KHA-CARI Guideline recommendations for renal biopsy

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1 | SCOPE OF THE GUIDELINE

This guideline addresses issues relevant to the preparation, intervention and care of patients undergoing native or transplant kidney biopsies. The guideline provides recommendations concerning the impact of education on patients and caregivers prior to undertaking renal biopsy and the use of anticoagulants, antiplatelets and desmopressin pre- and post-biopsy. It also examines the available evidence for comparing needle use, imaging techniques and the position of the patient during biopsy. Lastly, it addresses issues relevant to the management of post-renal biopsy care and outlines the evidence base for techniques to detect and reduce the possibility of bleeding; the most common complication following renal biopsy. An overview of the guideline development process is provided in Appendix A. A description of the grades and levels assigned to recommendations is provided in Tables A1 and A2.

2 | PART I: PRE-BIOSPY – MEDICATIONS AND PATIENT INFORMATION

Percutaneous renal biopsies are the gold standard for the investigation of causes of renal parenchymal disease, for native or transplant kidney biopsies. Despite this, there is limited evidence regarding patients’ experiences and requirements when undergoing a renal biopsy. Education, psychosocial support and self-management have been identified as a requirement for those in need of a renal biopsy.1,2 The method in which the information is conveyed to patients as well as the provision of support for the decision-making process are also important.3

Although the procedure is considered to be safe, especially since the introduction of spring-loaded needles and real-time imaging,4-11 bleeding is the most common complication. Routine care prior to biopsy involves measuring haemoglobin, platelet count, international normalized ratio (INR) and activated partial thromboplastin time. To minimize the risk of bleeding, patients are usually advised to stop antiplatelet and anticoagulant agents prior to renal biopsy. These agents are common in patients with kidney disease, who are at increased risk of vascular disease. Although policies and practices vary between centres, non-urgent biopsies are often postponed until antiplatelet and anticoagulant agents have been ceased for several days. This can lead to delays in diagnosis and treatment, unnecessary administration of blood products such as fresh frozen plasma or platelets, and may
increase the likelihood of ischaemic and thromboembolic events, in particular when there is discontinuation of aspirin.\textsuperscript{9,10} 

There is a lack of evidence that uremic bleeding is due to deficiency or abnormality of factor VIII and von Willebrand Factor (vWF), and that the similar biological effects of desmopressin and cryoprecipitate on these haemostatic proteins led some investigators to postulate that desmopressin might be therapeutically effective. Desmopressin acetate is a synthetic analogue of antidiuretic hormone which is occasionally administered prior to percutaneous renal biopsy to reduce the risk of bleeding complications.\textsuperscript{12,13} It acts as a selective agonist of endothelial vasopressin-2 receptors, augmenting plasma levels of factor VIII and vWF.\textsuperscript{14,15} Studies have demonstrated that infusion of desmopressin elicits a rapid but transient increase in the circulating levels of vWF and factor VIII, reaching a peak between 90 min and 2 h after administration.\textsuperscript{15} A single dose can be expected to increase the factor VIII level 3- to 6-fold. It has been shown to normalize bleeding time in uraemia for up to 4–8 h,\textsuperscript{14,16-18} presumably through its vasopressin-2 receptor agonist activity. The other effects of desmopressin include vasodilation, and an oxytocic effect at intranasal doses of 15–20 μg.

The aim of this guideline is to help to minimize harms associated with pre-biopsy care. Evidence on the emotional well-being and psychological impact of educational interventions and provision of information for patients undergoing a renal biopsy will be examined. Secondly, evidence surrounding antiplatelet and anticoagulant medication, along with desmopressin use prior to renal biopsy will be covered in this section.

2.1 | Biopsy information and education for patients and caregivers

**Guideline recommendations**

a. We recommend patients and their carers be provided with education and information about renal biopsies including reasons for its use, risks and complications, pre- and post-biopsy management with particular regard to psychological issues such as anxiety. The education and information provided should be in a format suited to their learning needs (1C).

**Ungraded suggestions for clinical care**

- We suggest healthcare providers consider following the process outlined in Figure 1 to establish methods of communication and interaction with patients undergoing a renal biopsy, to adequately prepare them for the procedure and alleviate unnecessary anxiety throughout the process.

