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Effects of Aspirin Therapy on Ultrasound–Guided Renal Allograft Biopsy Bleeding Complications

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Abstract

Purpose—To determine if patient aspirin exposure and timing affect bleeding risk after renal allograft biopsy.

Materials and Methods—Review of 6,700 renal allograft biopsies (in 2,362 unique patients) was performed. Median patient age was 53.0 years [interquartile range 43.0, 62.0]; 56.2% of patients were male. Of biopsies, 4,706 (70.2%) were performed in patients with no aspirin exposure within 10 days of biopsy; 664 (9.9%), were performed within 8–10 days of aspirin exposure; 855 (12.8%), within 4–7 days; and 475 (7.1%), within 0–3 days. Follow-up to 3 months after the procedure was completed in all patients. Biopsies were categorized as protocol or indication; 19.7% were indication biopsies. Bleeding complications were graded based on SIR criteria. Logistic regression models examined the association between aspirin use and bleeding events.

Results—Rate [95% confidence interval] of major bleeding complications was 0.24% [0.14, 0.39], and rate of any bleeding complication was 0.66% [0.46, 0.90]. Bleeding events were significantly associated with patients undergoing indication biopsies compared with protocol biopsies (odds ratio [OR] 2.27, $P = .012$). Patient factors associated with major bleeding complications in multivariate models included estimated glomerular filtration rate (OR 0.61, $P = .016$) and platelet count (OR 0.64, $P = .033$). Aspirin use was not significantly associated with increased risk of bleeding complication except for use of 325 mg of aspirin within 3 days of biopsy (any complication OR 3.87 [1.12, 13.4], $P = .032$; major complication OR 6.30 [1.27, 31.3], $P = .024$).

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None of the authors have identified a conflict of interest.

Conclusions—Renal allograft biopsy bleeding complications are very rare, particularly for protocol biopsies. Use of 325 mg of aspirin within 3 days of renal allograft biopsy was associated with increased bleeding complications.

Ultrasound-guided percutaneous biopsy is an important diagnostic tool for monitoring renal allografts (1,2). Biopsies can be performed as part of routine follow-up protocols or when allograft dysfunction occurs. Percutaneous renal allograft biopsies are considered to be safe procedures. Bleeding is the most common complication, with reported major bleeding complication rates of 0%–3% (3–6).

It has been suggested that cessation of aspirin may be unnecessary for many percutaneous organ biopsies (4). However, Burger et al (7) reported a 50% increase in bleeding complications related to periprocedural aspirin use and concluded that aspirin discontinuation should be considered before any biopsy or surgery. Current Society of Interventional Radiology (SIR) guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions recommend withholding aspirin for 5 days before procedures with significant bleeding risk (8,9). This recommendation is based on the approximate 10-day life span of platelets, such that with aspirin therapy cessation for 5 days, the pool of functional platelets would be approximately 30%–50% (8). Careful consideration is given to the decision of aspirin cessation in kidney transplant recipients before biopsy. First, aspirin therapy may decrease the risk of renal allograft vein thrombosis (10,11). Additionally, kidney transplant recipients frequently have significant arteriovascular disease, and prolonged discontinuation of antiplatelet therapy can result in significant cardiovascular events (12,13). To examine the effects of aspirin exposure and timing on bleeding complications after renal allograft biopsies, an institutional database of ultrasound-guided renal allograft biopsies was reviewed.

MATERIALS AND METHODS

Renal Allograft Biopsy Cases

This single-center study was approved by the local institutional review board and is compliant with the Health Insurance Portability and Accountability Act. Data were obtained from an institutional database of image-guided biopsy procedures. Retrospective review was performed of 6,700 renal allograft biopsies performed between January 1, 2005, and August 31, 2014. Follow-up to 3 months after the procedure was completed on all patients. Patients were eligible for inclusion if they had undergone renal allograft biopsy during which core tissue samples (18-gauge) were obtained under ultrasound guidance. Fine-needle aspiration biopsies were not included. Patients who declined to participate were excluded. A subset of the patient population was included in a prior study (14) that analyzed all parenchymal organ biopsies.

