-performed biopsies (3.8% versus 2.1%; $P = 0.239$). Of the two patients who suffered major bleeding after biopsy performed by a radiologist, one patient underwent renal arterial embolization and one received a blood transfusion.

Table 1. Baseline demographic data for 2563 included patients undergoing percutaneous renal biopsy

Baseline data	All patients ($n = 2563$)	Elective ($n = 1499$, 58.5%)	Emergency ($n = 1064$, 42.5%)	P-value (chi-square)
Male (%)	57.4	57.9	56.3	0.216
Mean age (years)	56.9 (17.2)	54.1 (16.8)	60.8 (17.0)	<0.001
Pre-Hb (g/L)	11.6 (2.4)	12.4 (2.2)	10.4 (2.1)	<0.001
Post-Hb (g/L)	11.0 (2.4)	11.9 (2.3)	10.0 (2.0)	<0.001
Hb change (g/L)	−0.2 (0.9)	−0.4 (0.8)	−0.3 (0.9)	0.001
eGFR (mL/min/1.73 m^2)	33.9 (30.4)	48.1 (30.7)	24.4 (24.8)	<0.001
Urine PCR (mg/mmol)	288 (116–641)	251 (109–565)	357 (130–801)	<0.001
Urine ACR (mg/mmol)	175 (52–443)	176 (56–411)	172 (43–181)	0.500
Platelets ($\times 10^9$/L)	266 (211–331)	270 (85)	303 (136)	<0.001
Prothrombin time (s)	11.3 (2.0)	11.0 (2.2)	11.8 (1.6)	<0.001
Systolic BP (mmHg)	139 (20)	139 (20)	139 (19)	0.836
Diastolic BP (mmHg)	77 (11)	78 (12)	76 (11)	0.717

Hb, haemoglobin; PCR, protein:creatinine ratio; ACR, albumin:creatinine ratio; BP, blood pressure.

Table 2. Major bleeding rate after percutaneous renal biopsy

Major bleeding type	All biopsies ($n = 2563$)	Elective ($n = 1499$)	Emergency ($n = 1064$)	P-value (chi-square)
Overall major bleeding	56 (2.2%)	17 (1.1%)	36 (3.4%)	<0.001
Transfusion	46 (1.8%)	14 (0.9%)	32 (3.0%)	<0.001
Embolization	9 (0.4%)	2 (0.1%)	7 (0.7%)	0.03
Death	1 (0.04%)	1 (0.04%)	0 (0.0%)	
Other morbidity	59 (2.3%)	48 (3.2%)	11 (1.0%)	<0.001
Haemoglobin decrease>2 g/L	74 (2.9%)	39 (2.6%)	35 (3.3%)	0.31

Complications were more common in emergency versus elective procedures.

Table 3. Major bleeding rate by diagnosis after percutaneous native renal biopsy

Diagnosis on biopsy	n	Major bleeding	Transfusion	Embolization
Glomerulonephritis including HSP	1143	13 (1.1%)	12 (1.0%)	2 (0.2%)
Vasculitis	336	17 (5.1%)	14 (4.2%)	2 (0.6%)
Interstitial disease including CPN	199	4 (2.0%)	4 (2.0%)	0 (0.0%)
Chronic ischaemia	145	2 (1.4%)	0 (0.0%)	1 (0.7%)
Diabetic nephropathy	139	4 (2.9%)	4 (2.9%)	0 (0.0%)
Amyloid/myeloma	140	1 (0.7%)	1 (0.7%)	0 (0.0%)
Lupus nephritis	111	2 (1.8%)	2 (2.6%)	1 (0.9%)
Acute tubular injury	96	0 (0.0%)	0 (0.0%)	0 (0.0%)
Others	88	**5 (5.7%)**	**4 (4.5%)**	**3 (3.4%)**
Non-diagnostic	164	5 (3.0%)	5 (3.0%)	0 (0.0%)

CPN, *Chlamydia pneumoniae*; HSP, Henoch–Schönlein Purpura.