2.2 | Pre-biopsy medication – Antiplatelet and anticoagulant agents

**Guideline recommendations**

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 h to 72 h before the renal biopsy
  - Unfractionated heparin 4–6 h before the renal biopsy
  - Low molecular weight heparin 24 h before the renal biopsy

- We suggest that antiplatelets and anticoagulants should not be restarted until 24–48 h 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 INR should be less than 1.5.

2.3 | Pre-biopsy medication – Desmopressin acetate

**Guideline recommendations**

No recommendations or suggestions can be made due to lack of evidence.

**Ungraded suggestions for clinical care**

- There is a lack of evidence to support the benefit or harm of desmopressin acetate 0.3 μg/kg administered intravenously over 30 min prior to renal biopsy. Units should continue their existing practice until a higher level of evidence is available. However, we...
suggest this is considered only for patients with Stage 3b chronic kidney disease and onwards.

- Careful attention to fluid balance should be paid if desmopressin is administered and excessive fluid intake should be discouraged for 6–8 h after its administration.

- There is no evidence in any reports of a negative effect by using desmopressin in patients with cardiovascular disease. However, due to the hypothetical potential risk of thrombosis, desmopressin acetate should be avoided in patients with significant occlusive cardiovascular disease, including those with a vascular stent in situ.

3 | PART II: RENAL BIOPSY – IMAGING, NEEDLES AND POSITIONING

Percutaneous renal biopsy is an important diagnostic and prognostic tool for nephrologists. While it is generally safe, it is an invasive procedure and bleeding complications are the most frequently reported in published literature.\(^{19,20}\) Although the purpose of a renal biopsy is to establish a diagnosis, in the published literature the adequacy of a sample is often described by the number of glomeruli sampled. In the setting of renal transplant biopsies, published guidelines are available describing an adequate sample.\(^{21,22}\) In the setting of native kidney biopsies descriptions of adequacy are more varied and often depend on the underlying pathology;\(^{23}\) however, more than 10 glomeruli is often used to define an adequate sample.\(^{24-26}\) There are many devices available for performing percutaneous renal biopsies and they come in three different size options; 14, 16 and 18 G, as well as different configurations of cutting surfaces. The length of the needle throw is generally not reported in the published studies, but devices are now becoming available with a variable throw which can be selected by the operator at the time of biopsy.

Historically, native and transplant renal biopsies were performed 'blind' or 'by palpation', but a variety of adjunctive imaging techniques have since been employed to improve efficacy and safety. As ultrasound has become increasingly available, it has developed into the 'standard of care' in most recent renal biopsy publications.\(^{27}\) Few direct comparisons between imaging modalities exist, with observational studies predominantly describing the contemporary imaging methods, changes in methods over a period, and comparisons with a historical cohort.\(^{5,28-31}\) Current imaging questions in renal biopsy relate to the contemporary imaging modalities of ultrasound and computed tomography (CT) and the biopsy methods employed in conjunction with these: ‘Real-time imaging’ (direct image-guided needle entry) versus localization or marking (image-guided marking on skin surface +/- depth estimation) followed by blind biopsy. Difficult patients who may require CT-guided biopsy include those with structural kidney disease, body mass index >30 kg/m\(^2\) and those situations where there is no access to any ultrasound services.

Percutaneous renal biopsy is an important tool in the diagnosis of diseases affecting native and transplanted kidneys. Early percutaneous native renal biopsies were performed with the patient in the sitting position\(^{32,33}\) but soon the prone position on a sandbag or pillow to splint the kidneys was used which may improve patient comfort, improve tissue yield and can make real-time ultrasound easier.\(^{34}\) The prone position may not always be comfortable or even possible in some patient groups, including obese patients, pregnant women and those with significant respiratory compromise. The supine antero-lateral position for obese and non-obese patients has been reported to provide superior compliance, comfort and respiratory comfort assessed by visual analogue scale compared with the prone position.\(^{35}\) Biopsy of a renal transplant has been described exclusively with the patients in the supine position,\(^{35-37}\) however, like native kidney biopsy patient position in transplant biopsy is frequently not reported.\(^{38,39}\)
3.1 | Renal biopsy: Needles

Guideline recommendations

a. We recommend the use of a spring-loaded automatic needle device for native renal biopsy because they are associated with fewer complications and better tissue samples (1B).

b. We recommend the use of a spring-loaded automatic needle device for transplant renal biopsy because they are associated with fewer complications and better tissue samples (1C).

c. We suggest using a 16 G needle for native and transplant renal biopsy provides the best balance between sample adequacy and risk of bleeding (2C).