Biopsy procedures were categorized as protocol or indication. Protocol biopsies refer to routine biopsies of renal allograft to monitor for early signs of rejection. The scheduled intervals for protocol renal allograft biopsies varied slightly during the study period, but biopsies were typically performed at month 4 and years 1, 2, 5, and 10 after transplantation. Indication biopsies were biopsies performed to evaluate allograft dysfunction.

Aspirin Exposure

Aspirin exposure was defined as aspirin use (81 mg or 325 mg) within 10 days of the biopsy. Several possible definitions of aspirin exposure were considered and examined; the decision to use a cutoff of 10 days as the definition for aspirin use was based on the permanent inactivation of platelets caused by aspirin and the 7–10 days required for a complete platelet turnover (15). To capture variability in quantity of circulation of functional platelets, before modeling, aspirin use was stratified as follows: 0–3 days, 4–7 days, 8–10 days, > 10 days, or no aspirin use.

Patient Demographics

The study cohort included 6,700 biopsies performed in 2,362 unique patients. The number of renal allograft biopsies per patient ranged from 1 to 12, with a median [interquartile range] of 3 [1, 4] biopsies per patient. Patient demographics are presented in Table 1 by aspirin exposure timing before biopsy. Median patient age at biopsy was 53.0 years [43.0, 62.0], 56.2% of patients were male, median number of passes per biopsy was 3 [3, 3] (range, 1–6), median international normalized ratio was 1.0 [0.9, 1.1], median platelet count was $212 \times 10^9/\text{L}$ [170, 260], median estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease equation (16) was 48.3 mL/min/1.73 m² [37.4, 59.3], median creatinine was 1.4 mg/dL [1.2, 1.8], and 19.7% were indication biopsies. Of the 6,700 biopsies, 4,706 (70.2%) were performed on patients who did not take aspirin or took it > 10 days before biopsy, 664 (9.9%) were performed within 8–10 days of aspirin exposure, 855 (12.8%) were performed within 4–7 days of aspirin exposure, and 475 (7.1%) were performed within 0–3 days of aspirin exposure. Of the 1,994 biopsies performed on patients who had consumed aspirin within 10 days of biopsy, 81 mg of aspirin had been taken in 1,545 (77.5%) cases, and 325 mg of aspirin had been taken in 449 (22.5%) cases.

Definitions of Biopsy Complications

Complications were defined as acute if they occurred within 24 hours of the procedure and delayed if they occurred between 24 hours and 3 months after the procedure. A dedicated radiology registered nurse reviewed the procedural record and contacted each patient or patient representative by telephone within 24–72 hours after the procedure to access for acute complications. A review of the patient's medical record was performed 3 months after the biopsy to assess for delayed complications. Bleeding complications were defined and graded based on the SIR Standards of Practice complication classification system (17). One author (F.I.B.) reviewed all recognized bleeding complications. In cases of ambiguity, 2 additional authors (G.D.S., T.D.A.) reviewed the case, and a decision was reached based on the majority.

Allograft Biopsy Technique

All biopsies were performed at an academic teaching hospital by staff radiologists with subspecialty training in ultrasound-guided procedures (median of 10 y experience; range, 3–30 y). Biopsies were performed using real-time ultrasound guidance (ACUSON Sequoia; Siemens Medical Solutions USA, Inc, Malvern, Pennsylvania, or LOGIQ E9; GE Healthcare, Wauwatosa, Wisconsin). An 18-gauge biopsy device (Bard Monopty; Bard

Biopsy Systems, Tempe, Arizona) was used in all cases. By protocol, 3 biopsy samples were obtained from the cortex of the renal allograft, with fewer or additional samples rarely taken based on the discretion of the proceduralist. Introducer needles and needle-tract plugging techniques were not commonly used. Per protocol, parenchymal organ biopsies, including renal allograft biopsies, were not performed in patients with systolic blood pressures > 160 mm Hg or diastolic pressures > 100 mm Hg. Patients were monitored for approximately 2 hours after renal allograft biopsy in the outpatient hospital surgical ward before being discharged.