There were no deaths. There was no significant difference in age or eGFR between patients who had native biopsy performed by a nephrologist on the nephrology ward versus by a radiologist in the radiology department, but those performed by a radiologist had a significantly higher mean BMI (28 versus 32; P = 0.02).

Elective versus emergency biopsy

Biopsies were more likely to be performed electively (58.5%). Those who had a biopsy conducted as an emergency were significantly older, had worse renal function and more proteinuria (Table 1). Major bleeding was more common in those undergoing emergency compared with elective renal biopsy (1.1 versus 3.4%; P < 0.001) (Table 2).

Primary renal diagnosis

Major bleeding was more common in 336 patients with renal vasculitis (5.1 versus 2.1%), with the majority requiring blood transfusion (Table 3). No differences were observed in the rate of complications for patients in whom other diagnoses were made.

Biopsy adequacy

Tissue was adequate for diagnosis in 93.6% of cases. In the 163 cases in which biopsy was non-diagnostic, there was no significant difference in the rate of major complications (3.0 versus 2.2%; P = 0.43).

Medicines

Complete medication data relating to antiplatelet or anticoagulant use were available for 1509 patients. There were 327 patients who were taking aspirin (75 mg) at the time of biopsy and there was no increased risk of major bleeding (Table 4). In patients taking aspirin, there was no significant increased risk of a haemoglobin decrease >2 g/L (2.4 versus 2.2%; P = 0.79) or other morbidity (1.5 versus 3.0%; P = 0.15). In all, 29 patients stopped

Table 4. Bleeding rate according to aspirin use at the time of biopsy

	Total [$n = 2536$ (no aspirin, $n = 1182$; aspirin, $n = 327$)]				Elective [total, $n = 1499$ (no aspirin, $n = 692$; aspirin, $n = 207$)]				Emergency [total, $n = 1064$ (no aspirin, $n = 490$; aspirin, $n = 120$)]			
Aspirin status	Death	Tfusion	Embn	Major bleed	Death	Tfusion	Embn	Major bleed	Death	Tfusion	Embn	Major bleed
No aspirin	1 (0.1%)	22 (1.9%)	7 (0.6%)	30 (2.5%)	1 (0.1%)	11 (1.6%)	2 (0.3%)	14 (2.0%)	0 (0.0%)	11 (2.2%)	5 (1.0%)	16 (3.3%)
Aspirin	0 (0.0%)	5 (1.5%)	0 (0.0%)	5 (1.6%)	0 (0.0%)	2 (1.0%)	0 (0.0%)	2 (1.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	3 (2.5%)
Unknown	0 (0.0%)	19 (1.8%)	2 (0.2%)	21 (2.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	18 (4.0%)	2 (0.4%)	20 (4.4%)
P-value (chi-square)	0.56	0.92	0.14	0.47	0.56	0.03	0.31	0.01		0.29	0.35	0.50

Tfusion, transfusion; Embn, embolization.

Table 5. Binary logistic regression analysis of factors associated with increased risk of major bleeding

Risk factor	Odds ratio	95% confidence interval	P-value
Increasing age	1.025	1.007–1.043	0.006
Decreasing eGFR	1.034	1.018–1.050	<0.001
Systolic BP	1.018	0.996–1.040	0.113
BMI > 30	0.363	0.105–1.254	0.154

BP, blood pressure.

clopidogrel (>5 days before) and 13 continued it during biopsy. In these cases, clopidogrel was continued due to a perceived increased risk of stopping, including recent acute coronary syndrome or previous coronary stenting. Warfarin was stopped temporarily in advance of biopsy in all 61 relevant cases. There was no increased bleeding risk associated with the use of clopidogrel or warfarin, although numbers are small (data not shown).

Obesity

Height and weight were available for 1045 patients. The mean BMI was 28.1 (SD 6.0) kg/m^2 (range 12.9 – 55.4). A total of 326 were healthy weight, 373 were overweight and 346 were obese. There were 46 patients who had a biopsy with a recorded BMI >40. Rates of complications were 3.4, 1.1 and 0.9%, respectively ($P = 0.06$), for healthy weight, overweight and obese, suggesting that renal biopsy in obese patients is associated with lower bleeding risk than in patients with a normal BMI.