Ungraded suggestions for clinical care

- Consideration should be given to the throw length of the biopsy needle in relation to the size of the kidney being biopsied and cortical thickness. Throw length is often fixed and related to a specific needle type, however, there are some devices that have an adjustable throw length, and these could be considered for smaller kidneys.

3.2 | Renal biopsy: Imaging

Guideline recommendations

a. We recommend percutaneous native renal biopsy to be image-guided (1B).

b. We recommend Real-Time Ultrasound Guidance be used as the first line imaging for percutaneous renal biopsy in patients with a kidney transplant (1C).

c. We suggest the use of Real-Time Ultrasound Guidance or ultrasound localization for native renal biopsy (2C).

d. We suggest the use of CT localization for native renal biopsy in ‘difficult cases’ (defined below) (2D).

Ungraded suggestions for clinical care

No ungraded suggestions for clinical care.

3.3 | Positioning for renal biopsy

Guideline recommendations

a. We suggest the supine anterolateral position for obese patients or those with respiratory difficulty for native renal biopsy (2B).

Ungraded suggestions for clinical care

- We recommend the prone position with a pillow or sandbag under the abdomen to splint the kidneys for native renal biopsy
- We recommend the supine position for transplant biopsy

- For exceptional situations (intubated, pregnant, and morbidly obese) we recommend any position which simultaneously optimizes view of the needle tip and kidney whilst maintaining patient comfort

- Due to the lack of comparator trials it is impossible to make evidence based statements in regard to patient position for biopsy. The current standard, prone for native and supine for transplant has evolved through experience and practicality and is used to the extent that patient position is frequently not reported in renal biopsy studies.

4 | PART III: POST-RENAL BIOPSY – PATIENT CARE AND BLEEDING

As renal biopsy techniques have evolved over the last 70 years, so too have recommendation and practices for post-biopsy care. Modern biopsy techniques involve the use of smaller gauge, spring-loaded biopsy needles often used under real time guidance with ultrasound or CT. With this evolution there has been a parallel reduction in the requirement for prolonged hospitalization and observation post-renal biopsy.40 Post-biopsy observations should be designed to detect the major common complications arising from renal biopsy including: macroscopic haematuria with or without urinary retention, loin pain in association with local haematoma and haemodynamic compromise associated with significant blood loss. The frequency and type of observations listed in the literature are numerous and mostly suggest more frequent observations in the immediate post-biopsy period tailing out to less frequent observations prior to discharge. The complications described in these cohorts are commonly minor such as macro-haematuria with few cases having major bleeding requiring intervention. Urethral bleeding typically is self-limiting. Collection of successive urine samples passed post-biopsy to confirm bleeding is reducing. Macroscopic haematuria will settle in most cases over a few hours and a longer post-biopsy observation period (with bed rest) may be required to ensure bleeding arrests. If the patient is sent home, they should be advised to seek medical advice if the bleeding recurs. Persistent macroscopic haematuria associated with hypotension should be managed similar to severe internal bleeding.

There is insufficient reported data to recommend the best method of detection or management of post-renal biopsy bleeding and most reports are retrospective reviews of single centre experience, utilizing local expertise and resources. Older studies imaging with CT scanning have shown peri-nephric bleeding rates between 57% and 91% compared with 70% on ultrasound imaging post-biopsy. Newer scanning technology with higher resolution is likely to detect more cases of bleeding; however, it is unlikely to be useful in identifying the more serious cases.40,41 Bleeding may require crystalloid or colloid infusions. Immediate or delayed intra-renal bleeding may result in hypertension (Page kidney) from renal parenchymal compression.19,42,43 Indications for intervention with embolization or surgery to arrest bleeding include prolonged post-biopsy hypotension or bleeding – identified as either a large peri-nephric haematoma or persistent macroscopic
We do not suggest routine measurement of haemoglobin follow-
c. We do not suggest routine performance of post-biopsy ultrasound
b. We suggest patients at highest risk for post-biopsy complications
a. We recommend that following a renal biopsy procedure, the

Guideline recommendations

a. We recommend that following a renal biopsy procedure, the
   patient remain in hospital for strict bed-rest with frequent obser-
   vations for a period ranging from 6 to 24 h. Accepted practice for
   low risk patients is a 6 to 8 h period of observation with same day
   discharge (1B).

b. We suggest patients at highest risk for post-biopsy complications
   be targeted for longer periods of hospitalization, usually up to
   24 h. These include patients with significant renal impairment,
   patients undergoing biopsy for acute kidney injury, patients with
   elevated blood pressure pre-biopsy, patients aged >70 years and
   patients with abnormal bleeding profile or requiring early re-
   commencement of anticoagulation (2C).

c. We do not suggest routine performance of post-biopsy ultrasound
   for early detection of asymptomatic renal hematomas (2C).

d. We do not suggest routine measurement of haemoglobin follow-
   ing an uncomplicated renal biopsy (2C).

