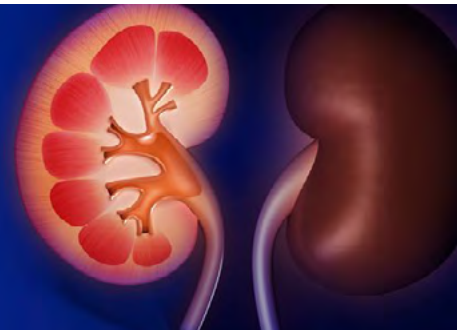
Nephrology Practice Review™



Making Education Easy

Issue 12 - 2024

In this issue:

Welcome to the 12th issue of Nephrology Practice Review.

This Review covers news and issues relevant to clinical practice in nephrology. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally on the back cover you will find our COVID-19 resources for Nephrologists and a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

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Editor
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Abbreviations used in this issue:

AAV = ANCA-associated vasculitis; **ACE** = angiotensin converting enzyme;
AKI = acute kidney injury; **ANCA** = antineutrophilic cytoplasmic antibody;
ARB = angiotensin II receptor blocker; **AVP-D** = arginine vasopressin deficiency;
BMI = body mass index; **CKD** = chronic kidney disease; **CV** = cardiovascular;
eGFR = estimated glomerular filtration; **FDA** = Food and Drug Administration;
KDIGO = Kidney Disease Improving Global Outcomes; **IV** = intravenous;
MPAA = mycophenolic acid analogs;
MSAC = Medical Services Advisory Committee;
NSAIDs = non-steroidal anti-inflammatory drugs;
PBAC = Pharmaceutical Benefits Advisory Committee;
PCR = protein-creatinine ratio;
RACGP = Royal Australian College of General Practitioners;
RAS = renin-angiotensin-system; **RSA** = Renal Society of Australia;
SLE = systemic lupus erythematous; **T2D** = type 2 diabetes.

Earn CPD

Nursing and Midwifery Board of Australia (NMBA) Journal reading and watching videos (including Research Reviews') may be considered a self-directed activity set out in the NMBA Registration Standard: Continuing Professional Development. One hour of active learning will equal one hour of CPD. Details at NMBA CPD page.

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Clinical Practice

KDIGO 2024 Clinical Practice Guideline for the evaluation and management of chronic kidney disease

The Kidney Disease Improving Global Outcomes (KDIGO) has published their 2024 update of the 2012 guideline for the evaluation and management of chronic kidney disease (CKD). The guideline covers optimal CKD evaluation and classification, kidney disease risk assessment, management of complications, medication management and drug stewardship in CKD, as well as strategies for delivering patient-centred care across diverse settings.

Key recommendations:

1. Evaluation of CKD
   a. In adults at risk of CKD, the use of creatinine-based glomerular filtration rate (eGFRcr) is recommended. The GFR category should be estimated by combining creatinine and cystatin C (eGFRcr-cys), if cystatin C is available.
   b. A kidney biopsy is suggested as an acceptable and safe diagnostic test to evaluate cause and guide treatment, when clinically appropriate.
   c. The use of eGFRcr-cys is recommended when eGFRcr is less accurate and GFR influences clinical decision making.
   d. A validated GFR estimating equation to derive GFR from serum filtration markers is recommended, instead of using serum filtration markers alone.
   e. Point-of-care testing can be used to measure creatinine and urine albumin where laboratory access is limited.
2. Risk assessment in people with CKD
   a. An assessment should be made at least annually of albuminuria in adults with CKD or albuminuria/proteinuria in children with CKD.
3. Delaying CKD progression and managing its complications
   a. Moderate-intensity physical activity for a cumulative duration ≥150 minutes per week or to a level appropriate to their cardiovascular (CV) and physical tolerance is recommended for people with CKD.
   b. A protein intake of 0.8 g/kg of bodyweight is suggested for adults with CKD G3-G5.
   c. A sodium intake <2 g/day (or <90 mmol of sodium per day or <5g NaCl per day) is suggested for people with CKD.
   d. A target systolic blood pressure <120 mmHg (when tolerated) is suggested for adults with CKD and elevated blood pressure.
   e. In children with CKD, 24-hour mean arterial pressure with ambulatory monitoring should be reduced to ≤50th percentile for age, sex and height.
   f. A renin-angiotensin-system (RAS) inhibitor is recommended for people with severely or moderately-to-severely increased albuminuria without diabetes.
   g. A RAS inhibitor is recommended for people with CKD and moderately-to-severely increased albuminuria with diabetes.
   h. Any combination of an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin II receptor blocker (ARB) or a direct renin inhibitor should be avoided in all patients with CKD, with or without diabetes.
   i. A sodium-glucose contransporter-2 inhibitor is recommended for patients with CKD, type 2 diabetes (T2D) and an eGFR ≥20 mL/min/1.73m^2
   j. A nonsteroidal mineralocorticoid receptor antagonist is recommended for patients with T2D, an eGFR >25 mL/min/1.73m^2, normal serum potassium, and albuminuria >30 mg/g, despite a maximum tolerated dose of a RAS inhibitor.