Analysis of other demographic factors associated with increased risk of bleeding

In binary logistic regression analyses, pre-biopsy platelet count, PT, blood pressure and proteinuria were not associated with a risk of bleeding. Increased age and decreased eGFR were associated with an increased risk of major bleeding (Table 5).

Comparison with previous cohort

The demographics of this larger cohort, including age, sex, eGFR at biopsy and urgency of biopsy are similar to those of our previously published cohort [6].

Discussion

In this study we demonstrated that native renal biopsy is a safe procedure. Older patients, those with worse renal function and those with vasculitis undergoing the procedure as an emergency are at greatest risk. Continuing aspirin is not associated with a risk of major bleeding and a BMI >30 kg/m^2 is not a risk factor for bleeding.

Our reported complication rates are in keeping with other available large-scale studies of native renal biopsy [1, 2, 7–9]. Our complication rates are similar to those described in the largest available meta-analysis, assessing 34 published studies of 9474 biopsies from 1980 to 2011 [3], which included a subset of the patients presented in the present analysis published in 2008 [6]. All included studies used real-time US guidance and biopsies were taken using automated spring-loaded devices, which would be in keeping with modern techniques. Other large, single-centre case series have reported much greater complication rates (transfusion rates 5–9%) [10–13]. It has been suggested that this may be because these large academic centres have a greater proportion of biopsy procedures performed by nephrology trainees and may have a greater proportion of high-risk patients [4]. The Glasgow Renal and Transplant Unit is the second largest renal centre in the UK, serving a population of ~1.6 million. More than 90% of our biopsies are performed by nephrology trainees and we have included all biopsies conducted in this time period regardless of risk stratification. We believe our data are representative of native renal biopsy complications in a large academic renal unit.

In a large case series of 15 181 percutaneous core biopsies, there was no increased risk of bleeding in 5832 renal biopsies (native and transplant) in patients taking aspirin ($n = 1270$) versus no aspirin use (1.0 versus 0.6%; $P = 0.53$) [14]. A recent review of best practice in native renal biopsy has been published and discusses the issue of using aspirin around the time of biopsy, concluding that there are insufficient data to safely answer this question [4]. Our practice is to continue aspirin and to discontinue other antiplatelets and anticoagulants. As a direct comparison with our own practice, our major bleeding rate has not increased since we changed our practice to routinely continue aspirin [6].

In this study we have focused on what we believe to be the major bleeding of native renal biopsy, in line with previously published reports. Although we have reported rates of haemoglobin decrease and other morbidity, this study was not designed to analyse these complications and it is likely that the rates of minor bleeding complications are underreported.

The increased rate of blood transfusion observed in patients with vasculitis may be confounded by the high transfusion requirements seen acutely in these patients when they present. Whether the vasculitic process in the kidney influences the risk of bleeding is unclear. Other primary renal diagnoses, such as amyloid, have also been associated with an increased risk of bleeding [15], although we found no evidence of such an association in this study.

Obesity is a worldwide problem and is associated with the development of renal diseases. As such, renal biopsy will be

required more frequently in patients with high BMIs. In this study we biopsied a large number of patients who were clinically obese but observed no increased risk of complications in these patients, which is reassuring.

We acknowledge constraints in the interpretation of these data. In this retrospective observational study, we did not observe an increased risk of complications in patients taking antiplatelet agents, but the absolute number of complications in this group was small. The nature and size of this study is not powered to give a definitive answer to the question of the safety of using aspirin at the time of biopsy: prospective confirmation would be required. Nevertheless, we believe we have described data that compare favourably with other published studies from a large cohort of patients who have undergone native renal biopsy in a 'real-world' setting.

In summary, the risk of major bleeding following native renal biopsy in the modern era is low. Complications are more common when biopsy is conducted as an emergency, which has implications for obtaining informed consent. Obesity does not appear to be a risk factor for major bleeding. In the absence of large-scale, randomized clinical trials, our data support the routine continuation of aspirin at the time of renal biopsy, particularly given that discontinuing it may increase the risk of thrombotic events in those at high risk of cardiovascular disease.

Conflict of interest statement

None declared.

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