Anticoagulation Practice Guidelines

SIR anticoagulation consensus guidelines were followed (8,9). This includes patients having a platelet count of $> 50 \times 10^9/L$ and international normalized ratio of < 1.5 before any solid organ biopsy. Patients were also required to discontinue common and novel anticoagulation medications for the time frame recommended in the SIR anticoagulation consensus guidelines. However, 5 patients underwent indication renal allograft biopsies without cessation of clopidogrel for at least 5 days. For elective biopsies, patients were typically asked to stop aspirin (81 mg or 325 mg) for 7–10 days before the procedure. Deviations from these guidelines were permitted based on the indication for aspirin therapy and for patients who lived far from the institution, for whom rescheduling of the biopsy would be impractical.

Statistical Analysis

Summary statistics for patient demographics and clinical characteristics were reported as number (%) or median/interquartile range and grouped by time frame of aspirin discontinuation before biopsy (aspirin exposure). Differences in demographics or clinical characteristics among the aspirin exposure groups were compared using χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. Bleeding complications were the primary outcome of interest and were examined as 2 outcomes: (a) any (major or minor) complication and (b) major complication. The 95% confidence intervals (CIs) for complication rates were calculated using the modified Clopper-Pearson method.

Logistic regression analysis using the generalized estimating equation method (18) was used to model the association of patient and procedure characteristics with bleeding outcomes. The generalized estimating equation method is an extension of generalized linear models that allows incorporation of within-subject covariance structures to account for correlated data, such as multiple biopsies per patient. Patient and procedure characteristics examined were age, sex, number of biopsy passes, international normalized ratio, platelet count ($\times 10^9/L$), biopsy performed by trainee versus biopsy performed by attending radiologist, creatinine (mg/dL), eGFR (mL/min/1.73 m²), indication biopsy, and aspirin exposure before biopsy.

Variables were reviewed for evidence of collinearity by means of variance inflation factors and principal components analysis before multivariate modeling. Owing to observed collinearity between creatinine, eGFR, and indication biopsy, although all were found to be

significant univariately, eGFR was selected as the most comprehensive indicator of kidney function and was the only one included in multivariate model fitting. Creatinine was log transformed before model fit. Platelets were both fit as a continuous variable and discretized into normal/abnormal (abnormal platelets $<50 \times 10^9/L$). Odds ratios (OR) are based on unit increases of $100 \times 10^9/L$ for platelets, 10 years for age, and $10 \text{ mL/min/1.73 m}^2$ for eGFR. Sex and age were not found to be significantly associated with either outcome. However, sex and age are known to be associated with bleeding complications (19,20). Owing to significant baseline differences in age and sex between aspirin exposure groups, they were adjusted for in multivariate models. Model fit was assessed using the quasi-likelihood under the independence model information criterion (21). Multiple correlation structures were examined, and an exchangeable correlation structure was selected. *P* values $< .05$ were considered significant. CIs and *P* values for ORs are Wald-based. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Bleeding complication events (any and major only) per aspirin exposure category are summarized in Table 2. There were 44 total complications in 41 unique patients, and 16 were major complications (occurring in 16 unique patients). The complication rate was 0.66% [95% CI 0.46, 0.90] for any complication and 0.24% [95% CI 0.14, 0.39] for major complications. Of the 16 major complications, 11 (69%) were the result of perinephric bleeding requiring angiography with or without embolization and/or blood transfusion, whereas 5 (31%) were the result of hematuria requiring continuous bladder irrigation with or without percutaneous nephrostomy tube placement. Of the 28 minor bleeding complications, 12 (43%) were due to perinephric bleeding/hematoma, and 16 (57%) were due to hematuria. All these patients were monitored overnight in the hospital without any intervention. There were no procedure-related permanent adverse sequelae or deaths. No bleeding complications were observed in the 5 patients who remained on clopidogrel at the time of biopsy. The rate of any bleeding complications in protocol surveillance biopsies was 0.52% (28 of 5,377 [95% CI 0.35, 0.75]) and in indication biopsies was 1.21% (16 of 1,323 [95% CI 0.69, 1.96]). The rate of major bleeding complications in protocol surveillance biopsies was 0.11% (6 of 5,377 [95% CI 0.04, 0.24]) and in indication biopsies was 0.76% (10 of 1,323 [95% CI 0.36, 1.39]).