Kidney Int. 2024 Apr; 105(4S):S117-S314.

The WKD 2024 advocacy brief on breaking barriers to equitable kidney care and advancing optimal therapeutic management of kidney diseases

The World Kidney Day 2024 Position Paper "The time is now: Paving the way for optimal kidney care for all" was released on March 7th. The document focuses on policies to ensure equitable access to kidney care, including recognising CKD as a global health priority, early detection, optimising therapeutic management, and quality care and medicines.

Six barriers to optimal access to kidney care are identified:

1. Disease-related - asymptomatic onset, disease complexity and polypharmacy.
2. Patient-related - poor health literacy, insufficient self-care and empowerment, mistrust in the health system and misinformation.
3. Clinician-related - inadequate diagnosis and control of common CKD risk factors, knowledge gaps, time pressure, insufficient numbers of nephrologists, low physician-patient density.
4. Socio-economic factors - cost, poverty, unemployment, food insecurity, education, racial and gender discrimination, geography.
5. Health systems – care fragmentation, missed opportunities for early detection, lack of renal registries.
6. Policy-related – CKD not being prioritised, lack of or non-implementation of national strategies and policies, lack of integration of CKD screening and management into other disease programmes and a lack of preventative focus.

The paper advocates for CKD to be acknowledged as a global health priority and to implement policies aimed at preventing CKD. This includes collecting robust data on CKD burden, ensuring financial stability for kidney care and integrating CKD screening into other global policy responses such as maternal health, HIV, tuberculosis and other non-communicable diseases. People at high risk of CKD should be screened including measurements of blood pressure, body mass index (BMI), diabetes, kidney function and presence of kidney injury. Optimal therapeutic management includes raising physician and patient awareness, improving access to lifestyle and dietary advice, improving healthcare training and better access to guideline-directed medical therapy.

Read more here.

The KDIGO 2024 Clinical Practice Guideline for the management of lupus nephritis

The KDIGO 2024 Clinical Practice Guideline for the management of lupus nephritis has been released as the first of a series of updates of the 2021 Clinical Practice Guideline for the management of glomerular diseases.

Testing for kidney involvement in a patient with systemic lupus erythematous (SLE) is indicated when the patient first presents with SLE, as part of regular surveillance and when there is a suspicion of disease flare. The testing panel should include serum creatinine and eGFR, urinalysis (dipstick and sediment), spot protein-creatinine ratio (PCR) and serology (anti-double-stranded DNA and complement). A kidney biopsy is useful as clinical findings do not always indicate the level of kidney involvement.

It is recommended that patients with SLE, including those with lupus nephritis, receive hydroxychloroquine or an equivalent antimalarial unless contraindicated. Adjunctive therapies should be considered on an individual basis depending on the patient's risk of CV disease, proteinuria and CKD progression, infection, bone injury, exposure to ultraviolet light, premature ovarian failure, unplanned pregnancy, and cancer. In patients with Class I or II lupus nephritis and a low level of proteinuria, immunosuppressive treatment is guided by the extrarenal features of SLE. If nephrotic syndrome is present, a maintenance combination of a low-dose glucocorticoid and another immunosuppressive agent should be considered. For patients with active Class III or IV lupus nephritis, with or without a membranous component, initial treatment should include glucocorticoids plus any one of mycophenolic acid analogs (MPAA), low-dose intravenous (IV) cyclophosphamide, belimumab and either MPAA or low-dose IV cyclophosphamide, or MPAA and a calcineurin inhibitor where renal function is not severely impaired. Reduced doses of glucocorticoids following a short course of methylprednisolone pulses may be considered initially for active lupus nephritis if both renal and extrarenal manifestations improve satisfactorily. MPAA maintenance therapy is recommended after completing initial therapy. An algorithm is provided for managing patients that have not responded satisfactorily to treatment. Guidance is also provided for special considerations involving the management of lupus nephritis, including the presence of thrombotic microangiopathy, pregnancy, lupus nephritis in children and kidney failure.

Kidney Int. 2024 Jan; 105(1S):S1-S69.

