2. PRE – BIOPSY MEDICATION – ANTIPLATELET AND ANTICOAGULANT AGENTS

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Authors: Emily See, Paul Champion de Crespigny, Pamela Lopez-Vargas, Talia Gutman, Karine Manera, Solomon Menahem, John Saunders, David Voss, Jeffrey Wong and Rob MacGinley.

GUIDELINES

a. We recommend continuation of aspirin in patients at high risk for a cardiovascular event, including those with a history of coronary stent (particularly within 3 months of bare metal stent or 12 months of drug eluting stent insertion), symptomatic myocardial ischaemia or peripheral vascular disease (including patients with a peripheral stent), or previous ischaemic stroke (1C).

b. We recommend cessation of aspirin for patients at low risk for a cardiovascular event either 3 days (to prevent major bleeding) or 7 days (to prevent minor bleeding) prior to the renal biopsy (1C).

c. We suggest the use of bridging anticoagulation in patients at highest risk for thromboembolism. This includes patients with a mechanical mitral valve, a mechanical aortic valve and additional stroke risk factors, antiphospholipid syndrome, an embolic event within the previous 3 months, atrial fibrillation (CHADS2 score 5 or 6), and a previous thromboembolic event with interruption of anticoagulation (2C).

UNGRADED SUGGESTIONS FOR CLINICAL CARE

- We suggest all patients stop taking:
  - Adenosine diphosphate (ADP) inhibitors (clopidogrel, prasugrel, ticagrelor) 5 to 7 days before the renal biopsy
  - Warfarin 5 days before the renal biopsy
  - Direct thrombin inhibitors (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban) 48-72 hours before the renal biopsy
  - Unfractionated heparin 4-6 hours before the renal biopsy
  - Low molecular weight heparin 24 hours before the renal biopsy
- We suggest that antiplatelets and anticoagulants should not be restarted until 24-48 hours following an uncomplicated biopsy, since most complications will occur within this time.
- We suggest that prior to renal biopsy, the platelet count should be above 50,000/μL and the international normalised ratio (INR) should be less than 1.5.

IMPLEMENTATION AND AUDIT

1. All centres and proceduralists should maintain records of use of antiplatelet and anticoagulant agents (including dates of cessation) and complications associated with all percutaneous native and allograft renal biopsies.
2. Outcomes and complications should be reviewed at regular audits and performance should be benchmarked to ensure safe practice.

BACKGROUND

Percutaneous renal biopsy is an important means of diagnosing kidney disease. Although it is considered to be a safe procedure, especially since the introduction of spring-loaded needles and real-time imaging,(1, 2) bleeding is the most common complication. Routine care prior to biopsy involves measuring haemoglobin, platelet count, international normalised ratio (INR) and activated partial thromboplastin time (APTT). The most appropriate pre-biopsy thresholds of platelet count and INR are debated. Advanced techniques, including measurement of skin bleeding time and platelet function assays, are not considered to be standard practice and are not covered by this guideline.

To minimise the risk of bleeding, the practice of advising patients to stop antiplatelet and anticoagulant agents prior to renal biopsy is common. These agents are common in patients with kidney disease, who are at increased risk of vascular disease. The most frequently prescribed antiplatelet agents include cyclooxygenase inhibitors (e.g. aspirin) and adenosine diphosphate (ADP) receptor inhibitors (e.g. clopidogrel, ticlopidine, prasugrel). Aspirin irreversibly inhibits platelet cyclooxygenase, a key enzyme in production of thromboxane A2, which mediates platelet activation and aggregation. Clopidogrel binds to platelet receptors and inhibits activation of the glycoprotein IIb/IIIa pathway. Both aspirin and clopidogrel modulate platelet activity for the duration of their lifespan. Withholding these agents for 5 to 7 days results in approximately 30-50% of platelets having normal function at the time of procedure.(3) Less common classes of antiplatelet agents include glycoprotein IIb/IIIa inhibitors (e.g. abciximab, eptifibatide, tirofiban), phosphodiesterase inhibitors (e.g. dipyridamole) and non-steroidal anti-inflammatory drugs. Non-steroidal anti-inflammatory drugs have not been shown to increase the risk of bleeding, except in patients with existing coagulopathies (e.g. haemophilia, Von Willebrand disease, or severe thrombocytopenia) and paradoxically tend to diminish the antiplatelet effect of aspirin.(4)