Ungraded suggestions for clinical care

- Observations performed post-biopsy should be aimed at detecting
  the known major complications of renal biopsy including
  haemodynamic compromise, macroscopic haematuria and severe
  loin pain. The frequency and type of observations can be guided by
  unit protocols.

- Patients who live some distance from hospital, are home alone or
  are likely to have significant psychosocial stress following biopsy
  should be targeted for overnight hospital stay.

- At discharge, patients should be provided with clear written
  instructions for post-biopsy care, for return to work and exercise,
  with Unit contacts in case of emergency. At discharge, patients
  should be provided with a clear plan for obtaining biopsy results.

- Following an uncomplicated renal biopsy, patients should abstain
  from heavy physical exercise or manual labour for 1–2 weeks.

4.2 | Biopsy bleeding management

Guideline recommendations

a. We suggest that moderate to severe bleeding, indicated by severe
   pain, large peri-nephric haematoma and/or post-biopsy hypoten-
   sion should be initially managed with intravenous resuscitation
   fluids of crystalloid or colloid (2B).

b. We recommend either radiological intervention or surgical management
   (according to local resources and expertise) to arrest bleeding and secure
   haemostasis in cases of severe bleeding with hypotension or a large peri-
   nephric blood collection not responding to conservative measures (1C).

c. We suggest that ultrasound scanning with Doppler is satisfactory
   to detect arteriovenous fistulae (AVF) without the requirement for
   invasive procedures such as angiography (2B).

d. We do not suggest routine screening for AVF or aneurysms in rou-
   tine uneventful biopsies (2B).

Ungraded suggestions for clinical care

- Patients with a pre-biopsy haemoglobin (Hb) <80 g/L are more likely
  to require a blood transfusion post-biopsy.1–4 Anaemia appears to
  be a surrogate marker for other bleeding risk factors (female gender,
  hypertension, impaired renal function, older age). We do not recom-
  mend routine blood transfusion for pre-biopsy anaemia.

- Large retrospective reviews from single centres would suggest
  detection of the peri-nephric bleed that can be by either ultra-
  sound or CT scan.

- The duration or severity of haematuria does not indicate the likeli-
  hood of asymptomatic AVF development. Intra-nephric fistulae are typi-
  cally asymptomatic and most spontaneously resolve. In cases of
  prolonged urinary tract bleeding or development of hypertension
  post-biopsy, AVF should be screened for. If present, radiological in-
  tra-vascular deployment of glue, gel or coils (depending upon local facili-
  ties and expertise) is suggested as initial management.44–48

- Unsuccessful angiographic intervention to maintain haemostasis will
  require urgent surgical intervention. Wherever possible nephron spar-
  ing surgery, for example, partial nephrectomy should be considered.

5 | DISCLOSURE

RMG, PJCdC, TG, PL-V, KM, SM, JS, ES, DV and JW have no relevant
financial affiliations that would cause a conflict of interest according
the conflict of interest statement set down by KHA-CARI Guide-
lines. For a full text version of the guideline, readers need to go to the

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A. | APPENDIX

A.1 | GUIDELINE DEVELOPMENT PROCESS

The overall approach to guideline development followed by KHA-CARI follows the GRADE framework as detailed in the KHA-CARI Development Manual (www.cari.org.au). In brief guideline development follows a five-stage process:

Stage 1: Scoping and identification of sub-topics.

Stage 2: Systematic literature review, evidence summaries and writing of draft guideline.

Stage 3: External peer review, consumer review and nephrology community comment.

Stage 4: KHA-CARI Steering Committee review and approval.

Stage 5: Publication of summary guideline in a peer reviewed journal and posting of complete guideline on the KHA-CARI Guidelines website.