Management of *de novo* nephrolithiasis after kidney transplantation: a comprehensive review from the European Renal Association CKD-MBD working group

This narrative review summarises what is currently known about the epidemiology, clinical presentation, diagnosis, prevention and treatment of nephrolithiasis following kidney transplantation, including the management of asymptomatic stones in kidney donors.

The denervation of the kidney and ureter graft substantially reduces the development of symptoms due to nephrolithiasis, therefore the reported prevalence of 1-2% following kidney transplantation should be interpreted cautiously, as should the apparent lack of adverse effects on allograft function. Prevention of stone formation in the transplanted kidney may include increased fluid intake, controlling diuretic use, maintaining a normal BMI, probiotic intake and a balanced dietary intake of oxalate, calcium, sodium, citrate and animal protein, as well as citrate supplementation and thiazide diuretic use.

Conservative management is recommended for non-obstructive stones <4 mm. Non-steroidal anti-inflammatory drugs (NSAIDs) are not recommended for pain relief in transplant recipients due to the potential for nephrotoxicity. Alpha-blockers are the first-line medical expulsive therapy. Non-invasive methods for treating stones in the transplanted kidney include extracorporeal shock wave lithotripsy (most common with low rates of complications), thiazide diuretics, urinary alkalisation and increased hydration. Invasive management approaches include semi-rigid ureteroscopy, retrograde intrarenal surgery, percutaneous nephrolithotomy (preferred for stones >2 cm), endoscopic combined intrarenal surgery, open-laparoscopic and robotic surgery and *ex-vivo* allograft stone treatment.

The stone-free rate following all active therapies for nephrolithiasis is relatively high. The choice of treatment modality should therefore account for the patient and surgeon preferences, the features of the stone and the patient's clinical characteristics.

Clin Kidney J. 2024 Feb 6; 17(2):sfae023.

The KDIGO 2024 Clinical Practice Guideline for antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis

The KDIGO 2024 Clinical Practice Guideline for antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis is an update to the ANCA vasculitis chapter in the 2021 Clinical Practice Guideline for the management of glomerular diseases. No major changes have been made relating to the diagnosis and assessment of prognosis in ANCA-associated vasculitis (AAV).

The most significant updates to the new guideline relate to induction therapy. While the recommendation that glucocorticoids be used in combination with cyclophosphamide or rituximab for the initial treatment of new-onset AAV remains, there is now a stronger emphasis placed on the rapid reduction in glucocorticoid dose, to reduce the rate of severe infections. The use of avacopan for induction therapy in AAV is included as a practice point, with a note that patients with an increased risk of glucocorticoid toxicity are most likely to benefit.

There are no changes in practice for maintenance therapy in AAV and either rituximab or azathioprine and low-dose glucocorticoids are recommended following induction of remission. No new information relating to the management of relapsing or refractory disease or following kidney transplantation was identified by the guideline authors.

Kidney Int. 2024 Mar;105(3S):S71-S116.

Arginine or hypertonic saline-stimulated copeptin to diagnose AVP deficiency

Differentiating arginine vasopressin deficiency (AVP-D) from primary polydipsia in patients with both polyuria and polydipsia can be challenging. If plasma copeptin levels can be measured reliably, the two disorders can be distinguished by plasma copeptin following hypertonic saline infusion (causing hypernatremia) or after IV infusion of arginine. Hypertonic saline infusion has a high degree of accuracy but requires close monitoring of sodium. Arginine-stimulated copeptin is a simpler test.

This study was a head-to-head comparison of the two methods with the primary endpoint being overall diagnostic accuracy with pre-defined cut-offs of 4.9 pmol/L after sodium was >149 mmol/L for hypertonic saline stimulation and 3.8 pmol/L after 60 minutes for arginine. There were 158 patients who underwent both testing methods. The diagnostic accuracy for differentiating AVP-D from primary polydipsia was 95.6% for hypertonic saline stimulated copeptin and 74.4% for arginine. Adverse events were considered mild for both tests, and arginine was preferred to hypertonic saline stimulation by 72% of patients. Post arginine-stimulated copeptin >5.2 pmol/L diagnosed primary polydipsia with a specificity of 91.4% and levels ≤3.0 pmol/L diagnosed AVP-D with a specificity of 90.9%.

Despite hypertonic saline infusion being superior in terms of diagnostic accuracy, arginine infusion may still be favoured as the initial investigation in clinical practice as it is simpler, patients prefer it over hypertonic saline infusion, and it is highly accurate if post-arginine copeptin levels are <3 pmol/L (AVP-D) or >5.2 pmol/L (primary polydipsia). If the patient's post-arginine copeptin level falls between these two values, hypertonic saline infusion can be employed to clarify the diagnosis.