Anticoagulant medications include vitamin K antagonists (e.g. warfarin), heparin (e.g. unfractionated, low molecular weight), direct thrombin inhibitors (e.g. dabigatran, argatroban, bivalirudin), and factor Xa inhibitors (e.g. apixaban, rivaroxaban). The anticoagulant effect of warfarin is mediated by antagonism of the production of vitamin K-dependent extrinsic pathway clotting factors and protein C and S in the liver. Unfractionated and low molecular weight heparin accelerate inhibition of factor X, potentiating the action of anti-thrombin III. Direct thrombin inhibitors directly inhibit the enzyme thrombin, while factor Xa inhibitors act directly upon factor X without using anti-thrombin as a mediator.(5)

Although policies and practices vary between centres, it is common to delay non-urgent biopsies until antiplatelet and anticoagulant agents have been ceased for several days. This approach may lead to important delays in diagnosis and treatment, or unnecessary administration of blood products such as fresh frozen plasma or platelets. Of greater concern, withholding antiplatelet or anticoagulant medications has been associated with precipitation of ischaemic and thromboembolic events.(6-10) In a case-control study of 309 patients admitted with an ischaemic stroke or transient ischaemic attack, Llinas *et al.*(9) found that discontinuation of aspirin increased the odds of having a repeat stroke 3.34 times (odds ratio 3.34, 95% confidence interval [CI] 1.07-10.39). Garcia Rodriguez *et al.*(8) conducted a case-control study of 39,513 patients who were prescribed aspirin for secondary prevention of cardiovascular events. They found that patients who had recently stopped taking aspirin were at significantly greater risk of fatal and non-fatal myocardial infarction (rate ratio 1.43, 95% CI 1.12-1.84) compared to individuals who had continued aspirin therapy. The risk of an ischaemic event appears to be greatest in the one to two weeks after stopping antiplatelet therapy(7, 10) and in the first month after cardiac intervention.(11) In patients who have undergone percutaneous coronary intervention, the risk of a major adverse cardiovascular event with discontinuation of dual antiplatelet therapy for 7 days was 6 times greater compared to individuals who continued therapy (hazard ratio 7.04, 95% CI 3.31-14.95).(10) A meta-analysis of trials including almost 50,000 patients suggested that in patients who developed acute coronary syndrome following withdrawal of aspirin, the mean time to event was 8.5 days.(7)

Interruption of anticoagulation therapy may be associated with similar risks.(12) In some studies, temporary cessation of warfarin has been shown to result in a return to pre-therapy risk of thromboembolism (13) Patients at greatest risk include those with a history of a mechanical mitral valve, a mechanical aortic valve and additional stroke risk factors, antiphospholipid syndrome, an embolic event within the previous 3 months, atrial fibrillation (CHADS2 score 5 or 6), and previous thromboembolism. Conversion of a long-acting anticoagulant to a short-acting agent is often performed

at the time of invasive procedures, with the intent of reducing this risk.(14). However, 'bridging therapy' requires monitoring and is associated with cost to patients and health care services.

SEARCH STRATEGY

Databases searched: The search was carried out in Medline (1946 – May 2017), The Cochrane Library (Central) and the Cochrane Kidney and Transplant Register of Studies, Embase (May2017). Text words for renal biopsy were combined with MeSH terms and text words for aspirin, clopidogrel and anti-platelet therapy. No language restrictions were placed on the search.
The search strategy is provided in the Appendices.

Date of search/es: May 2017

WHAT IS THE EVIDENCE?

Coagulation profile in the setting of renal biopsy

Mejia-Vilet *et al*.(15) performed a retrospective observational study of 1205 ultrasound-guided percutaneous renal biopsies undertaken in adult patients with a 16-gauge needle at a single centre in Mexico. The median platelet count was 253 and INR was normal (not specified by authors). The primary outcome was development of a major complication, defined as any complication that required medical intervention (blood transfusion, arterial embolization, or surgery). The authors found that a platelet count <150,000/µL was associated with a higher risk of major complications compared to a platelet count ≥150,000/µL (OR 2.78, 95% CI 1.04 to 7.43, p=0.041), after adjustment for chronic kidney disease features on pre-biopsy ultrasound, blood urea nitrogen >50 mg/dL, haemoglobin <11 g/dL, and perirenal haematoma in post-biopsy ultrasound.