A.2 | EXPLANATION OF GRADES

The evidence and recommendations in this KHA-CARI Guideline have been evaluated and graded following the approach detailed by the GRADE working group (www.gradeworkinggroup.org). A description of the grades and levels assigned to recommendations is provided in Tables A1 and A2.

TABLE A1 Final grade for overall quality of evidence†

<table>
<thead>
<tr>
<th>Overall evidence grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High quality of evidence</td>
</tr>
<tr>
<td></td>
<td>We are confident that the true effect lies close to that of the estimate of the effect</td>
</tr>
<tr>
<td>B</td>
<td>Moderate quality of evidence</td>
</tr>
<tr>
<td></td>
<td>The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</td>
</tr>
<tr>
<td>C</td>
<td>Low quality of evidence</td>
</tr>
<tr>
<td></td>
<td>The true effect may be substantially different from the estimate of the effect</td>
</tr>
<tr>
<td>D</td>
<td>Very low quality of evidence</td>
</tr>
<tr>
<td></td>
<td>The estimate of effect is very uncertain, and often will be far from the truth</td>
</tr>
</tbody>
</table>

†Adapted from GRADE working group (www.gradeworkinggroup.org).

A.3 | RENAL BIOPSY GUIDELINE OVERVIEW – COMPLIANCE WITH AGREEII REPORTING CHECKLIST

(https://www.agreetrust.org/resource-centre/agree-reporting-checklist/)

A.3.1 | Domain 1: Scope and purpose

Objectives:

- To ensure clinical practice aligns with the best available evidence;
- To reduce adverse events, complications and burden to patients (bleeding, time in hospital, worry);

TABLE A2 Nomenclature and description for grading recommendations†

<table>
<thead>
<tr>
<th>Grade</th>
<th>Implications</th>
<th>Patients</th>
<th>Clinicians</th>
<th>Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1: We recommend</td>
<td>Most people in your situation would want the recommended course of action and only a small proportion would not</td>
<td>Most patients should receive the recommended course of action</td>
<td>The recommendation can be adopted as a policy in most situations</td>
<td></td>
</tr>
<tr>
<td>Level 2: We suggest</td>
<td>The majority of people in your situation would want the recommended course of action, but many would not</td>
<td>Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences</td>
<td>The recommendation is likely to require debate and involvement of stakeholders before policy can be determined</td>
<td></td>
</tr>
</tbody>
</table>

†Adapted from GRADE working group (www.gradeworkinggroup.org).
To provide a definitive diagnosis for patients with kidney disease; and
To monitor kidney function post-renal transplant.

Questions: Research questions to determine scope of the guideline were developed by the guideline writing group comprised of seven nephrologists, and informed by a workshop with patients and caregivers to address:

- Use of desmopressin acetate pre-biopsy;
- Use of antiplatelets and anticoagulants pre-biopsy;
- Needle size and type;
- Imaging modality;
- Patient position;
- Bleeding complications;
- Post-operative care;
- Biopsy information and education for patients and caregivers.

Outcomes, interventions, comparisons and context are outlined in the relevant guideline subtopic.

Population: All patients with chronic kidney disease (including stages 1–5 non-dialysis-dependant, on dialysis or who have received a transplant) undergoing a percutaneous renal biopsy.

A.3.2 | Domain 2: Stakeholder involvement

Group membership: The guideline writing group consisted of seven nephrologists from Australia and New Zealand, supported by research staff in the KHA-CARI office:

- Rob MacGinley, Convenor. Eastern Health Clinical School, Monash University, Melbourne, VIC, Australia.
- Paul Champion de Crespiginy, Department of Nephrology, The Royal Melbourne Hospital, Melbourne, VIC, Australia. Desmopressin, antiplatelets, patient care and education guidelines.
- Emily See, Department of Nephrology, Monash Health, Melbourne, VIC, Australia. DDAVP, antiplatelets/anticoagulants, information and education guidelines.
- John Saunders, Renal Unit, Royal Prince Alfred Hospital, Sydney, NSW, Australia. Needles, imaging, positioning guidelines.
- Jeffrey Wong, Department of Nephrology, Liverpool Hospital, Sydney, NSW, Australia. Needles, imaging, positioning guidelines.
- Solomon Menahem, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia. Bleeding, post-operative care guidelines.
- David Voss, Department of Renal Medicine, Counties Manukau Health, Auckland, New Zealand. Bleeding, post-operative care guidelines.