Factors Associated with Any Bleeding Complication

For the outcome of any complication, platelet count (OR [95% CI] 0.62 [0.42, 0.93], *P* = .020), creatinine (2.84 [1.52, 5.31], *P* = .001), eGFR (0.76 [0.61, 0.95], *P* = .017), and indication biopsy (2.27 [1.19, 4.33], *P* = .013) all were significantly associated. Univariate association of aspirin exposure and any bleeding complication was also statistically significant (*P* = .014) (Table 3). Specific ORs for multivariate models fit based on aspirin exposure in the 0–3 days, 4–7 days, and 8–10 days groups versus the > 10 days group are presented in Table 4. In the final model, adjusting for age, sex, eGFR, and platelet count, overall aspirin exposure (aspirin use within 10 d of biopsy) was no longer significant (*P* = .19). Because the initial univariate analysis showed aspirin exposure within 3 days of biopsy to be associated with any bleeding complication, an additional multivariate model was

performed with aspirin exposure dichotomized by 325 mg aspirin only received within 3 days before biopsy (Table 5). This showed a significant association between patients who had taken 325 mg of aspirin within 3 days of biopsy and any bleeding complication (OR 3.87 [95% CI 1.12, 13.4], $P = .032$).

Factors Associated with Major Bleeding Complication

Univariately, aspirin exposure was not revealed to be significantly associated with major bleeding complications ($P = .08$). Platelet count (OR [95% CI] 0.46 [0.24, 0.88], $P = .019$), eGFR (0.60 [0.40, 0.89], $P = .012$), creatinine (5.42 [2.39, 12.3], $P = .001$), and indication biopsy (6.84 [2.48, 18.9], $P < .001$) all were revealed to be significantly associated with major bleeding complications (Table 3). In a multivariate model (Table 4) including age, sex, platelet count, and eGFR, both eGFR and platelet count remained significant (eGFR, 0.61 [0.40, 0.91], $P = .016$; platelet count, 0.64 [0.43, 0.97], $P = .033$). Because the initial univariate analysis showed aspirin exposure within 3 days of biopsy to be associated with major bleeding complication, an additional multivariate model with aspirin exposure dichotomized by 325 mg aspirin only within 3 days of biopsy (Table 5) was performed. This showed a significant association with major bleeding complications (OR 6.30 [95% CI 1.27, 31.3], $P = .024$).

DISCUSSION

This evaluation of 6,700 renal allograft biopsies demonstrates a very low (< 1%) overall bleeding complication rate, and aspirin exposure and the duration of abstinence were generally not revealed to be significantly associated with bleeding complications. However, a significant association was noted only in the group of patients taking 325 mg of aspirin within 3 days before the biopsy. Other factors that were associated with increased bleeding complications in a multivariable analysis included lower platelet count and lower kidney function.

The 0.24% major bleeding complication rate found in this cohort is lower than that previously reported in the literature. Furness et al (3) reported a 0.40% major complication rate in a review of 2,127 renal allograft biopsies. Morgan et al (6) found a 1.9% major complication rate after 2,514 renal allograft biopsies, and Wilczek (4) reported a 2.8% major complication rate after 1,129 renal allograft biopsies. This disparity in outcomes likely stems from differences in how major complications were defined in each study (ie, complication classification system used) and differences in the biopsy technique. In a review of 5,832 kidney biopsies, including native and allograft biopsies, Atwell et al (14) reported a major bleeding complication rate of 0.7%. The major complication rate for patients who had taken aspirin within 10 days of biopsy was 1.0% compared with 0.6% for patients who had not taken aspirin within 10 days of the procedure. The conclusion from the study by Atwell et al was that cessation of aspirin was probably unnecessary before renal biopsy, although the authors acknowledged that a shorter period of abstinence would also be reasonable. In contrast to the study by Atwell et al (14), aspirin use was stratified in the present cohort in an effort to capture variability in quantity of circulating functional platelets. However, there

was no statistically significant difference identified in bleeding complication rates except in patients taking 325 mg of aspirin within 3 days before the biopsy.