In a two-centre prospective observational study by Moledina *et al*,(16) 159 adult who underwent ultrasound or computed tomography guided percutaneous renal biopsy to investigate acute kidney disease, using either 16- or 18-gauge needles were included. The median platelet count was 202,000/µL and INR was 1.1. A greater proportion of patients who required a post-biopsy blood transfusion had a platelet count <120,000/µL at the time of biopsy (23% vs 4%, p=0.002) and a lower platelet count (per 10,000/µL drop) was associated with a greater risk of blood transfusion (OR 4.6, 95% CI 1.6-13.4), after adjustment for female gender and blood urea nitrogen (per 10 mg/dL increase).

Although lower platelet count has been associated with an increased risk of major complications, no studies have determined the threshold of platelet count or INR at which it is safe to proceed with renal biopsy. The two largest renal biopsy studies, which investigated the impact of antiplatelet agents on bleeding risk, excluded patients with a platelet count ≤50,000/µL or INR ≥1.5,(17, 18) which is consistent with recommendations for other solid organ percutaneous biopsies.(19-21) It must be noted, however, that the median platelet count in both studies was much higher than this threshold (212,000/µL and 241,000/µL, respectively), and the median INR in both studies was normal (1.0 and 0.9, respectively).(17, 18) In the study by MacKinnon *et al*,(22) patients were not biopsied if their platelet count was <100,000/µL or if their INR was >1.4. Again, the mean platelet count in the study was much higher at 285,000/µL and the mean INR was much lower (1.3) than these thresholds. In the absence of sufficient evidence to inform a threshold at which proceeding with renal biopsy is safe, platelet and INR thresholds should be individualised, taking into account other factors associated with the risk and consequences of bleeding, including the use of antiplatelet and anticoagulant therapy, and the presence of hypertension, uraemia, complicated anatomy, and low haemoglobin.

Antiplatelet studies in the setting of renal biopsy

Atwell *et al*.(17) performed a large single-centre retrospective study of 15,181 patients undergoing ultrasound or CT-guided percutaneous solid organ biopsies at a single centre between 2002 and 2006. Of these, 5,832 were native or allograft renal biopsies. Patients were required to have a platelet count greater than 50 x 10^9/L and an INR less than 1.6. Up to 2 cores were taken, using a needle size of 20-gauge or larger, under CT or ultrasound guidance. A major bleeding complication was defined as the

requirement for transfusion, an interventional radiology procedure, or an operative intervention. The use of aspirin (81mg or 325mg) within 10 days prior to the procedure was not associated with a significant difference in the incidence of major bleeding compared to the absence of aspirin in the entire cohort (0.6% vs. 0.4%, p=0.34) or in the renal biopsy cohort (1.0% vs 0.6%, p=0.53). The association between aspirin use and risk of bleeding remained non-significant, even after adjustment for platelet count, INR, needle size, and number of passes. Although not a primary objective of this study, data were also collected on the use of ADP-inhibitors. Of 246 patients in the overall cohort who had recently taken clopidogrel, only 1 (0.4%) developed a major bleeding complication.

In a single-centre retrospective study of 6,700 renal allograft biopsies performed in 2,362 patients between 2005 and 2014, Baffour *et al*.(18) examined the association between aspirin use and bleeding events. All biopsies were ultrasound guided and most were protocol biopsies (81.3%). The INR was less than 1.5 and platelet count greater than 50 x 10^9/L in all patients. Three biopsy cores were obtained from each patient, using a needle size of ≥18 gauge. Aspirin doses were either 81mg or 325mg. Any bleeding complication was observed in 1.7% of patients receiving aspirin within 3 days of biopsy, 0.3% in patients receiving aspiring 4-7 days before biopsy, and 0.3% in patients receiving aspirin within 8-10 days of aspirin, compared to 0.7% in patients not on aspirin. In a multivariable logistic model, there was no association between aspirin use and the risk of bleeding complications, except in patients who received 325mg daily of aspirin within 3 days of biopsy who experienced an increased risk of any bleeding complication (OR 3.87 [95% CI 1.12-13.4, p=0.032]) and major bleeding complications (OR 6.30 [95% CI 1.27-31.3, p=0.024]).