Target population preferences and views: The literature searches included qualitative studies addressing patient and caregiver perspectives and preferences for renal biopsy, however, no relevant papers were found. Patient and caregivers who had recently undergone a renal biopsy participated in a workshop consisting of simultaneous focus group discussions to elicit their preferences and priorities for guideline development for renal biopsy. These discussions broadened the scope of the guideline to include an additional topic on biopsy information and education for patients and caregivers. Patients and public were invited to provide feedback and comment on the draft version of the guidelines posted on the KHA-CARI website and through Kidney Health Australia. Patients and caregivers will be included in the development of a patient version of the guideline.

Target users: The guidelines may be used by nephrologists and radiologists performing renal biopsies and by nurses caring for biopsy patients, to inform standards of care and clinical decisions related to percutaneous renal biopsy. Health professionals were involved in the peer review of the guidelines, and invited to provide comment and feedback in the draft through professional societies including the Australian and New Zealand Society of Nephrology, Australian and New Zealand Society of Interventional Nephrology, the Renal Society of Australia, Royal Australian and New Zealand College of Radiologists, Transplant Nurses’ Association and Transplant Society of Australia and New Zealand. The comments were discussed by the writing group and used to update and improve the evidence for the recommendations.

A.3.3 | Domain 3: Rigour of development

Search methods: Search methods for each subtopic, including a full search strategy are reported with the relevant subtopic guideline.

Evidence selection criteria: All study designs, comparisons and outcomes for studies including patients undergoing percutaneous renal biopsy that addressed the selected subtopics were included. No language restrictions were applied.

Strengths and limitations of the evidence: Critical appraisal of the evidence is reported in the evidence tables (attached as Appendix I) in each guideline subtopic, and within the guideline evidence summaries using the GRADE Assessment.

Formulations of recommendations: Recommendations were formulated based on the GRADE assessment of the evidence.

Consideration of benefits and harms: Complications were reported within each guideline subtopic, and considered in the recommendations based on the evidence.

Link between recommendations and evidence: The evidence for each subtopic was systematically screened, extracted and summarized with appraisal, and recommendations used the GRADE Assessment to qualify the certainty of the evidence in relation to the recommendation. Evidence tables are provided for each guideline subtopic.

External review: 10 peer reviewers with expertise in the subtopic/field were identified by the convenor (including nephrologists, interventionists) from hospitals around Australia. Reviewers were invited to complete a review form, and/or provide comment...
directly on the draft guideline manuscript. Each subtopic underwent external peer review by at least two reviewers to improve the quality of the guidelines and ensure the recommendations reflected the evidence. Final drafts were posted for public review for 1 month following the peer review process. Comments, suggestions and feedback were integrated into the final versions of the manuscript.

Updating procedure: This guideline will be reviewed and updated to account for new evidence relating to the topic that may:

- Warrant inclusion of additional recommendations;
- Alter the strength of a recommendation, that is, upgrade a suggestion to a recommendation or conversely downgrade a recommendation to a suggestion;
- Warrant removal or change to a recommendation or suggestion.

In line with NHMRC guidance, KHA-CARI Guidelines should be considered for review and update no later than 5 years after publication.

A.3.4. | Domain 4: Clarity of presentation

Graded recommendations and suggestions are provided in a box at the beginning of each guideline subtopic, with reference to the population or subgroup where relevant. Where there is uncertainty in the evidence, this is reflected in the grade of the evidence, and may be supported by ungraded suggestions for care.

A.3.5. | Domain 5: Applicability

Facilitators and barriers to application: These guidelines are based on the best available evidence, with consideration from the authors regarding potential barriers to application such as cost and time, and facilitators such as current practice. Further relevant details may be discussed within guideline subtopics.

Implementation advice/tools: Each guideline subtopic contains suggestions for implementation and future research.

Resource implications: This is not relevant for most guideline subtopics as they are based on clinical practice. There may be some cost implications for patient education which may warrant further exploration.

Monitoring auditing criteria: Each guideline subtopic contains suggestions for audit.

A.3.6. | Domain 6: Editorial independence

The development of the KHA-CARI Guideline for renal biopsy was funded by Kidney Health Australia, The Australian and New Zealand Society of Nephrology, and the Better Evidence and Translation in Chronic Kidney Disease program. The funding bodies did not influence the content or scope of the guideline.

Competing interests: The authors have no competing interests to declare as identified by the KHA-CARI conflict of interest form completed by all authors.