There are potential serious implications to withholding aspirin therapy before renal transplant biopsy. First, there is evidence suggesting that aspirin therapy reduces the incidence of renal vein thrombosis in transplant recipients (11). Additionally, even a temporary interruption of long-term aspirin treatment has been revealed to triple a patient's risk of a transient ischemic attack or stroke (22). Following a review of the literature, Nayak-Rao (23) concluded that cessation of aspirin may be unnecessary in patients with low bleeding risk patients native renal biopsies. Given the very low rate of major bleeding complications seen in this study, it may be reasonable to continue aspirin in renal transplant recipients with an otherwise low bleeding risk who are undergoing biopsy. However, this study would suggest that patients taking 325 mg of aspirin within 3 days of biopsy may represent a unique higher risk cohort.

Other variables evaluated that remained significant for bleeding complications were patient eGFR and platelet count. The observed association between eGFR and increased bleeding risk is not an unexpected finding. Uremia causes platelet dysfunction by impairing platelet adhesiveness and causing abnormal platelet-endothelial interactions (24,25). The association identified between decreased platelet count and increased bleeding risk is also well documented (26).

Limitations of this study include the retrospective design and associated potential biases. Also, arbitrary stratification of patient aspirin exposure into 4 groups may have confounded results, especially as the number of biopsies in the 3 groups in which patients had taken aspirin within 10 days of the procedure was significantly lower than the group in which patients had not taken aspirin. The low number of complications also limited the models that could be fit, including possible higher level interaction effects between variables. Finally, other patient factors that may have affected bleeding risk, including blood pressure, were not included in the database until more recently and therefore were not included in these analyses.

In conclusion, the goal of this study was to determine whether aspirin exposure increases the risk of bleeding complications after ultrasound-guided renal allograft biopsy. The results demonstrate a significantly increased risk only in patients taking 325 mg of aspirin within 3 days of the biopsy.

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ABBREVIATIONS

CI	confidence interval
eGFR	estimated glomerular filtration rate

OR odds ratio

References

1. Rea DJ, Heimbach JK, Grande JP, et al. Glomerular volume and renal histology in obese and non-obese living kidney donors. *Kidney Int.* 2006; 70:1636–1641. [PubMed: 16955108]
2. Stegall MD, Park WD, Larson TS, et al. The histology of solitary renal allografts at 1 and 5 years after transplantation. *Am J Transplant.* 2011; 11:698–707. [PubMed: 21062418]
3. Furness PN, Philpott CM, Chorbajian MT, et al. Protocol biopsy of the stable renal transplant: a multicenter study of methods and complication rates. *Transplantation.* 2003; 76:969–973. [PubMed: 14508363]
4. Wilczek HE. Percutaneous needle biopsy of the renal allograft. A clinical safety evaluation of 1129 biopsies. *Transplantation.* 1990; 50:790–797. [PubMed: 2238054]
5. Nahas WC, Mazzucchi E, Henrique A, et al. Percutaneous needle biopsy of the renal allograft using the automated needle system: evaluation of 87 procedures. *J Urol.* 1993; 150(2 Pt 1):313–315. [PubMed: 8326550]
6. Morgan TA, Chandran S, Burger I, Goldstein R. Complications of ultrasound guided renal transplant biopsies. *Am J Transplant.* 2016; 16:1298–1305. [PubMed: 26601796]
7. Burger W, Chemnitz JM, Kneissl GD, Rucker G. Low-dose aspirin for secondary cardiovascular prevention—cardiovascular risks after its peri-operative withdrawal versus bleeding risks with its continuation—review and meta-analysis. *J Intern Med.* 2005; 257:399–414. [PubMed: 15836656]
8. Patel IJ, Davidson JC, Nikolic B, et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. *J Vasc Interv Radiol.* 2012; 23:727–736. [PubMed: 22513394]
9. Patel IJ, Davidson JC, Nikolic B, et al. Addendum of newer anticoagulants to the SIR consensus guideline. *J Vasc Interv Radiol.* 2013; 24:641–645. [PubMed: 23622037]
10. Grotz W, Siebig S, Olschewski M, Strey CW, Peter K. Low-dose aspirin therapy is associated with improved allograft function and prolonged allograft survival after kidney transplantation. *Transplantation.* 2004; 77:1848–1853. [PubMed: 15223902]
11. Robertson AJ, Nargund V, Gray DW, Morris PJ. Low dose aspirin as prophylaxis against renal-vein thrombosis in renal-transplant recipients. *Nephrol Dial Transplant.* 2000; 15:1865–1868. [PubMed: 11071979]
12. Ferrari E, Benhamou M, Cerboni P, Marcel B. Coronary syndromes following aspirin withdrawal: a special risk for late stent thrombosis. *J Am Coll Cardiol.* 2005; 45:456–459. [PubMed: 15680728]
13. Bachman DS. Discontinuing chronic aspirin therapy: another risk factor for stroke? *Ann Neurol.* 2002; 51:137–138.
14. Atwell TD, Smith RL, Hesley GK, et al. Incidence of bleeding after 15,181 percutaneous biopsies and the role of aspirin. *AJR Am J Roentgenol.* 2010; 194:784–789. [PubMed: 20173160]
15. Schafer AI. Effects of nonsteroidal anti-inflammatory therapy on platelets. *Am J Med.* 1999; 106:25S–36S. [PubMed: 10390125]
16. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999; 130:461–470. [PubMed: 10075613]
17. Omary RA, Bettmann MA, Cardella JF, et al. Quality improvement guidelines for the reporting and archiving of interventional radiology procedures. *J Vasc Interv Radiol.* 2003; 14(9 Pt 2):S293–295. [PubMed: 14514836]
18. Hardin, JW., Hilbe, JM. *Generalized Estimating Equations.* Boca Raton, FL: Chapman & Hall/CRC; 2003.
19. Manno C, Strippoli GF, Arnesano L, et al. Predictors of bleeding complications in percutaneous ultrasound-guided renal biopsy. *Kidney Int.* 2004; 66:1570–1577. [PubMed: 15458453]
20. Zhu MS, Chen JZ, Xu AP. Factors that can minimize bleeding complications after renal biopsy. *Int Urol Nephrol.* 2014; 46:1969–1975. [PubMed: 25150849]