Mackinnon *et al.*(22) retrospectively compared complication rates following 1120 biopsies between centres that routinely withheld or continued antiplatelet agents at the time of native percutaneous renal biopsy. In total, 60 patients in the first centre were on antiplatelet agents (aspirin n=54, dipyridamole n=4, clopidogrel n=2), which were withheld for 5 days, while 75 patients continued their antiplatelet agents (aspirin n=68, clopidogrel n=7). Biopsies were ultrasound-guided, needle size was 16-gauge, and the median number of passes was 2 to 3. Patients were not biopsied if their blood pressure was >160/90mmHg, if their INR was greater than 1.4 or if their platelet count was less than 100 x 10^9/L. Major complications were defined as the requirement for blood transfusion, surgical or radiological intervention. Minor bleeding was defined as a fall in haemoglobin of ≥1.0g/dL. They found that continuation of antiplatelet agents was associated with a greater absolute decrease in haemoglobin (-0.50 ± 0.81 vs -0.30 ± 0.69 g/dL, p=0.015) and the percentage of patients with a minor bleeding complication (31.0% vs 11.7%, p=0.008), however there was no difference in the proportion of patients in either group with a major complication, either in urgent (5.2% vs 3.4%, p=0.17) or elective (1.3% vs 0%, p=0.56) settings.

A meta-analysis by Corapi *et al*.(23) examined the factors associated with macroscopic haematuria and blood transfusion following native kidney biopsy. Of the 16 studies which reported antiplatelet practice, the rate of transfusion did not differ between the 9 studies (n=2116 biopsies) which withheld antiplatelet agents for ≥7 days prior to biopsy compared to the 7 studies (n=4,009 biopsies) in which antiplatelet agents were not withheld for ≥7 days (p value for difference 0.7). Similarly, there was no difference in macroscopic haematuria rates between studies utilising either antiplatelet withholding practice (p value for difference 0.3).

Moledina *et al.*(16) reported the findings of a prospective observational study performed in two centres in the United States. They studied 159 adult patients who underwent ultrasound or computed tomography guided percutaneous renal biopsy to investigate acute kidney disease, using either 16- or 18-gauge needles. Compared to patients who did not require a transfusion, those who received a transfusion following biopsy were not more likely to have received antiplatelet medications within the 7 days prior to the procedure in an unadjusted analysis (9% vs 14%, p=0.57).

Despite their increasing use in clinical practice, no studies have reported the incidence of bleeding complications following renal biopsy in patients managed with newer antiplatelet agents (ticagrelor, prasugrel). Therefore, recommendations about the need for, and timing of, antiplatelet interruption can only be based on the pharmacological profile of these agents.

Anticoagulant studies in the setting of renal biopsy

Although Moledina *et al.*(16) did not report an increased risk of transfusion in patients who had taken an anticoagulant medication within the 7 days prior to biopsy (50 vs 53%; p=0.84), no studies have reported the incidence of bleeding complications in patients taking warfarin or newer anticoagulant agents (dabigatran, apixaban, rivaroxaban) at the time of biopsy. Therefore, recommendations about the timing of treatment interruption can only be based on the pharmacological profile of these agents. The utility of bridging anticoagulation during warfarin interruption has been investigated by a randomised, double-blind, placebo-controlled trial of patients with atrial fibrillation (AF) or flutter (CHADS2 score ≥1) who required perioperative interruption of warfarin treatment for an elective procedure. This study found that discontinuing warfarin treatment without the use of bridging anticoagulation was non-inferior to the use of bridging anticoagulation for the prevention of arterial thromboembolism.(24) The mean CHADS2 score in this study was 2.3 and only 13% of patients had a CHADS2 score >3, so the findings of this study should be interpreted with caution in high-risk patients with AF and these findings are not generalisable to other indications for anticoagulation, including mechanical valves, anti-phospholipid syndrome and deep vein thrombosis or pulmonary embolism.