N Engl J Med. 2024 Jan 18.

Diabetic kidney disease: strategies for holistic management

Diabetic kidney disease is the primary driver of CKD and accounts for 40% of dialysis initiations in Australia. As the prevalence of diabetes has increased the number of patients with end-stage kidney disease has also increased at a time when mortality rates due to other chronic CV and respiratory diseases has fallen. This article outlines management strategies to reduce the morbidity and mortality rates associated with diabetic kidney disease.

Early detection and intervention are critical to prevent progression and improve outcomes for patients. The criteria for diagnosing diabetic kidney disease are a reduced eGFR or an elevated urinary albumin level in a patient with diabetes. Treatment aims to reduce albuminuria and CV risk, while slowing the decline in kidney function. A multidisciplinary approach to management is recommended including lifestyle modification, glycaemic control, blood pressure control, lipid management and the use of renoprotective medicines. An ACE inhibitor or ARB is recommended as the first-line medicine, a sodium-glucose contransporter-2 (SGLT-2) inhibitor as second-line therapy and a mineralocorticoid antagonist as the third.

Read more here.

Regulatory News

A new class of antihypertensive approved to treat resistant hypertension

The United States Food and Drug Administration (FDA) has approved aprocitentan for the treatment of hypertension in combination with other antihypertensive medicines for adults who are not adequately controlled with other medicines. Aprocitentan is a novel dual endothelin receptor antagonist that prevents endothelin-1 (ET-1) binding to ET_A and ET_B receptors. This is the first new class of antihypertensive medicine approved in decades.

The recommended dose of aprocitentan is 12.5 mg taken orally, once daily. Aprocitentan will be available in the United States via a risk evaluation and mitigation strategy due to the possibility that it may cause major birth defects in pregnant patients.

The approval of aprocitentan was based on the PRECISION trial involving 730 participants with a systolic blood pressure ≥140 mmHg despite treatment with 3 antihypertensives. An approximate 4 mmHg reduction in office systolic blood pressure was reported after adjusting for change in placebo. Interestingly, a -28% reduction from baseline in the urine albumin-creatinine ratio was also reported, compared to a 5% increase in the placebo group.

Read more here.

Paediatric acute kidney injury device granted humanitarian exemption

The FDA has granted a Humanitarian Device Exemption Approval for a selective cytopheretic device for children with acute kidney injury (AKI). The device is indicated for patients weighing ≥10 kg and aged ≤22 years with AKI caused by sepsis or a septic condition who are receiving antibiotics and require renal replacement therapy. The device works by targeting proinflammatory monocytes and neutrophils to minimise hyperfiltration. The exemption only requires the manufacturer to demonstrate that the device has a probable benefit, without significant risk.

Read more here.

News in Brief

Chronic kidney disease management in primary care handbook released

The Stroke Foundation has published a guide entitled *Chronic kidney disease (CKD) management in primary care*. This guideline is endorsed by the Royal Australian College of General Practitioners (RACGP).

Read more here.

Porcine kidney successfully transplanted for the first time

The first successful transplantation of a genetically-modified pig kidney into a living patient has been completed by surgeons in Boston. The kidney was taken from a pig with 69 genetic edits to improve human compatibility. This advancement in xenotransplantation may provide a solution to the shortage in organs for transplantation.

Read more here.

Chairs of PBAC and MSAC announced

Professor Robyn Ward has been announced as the Chair of the Pharmaceutical Benefits Advisory Committee (PBAC). Professor Jonathan Craig has been announced as the Chair of the Medical Services Advisory Committee (MSAC).

Read more here.

The major global burden of chronic kidney disease

The International Society of Nephrology Global Kidney Health Atlas has been updated. This resource assesses disparities in kidney disease burden and care in approximately 200 countries.

Read more here.

COVID-19 Resources for Nephrologists

Australian and New Zealand Society of Nephrology

Renal Society of Australasia

Transplantation Society of Australia and New Zealand

Conferences, Workshops, and CPD

Click on the links below for upcoming local and international nephrology meetings, workshops and CPD.

ANZSN - Upcoming Conferences and Meetings

Renal Society of Australasia - Events

Transplantation Society of Australia and New Zealand

COMS - Conferences and Meetings on Nephrology

Research Review Publications

Nephrology Research Review with Professor David Mudge and Drs Emily See and Sradha Kotwal

Renal Cancer Research Review with Associate Professors Craig Gedye and Alexander Guminski

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