21. Pan W. Akaike's information criterion in generalized estimating equations. *Biometrics*. 2001; 57:120–125. [PubMed: 11252586]
22. Maulaz AB, Bezerra DC, Michel P, Bogousslavsky J. Effect of discontinuing aspirin therapy on the risk of brain ischemic stroke. *Arch Neurol*. 2005; 62:1217–1220. [PubMed: 16087761]
23. Nayak-Rao S. Percutaneous native kidney biopsy in patients receiving antiplatelet agents—is it necessary to stop them routinely? *Indian J Nephrol*. 2015; 25:129–132. [PubMed: 26060359]
24. Weigert AL, Schafer AI. Uremic bleeding: pathogenesis and therapy. *Am J Med Sci*. 1998; 316:94–104. [PubMed: 9704663]
25. Boccardo P, Remuzzi R, Galbusera M. Platelet dysfunction in renal failure. *Semin Thromb Hemost*. 2004; 30:579–589. [PubMed: 15497100]
26. Slichter SJ. Relationship between platelet count and bleeding risk in thrombocytopenic patients. *Transfus Med Rev*. 2004; 18:153–167. [PubMed: 15248165]

Table 1

Baseline Demographic, Clinical, and Procedural Characteristics by Time Frame of Patient Aspirin Exposure before Biopsy