SUMMARY OF THE EVIDENCE

The majority of studies have only examined the peri-procedure management of aspirin in patients undergoing renal biopsies. The evidence comes mainly from low quality, single-centre retrospective studies and one systematic review. Aspirin continuation at the time of biopsy was not associated with an increased risk of major bleeding events, defined as the requirement for transfusion, an interventional radiology procedure, or an operative intervention. Aspirin use within 3-7 days of renal biopsy was associated with an increased risk of any bleeding complication or a minor bleeding complication (haemoglobin drop ≥1.0g/dL). Withholding aspirin in patients at high risk of cardiovascular disease is associated with an increased risk of peri-procedural ischaemic event.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: No recommendation.
UK Renal Association: No recommendation.
Canadian Society of Nephrology: No recommendation.
European Best Practice Guidelines: No recommendation.
International Guidelines: No recommendation.
Society of Interventional Radiology(25): withhold aspirin and clopidogrel for 5 days before procedures with significant bleeding risk. Withhold therapeutically dosed low molecular weight heparin for 24 hours or up to 2 doses. Withhold warfarin for 5 days and correct INR to <1.5. Withhold unfractionated heparin for 4 hours and correct APTT values >1.5x control.

SUGGESTIONS FOR FUTURE RESEARCH

There is a paucity of data on the peri-procedure management of patients on clopidogrel, direct thrombin inhibitors and factor Xa inhibitors. With the increasing prescription of these agents in clinical practice, future work should investigate the optimal time of drug cessation prior to renal biopsy.

CONFLICT OF INTEREST

Emily See, Paul Champion de Crespigny, Pamela Lopez-Vargas, Talia Gutman, Karine Manera, Solomon Menahem, John Saunders, David Voss, Jeffrey Wong and Rob MacGinley have no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by KHA-CARI.

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APPENDICES

Table 1. Characteristics of included studies

Study ID	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Primary outcomes
Atwell et al (2010)(17)	15,181 percutaneous core biopsies *5,832 renal biopsies	Retrospective review	Single centre,	*Patients underwent percutaneous core biopsies for liver, kidney, lung, pancreas and other organs. *Procedure done using 20-gauge or larger under CT or ultrasound guidance. *platelet count >50x10^9/L and INR <1.6	Not on aspirin	Use of aspirin (81 or 325 mg) ingested within 10 days before biopsy	• Bleeding
Baffour et al (2017)(18)	6700 (renal allograft biopsies) 2,362 patients	Retrospective Review	Single Centre, USA	Patients with renal transplant	biopsy, withholding aspirin (81mg or 325mg) for >10 days, 8-10 days, 4-7 days, 0-3 days	no aspririn use	• Any bleeding complication • Major bleeding complication
Mackinnon et al (2008)(22)	1,120 biopsies	Retrospective study	Multicentre, Scotland	*Patients undergoing elective or emergency native renal biopsy. *Biopsy done using disposable spring-loaded biopsy gun with a 16-gauge needle under direct ultrasound guidance. *Maximum number of passes was five.	Stop antiplatelet agents 5 days prior to kidney biopsy	Continue antiplatelet use prior biopsy	• Major and minor bleeding
Corapi et al (2012)(23)	34 studies (9,474 biopsies) 13 studies - antiplatelet agents	Systematic review and Meta-analysis		Adults undergoing native kidney biopsy as an inpatient or outpatient	Antiplatelet agents held for ≥ 7 days	Antiplatelet agents not held for ≥ 7 days	• Macroscopic haematuria • Erythrocyte transfusion rates
Mejia-Vilet et al (2018)(15)	1205 percutaneous renal biopsies	Retrospective & prospective observational study	Single centre, Mexico	Patients undergoing percutaneous renal biopsy.	Antiplatelet agents were suspended at least 7 days before the procedure	No comparator	• Blood transfusion • Nephrectomy • Death • Arterial embolization • Perinephric haematoma

Study ID	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Primary outcomes
							• Gross haematuria
Moledina et al (2018)(16)	159 patients	Prospective observational study	Multicentre, USA	Patients with acute kidney disease undergoing renal biopsy	Ultrasound or computed tomography with 16 or 18 gauge needle	No comparator	• Blood transfusion

Table 2. Risk of bias- Systematic reviews AMSTAR

Study ID	Priori design provided	Duplication-selection, extraction	Comprehensive literature search	Grey literature inclusion	List of included and excluded studies	Characteristics of included studies	Scientific quality	Appropriate conclusions	Methods appropriate	Publication bias	Conflict of interest
Corapi et al (2012) (23)	Yes	Yes	No	Yes	Can't answer	Yes	Yes	Yes	Yes	Can't answer	Can't answer

Table 3. Risk of bias- Other studies

Study ID	N	Study type	Quality	Comments
Atwell et al (2010)(17)	15,181 percutaneous core biopsies 5,832 renal biopsies	Retrospective review	Low	No quality appraisal tool available
Baffour et al (2017)(18)	6700 (renal allograft biopsies) 2,362 patients	Retrospective review	Low	No quality appraisal tool available; arbitrary stratification of exposure groups
Mackinnon et al (2008)(22)	1,120 biopsies	Retrospective study	Low	No quality appraisal tool available
Mejia-Vilet et al (2018)(15)	1205 percutaneous renal biopsies	Retrospective/prospective study	Low	No quality appraisal tool available
Moledina et al (2018)(16)	159 patients	Prospective observational study	Low	No quality appraisal tool available

Table 4. Major bleeding outcomes

Study ID	N	Study type	Intervention	Control	Outcome	Results	Quality
Atwell et al (2010)(17)	15,181 percutaneous core biopsies *5,832 renal biopsies	Retrospective review	Percutaneous core biopsies in patients taking aspirin 81 or 325mg within 10 days before biopsy.	Not on aspirin	Major bleeding complications	• 5,832 native and transplant renal biopsies were conducted (38%) • 70 major haemorrhages (0.5%) Common Terminology Criteria for Adverse Events (CTCAE) grade ≥3 within 3 months of the biopsy • 14/70 (20%) major bleeding complications occurred more than 24 hours after biopsy, this included 10/39 (26%) after kidney biopsy • 3 people died (3/15,181, 0.02%) • incidence of bleeding after kidney biopsy was 0.7% • There was an association between major bleeding and platelet count (mean 194 x 10^9/L for haemorrhage versus 257 x 10^9/L for no haemorrhage, p <0.001) and higher international normalized ratio (mean 1.2 for bleeding versus INR 1.0 for no haemorrhage; p<0.001) • Recent aspirin therapy does not appear to significantly increase the risk of bleeding complications.	Low
Baffour et al (2017)(18)	6700 (renal allograft biopsies) 2,362 patients	Retrospective Review	biopsy, withholding aspirin (81mg or 325mg) for >10 days, 8-10 days, 4-7 days, 0-3 days	No aspirin use	Major bleeding complication	• 44 total number of complications in 41 patients; 16 were major • major complication = 0.24% (95%CI: 0.14 - 0.39) • Major complications were: 11/16 (69%) perinephric bleeding - requiring angiography +/- embolization, +/- blood transfusion; 5/16 were haematuria requiring bladder irrigation +/- percutaneous nephrostomy tube placement. • Platelet count OR 0.46 (95%CI: 0.24 - 0.88), P = 0.019; Creatinine 5.42 (95%CI: 2.39 - 12.3), P ≤ 0.001; eGFR 0.60 (95%CI:0.40 - 0.89), P = 0.012; Indication biopsy 6.84 (95%CI: 2.48 - 18.9), P<0.001; were all significantly associated with major bleeding complication. • 325mg aspirin exposure within 3 days of biopsy was associated with major bleeding complication OR 6.30 (95%CI: 1.27 - 31.3), P = 0.024.	Low
					Any bleeding complication	• any complication = 0.66% (95%CI:0.46 - 0.90) • Platelet count OR 0.62 (95%CI: 0.42 - 0.93), P = 0.02; creatinine 2.84 (95%CI: 1.52 - 5.31), P ≤ 0.001; eGFR 0.76 (95%CI: 0.61 - 0.95), P = 0.007; Indication biopsy 2.27 (95%CI: 1.19 - 4.33), P=0.013; were all significantly associated with any bleeding complication. • 325mg aspirin exposure within 3 days of biopsy was associated with any bleeding complication OR 3.87 (95%CI: 1.12 - 13.4), P = 0.032;	
Mackinnon et al (2008)(22)	1,120 biopsies	Retrospective study	Stop antiplatelet agents 5 days prior to kidney	Continue antiplatelet use prior biopsy	Major bleeding requiring transfusion,	• Major bleeding more common in patients undergoing urgent than elective biopsy. • For patients who had an urgent biopsy, the rate of major bleeding	Low