Characteristic	0–3 d (n = 476)	4–7 d (n = 858)	8–10 d (n = 664)	> 10 d or none taken (n = 4,702)	Total (N = 6,700)	P Value
Age, y	57.0 [47.0, 65.0]	59.0 [50.0, 67.0]	59.0 [50.0, 67.0]	50.0 [39.0, 60.0]	53.0 [43.0, 62.0]	< .001
Male sex	301 (63.2%)	527 (61.4%)	394 (59.3%)	2,545 (54.1%)	3,767 (56.2%)	< .001
No. passes*	3.0 (1–6)	3.0 (2–6)	3.0 (1–5)	3.0 (1–6)	3.0 (1–6)	.476
INR	1.0 [0.9, 1.1]	1.0 [0.9, 1.0]	1.0 [0.9, 1.0]	1.0 [0.9, 1.1]	1.0 [0.9, 1.1]	.056
Platelets, 10 ⁹ /L	210.0 [168.0, 256.0]	208.0 [171.0, 258.5]	208.0 [168.0, 250.0]	214.0 [170.0, 263.0]	212.0 [170.0, 260.0]	.136
Biopsy performed by trainee	123 (25.8%)	239 (27.9%)	210 (31.6%)	1,311 (27.9%)	1,883 (28.1%)	.143
eGFR (mL/min/1.73 m ²)	41.2 [27.2, 55.0]	50.1 [38.2, 60.8]	49.6 [41.0, 59.8]	48.1 [37.5, 59.3]	48.3 [37.4, 59.3]	< .001
Creatinine (mg/dL)	1.6 [1.3, 2.4]	1.4 [1.2, 1.7]	1.4 [1.1, 1.7]	1.4 [1.2, 1.8]	1.4 [1.2, 1.8]	< .001
Indication biopsy	214 (45.0%)	126 (14.7%)	53 (8.0%)	930 (19.8%)	1,323 (19.7%)	< .001

Note—Values are presented as number (%) or median [IQR].

eGFR = estimated glomerular filtration rate; INR = international normalized ratio; IQR = interquartile range.

* Ranges displayed in place of IQR, as median/IQR of all categories was 3 [3, 3].

Table 2

Observed Number of Bleeding Complications by Time Frame of Aspirin Exposure before Biopsy

Complication Type	0-3 d (n = 476)	4-7 d (n = 858)	8-10 d (n = 664)	No Recent Use (n = 4,702)	Total (N = 6,700)
Any complication (major or minor)	8 (1.7%)	3 (0.3%)	2 (0.3%)	31 (0.7%)	44 (0.7%)
Major complication	4 (0.8%)	1 (0.1%)	1 (0.2%)	10 (0.2%)	16 (0.2%)
Minor complication	4 (0.8%)	2 (0.2%)	1 (0.2%)	21 (0.4%)	28 (0.4%)

Table 3

Univariate GEE Model Results for Association of Demographic, Clinical, and Procedural Characteristics with Complications (Any or Major Only) after Renal Allograft Biopsy

Outcome	Risk Factor	OR [95% CI]	P Value
Any complication	Aspirin exposure (4-category)		.014
	8–10 vs > 10/never	0.405 [0.085, 1.93]	
	4–7 vs > 10/never	0.518 [0.166, 1.62]	
	0–3 vs > 10/never	2.52 [1.14, 5.58]	
	Aspirin 10 d prior	0.96 [0.478, 1.93]	.909
	Aspirin 7 d prior	1.36 [0.666, 2.8]	.396
	Aspirin 3 d prior	2.97 [1.41, 6.27]	.004
	Aspirin (325 mg) 3 d prior	4.43 [1.27, 15.4]	.019
	Male sex	1.02 [0.528, 1.98]	.946
	INR	6.98 [0.860, 56.7]	.069
	Log (creatinine)	2.84 [1.52, 5.31]	.001
	No. passes/cores	1.27 [0.872, 1.86]	.212
	Platelets > 50	0.747 [0.327, 1.71]	.490
	Biopsy performed by trainee	0.941 [0.469, 1.89]	.864
	Indication biopsy	2.27 [1.19, 4.33]	.012
	Age (/10 y)	1.06 [0.872, 1.28]	.574
	eGFR (/10)	0.762 [0.61, 0.952]	.017
	Platelets (/100)	0.623 [0.418, 0.929]	.020
Major complication	Aspirin exposure (4-category)		.079
	8–10 vs > 10/never	0.71 [0.091, 5.53]	
	4–7 vs > 10/never	0.546 [0.0693, 4.3]	
	0–3 vs > 10/never	3.98 [1.25, 12.7]	
	Aspirin 10 d prior	1.41 [0.513, 3.9]	.504
	Aspirin 7 d prior	1.83 [0.635, 5.28]	.263
	Aspirin 3 d prior	4.39 [1.41, 13.6]	.010
	Aspirin (325 mg) 3 d prior	8.88 [2, 39.3]	.004
	Male sex	1.3 [0.472, 3.58]	.611
	INR	9.26 [0.528, 162]	.128
	Log (creatinine)	5.42 [2.39, 12.3]	< .001
	No. passes/cores	1.36 [0.851, 2.16]	.201
	Platelets > 50	0.543 [0.175, 1.69]	.291
	Biopsy performed by trainee	1.16 [0.403, 3.35]	.780
	Indication biopsy	6.84 [2.48, 18.9]	< .001
	Age (/10 y)	1.15 [0.878, 1.5]	.312
	eGFR (/10)	0.597 [0.399, 0.894]	.012
	Platelets (/100)	0.455 [0.236, 0.876]	.018