Study ID	N	Study type	Intervention	Control	Outcome	Results	Quality
			biopsy		surgery or radiological intervention	was 5.2% in the control group versus 3.4% in the intervention group, P=0.17. • For patients who had elective biopsy the rate of major complication was 1.3% (1/75) for those in the control group versus 0% (0/60) for those in the intervention group, P=0.56. • **Conclusion:** no significant difference in the rate of major bleeding between the two groups. But there is a significant difference in the rate of minor complications.	
Corapi et al (2012)(23)	34 studies (9,474 biopsies) 13 studies - antiplatelet agents	Systematic review and Meta-analysis	Antiplatelet agents held for ≥ 7 days	Antiplatelet agents not held for ≥ 7 days	Macroscopic haematuria	• 9 studies withheld antiplatelet agents for ≥ 7 days; macroscopic haematuria rate 3.8 (95%CI: 1.5 - 7.1); • 4 studies did not withhold antiplatelets agents for ≥ 7 days; macroscopic haematuria rate 1.6 (95%CI: 0.1 - 5.3) • There was no difference between the two groups for macroscopic haematuria rate P = 0.3	Moderate
					Erythrocyte transfusion rates	• 9 studies held antiplatelet agents for ≥ 7 days; transfusion rates 0.5 (95%CI: 0.1 - 1.3); • 7 studies did not withhold antiplatelets for ≥ 7 days; transfusion rates 0.7 (95%CI: 0.1 - 1.8) • There was no difference between the two groups for transfusion rates P = 0.7	
Mejia-Vilet et al (2018)(15)	1205 percutaneous renal biopsies	Retrospective & prospective observational study	Antiplatelet agents were suspended at least 7 days before the procedure	No comparator	Major complication requiring blood transfusion, embolization or surgery	• Major complications included: 1 patient (0.08%) with haematuria and 38 (3.15%) with perinephric haematomas requiring blood transfusions. • 6 (0.48%) renal angiographies with embolisation were performed • Platelet count < 150,000/µL - higher risk of major complications OR 2.78 (95%CI: 1.04 - 7.43, p=0.04)	Low
Moledina et al (2018)(16)	159 patients	Prospective observational study	Ultrasound or computed tomography with 16 or 18 gauge needle	No comparator	Blood transfusion	• 12 (8%, [95%CI: 4 - 13]) patients required a blood transfusion • 11 (7%) had a haematoma, 8 (73%) had a transfusion versus 3 (2%), p <0.001 • 3 (2%) required angiographic intervention also had a transfusion, p<0.001. • Patients with platelet count <120,000/µL at time of biopsy had increased risk of blood transfusion (23% vs 4%, P= 0.002) • A lower platelet count (per 10,000/µL drop) was associated with an increased risk of blood transfusion adj OR 4.6 ([95%CI: 1.6 - 13.4], p = 0.03) • **Comment**: platelet count, sex and BUN level were independently associated with transfusions after biopsy.	Low