Note—ORs and 95% Wald CIs are presented. For the 4-category aspirin exposure, > 10 days or never was used as the baseline level, and presented ORs for each level are based on the contrast between the listed exposure level and baseline. Units for creatinine are mg/dL, for platelets are $10^9/L$, and for eGFR are mL/min/1.73 m².

CI = confidence interval; eGFR = estimated glomerular filtration rate; GEE = generalized estimating equation; INR = international normalized ratio; OR = odds ratio.

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Table 4

Multivariate GEE Model Results for Association of Demographic and Clinical Characteristics with Complications (Any or Major Only) after Renal Allograft Biopsy

Outcome	Risk Factor	OR [95% CI]	P Value
Any complication	Aspirin exposure (4 groups)		.192
	8–10 vs > 10/never	0.465 [0.107, 2.02]	
	4–7 vs > 10/never	0.378 [0.0973, 1.47]	
	0–3 vs > 10/never	1.67 [0.663, 4.2]	
	eGFR (/10)	0.798 [0.643, 0.989]	.040
	Platelets (/100)	0.757 [0.549, 1.04]	.091
	Age (/10 y)	1.07 [0.87, 1.32]	.511
Major complication	Male sex	0.982 [0.475, 2.03]	.961
	eGFR (/10)	0.608 [0.405, 0.912]	.016
	Platelets (/100)	0.641 [0.425, 0.965]	.033
	Age (/10 y)	1.13 [0.821, 1.55]	.455
	Male sex	1.35 [0.413, 4.41]	.620

Note—ORs and 95% Wald CIs are presented. For the 4-category aspirin exposure, > 10 days or never was used as the baseline level, and presented ORs for each level are based on the contrast between the listed exposure level and baseline. Aspirin exposure was not included in the multivariate model for major complications because it did not reach univariate significance. Units for eGFR are mL/min/1.73m² and for platelets are 10⁹/L.

CI = confidence interval; eGFR = estimated glomerular filtration rate; GEE = generalized estimating equation; OR = odds ratio.

Table 5

Multivariate GEE Model Results for Association of Demographic and Clinical Characteristics with Complications (Any or Major Only) after Renal Allograft Biopsy with Aspirin Exposure Dichotomized by 325 mg Aspirin Received within 3 Days before Biopsy

Outcome	Risk Factor	OR [95% CI]	P Value
Any complication	325 mg ASA 3 d	3.87 [1.12, 13.4]	.032
	eGFR (/10)	0.789 [0.635, 0.98]	.032
	Platelets (/100)	0.747 [0.543, 1.03]	.072
	Age (/10 y)	1.04 [0.84, 1.28]	.733
	Male sex	0.973 [0.466, 2.03]	.942
Major complication	325 mg ASA 3 d	6.30 [1.27, 31.3]	.024
	eGFR (/10)	0.617 [0.414, 0.919]	.017
	Platelets (/100)	0.639 [0.422, 0.965]	.033
	Age (/10 y)	1.12 [0.817, 1.55]	.474
	Male sex	1.32 [0.4, 4.35]	.649

Note—ORs and 95% Wald CIs are presented. Units for eGFR are mL/min/1.73 m² and for platelets are 10⁹/L.

ASA = acetylsalicylic acid; CI = confidence interval; eGFR = estimated glomerular filtration rate; GEE = generalized estimating equation; OR = odds ratio.