Table 5. Minor bleeding

Study ID	N	Study type	Intervention	Control	Outcome	Results	Quality
Atwell et al (2010)(17)	15,181 percutaneous core biopsies *5,832 renal biopsies	Retrospective review	Not on aspirin	Use of aspirin (81 or 325 mg) ingested within 10 days before biopsy	Bleeding	• No significant difference in the incidence of bleeding for patients taking aspirin within 10 prior biopsy 0.6% (18/3,195) versus 0.4% (52/11,986) those not taking aspirin, P = 0.34. • No significant difference in bleeding post Kidney biopsies for: the aspirin use group 1.0% (13/1,270) versus 0.6% (26/4,562) in the non-aspirin group, P = 0.53. • After multivariate analysis including aspirin use and patient and biopsy characteristics - platelet count, INR, biopsy needle size, number of passes - a non-significant association between aspirin and bleeding remained (P > 0.05). • **Conclusion**: there was no significant association between aspirin use and significant bleeding after biopsy of any of the specific organs.	Low
Baffour et al (2017)(18)	6700 (renal allograft biopsies) 2,362 patients	Retrospective Review	Biopsy, withholding aspirin (81mg or 325mg) for >10 days, 8-10 days, 4-7 days, 0-3 days	No aspirin use	Minor bleeding complication	• Minor: 12/28 (43%) due to perinephric bleeding/haematoma; 16/28 (57%) due to haematuria.	Low
Mackinnon et al (2008)(22)	1,120 biopsies	Retrospective study	Stop antiplatelet agents 5 days prior to kidney biopsy	Continue antiplatelet use prior biopsy	Minor bleeding defined as an ≥1.0 g/dL fall in haemoglobin not requiring transfusion or other intervention.	• 31.0% (23/75) minor complications in the control group versus 11.7% (7/60) in the intervention group, P=0.008.	Low

Search Strategies

MEDLINE 1946 – May 2017

#	Searches
1	kidney diseases/
2	exp Renal Replacement Therapy/
3	Renal Insufficiency/
4	exp Renal Insufficiency, Chronic/
5	Diabetic nephropathies/
6	exp hypertension, renal/
7	(kidney disease* or renal disease* or kidney failure or renal failure).tw.
8	(ESRF or ESKF or ESRD or ESKD).tw.
9	(CKF or CKD or CRF or CRD).tw.
10	(pre-dialysis or predialysis).tw.
11	exp acute kidney injury/
12	(acute kidney failure or acute renal failure).tw.
13	(acute kidney injur$ or acute renal injur$).tw.
14	(acute kidney insufficie$ or acute renal insufficie$).tw.
15	acute tubular necrosis.tw.
16	(ARI or AKI or ARF or AKF or ATN).tw.
17	or/1-16
18	biopsy/
19	renal biops$.tw.
20	kidney biops$.tw.
21	or/18-20
22	17 and 21
23	exp platelet aggregation inhibitors/ or exp alprostadil/ or exp aspirin/ or exp aspirin, dipyridamole drug combination/ or exp dipyridamole/ or exp disintegrins/ or exp epoprostenol/ or exp iloprost/ or exp ketanserin/ or exp milrinone/ or exp pentoxifylline/ or exp prasugrel hydrochloride/ or exp s-nitrosoglutathione/ or exp s-nitrosothiols/ or exp ticlopidine/ or exp trapidil/
24	clopidogrel.tw.
25	ticagrelor.tw.
26	or/23-25
27	22 and 26
28	limit 27 to humans

#	Searches
1	kidney disease/
2	chronic kidney disease/
3	kidney failure/
4	chronic kidney failure/
5	mild renal impairment/
6	stage 1 kidney disease/
7	moderate renal impairment/
8	severe renal impairment/
9	end stage renal disease/
10	diabetic nephropathy/
11	kidney transplantation/
12	renovascular hypertension/
13	(kidney disease* or renal disease* or renal failure or kidney failure).tw.
14	(CKF or CKD or CRF or CRD).tw.
15	(ESRF or ESKF or ESRD or ESKD).tw.
16	(pre-dialysis or predialysis).tw.
17	((kidney or renal) adj (transplant* or graft* or allograft*)).tw.
18	acute kidney failure/
19	acute kidney tubule necrosis/
20	(acute kidney failure or acute renal failure).tw.
21	(acute kidney injur$ or acute renal injur$).tw.
22	(acute kidney insufficie$ or acute renal insufficie$).tw.
23	acute tubular necrosis.tw.
24	(ARI or AKI or ARF or AKF or ATN).tw.
25	or/1-24
26	renal biopsy.mp.
27	exp kidney biopsy/
28	renal biops$.tw.
29	kidney biops$.tw.
30	26 or 27 or 28 or 29
31	25 and 30
32	exp thrombocyte/ or exp acetylsalicylic acid/ or exp dipyridamole/ or exp dual antiplatelet therapy/ or exp clopidogrel/ or exp antithrombocytic agent/ or exp ticlopidine/
33	antiplatelet$.tw.
34	antiplatelets.mp.
35	32 or 33 or 34
36	31 and 35
37	limit 36 to human