VA/DOD Clinical Practice Guidelines

PRIMARY CARE MANAGEMENT OF CHRONIC KIDNEY DISEASE

Provider Summary

Version 5.0 | 2025

VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE PRIMARY CARE MANAGEMENT OF CHRONIC KIDNEY DISEASE

Department of Veterans Affairs

Department of Defense

Provider Summary

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and the Department of Defense (DOD) guidelines are based on the best information available at the time of publication. The guidelines are designed to provide information and assist decision-making. They are not intended to define a standard of care and should not be construed as such. Neither should they be interpreted as prescribing an exclusive course of management.

This clinical practice guideline is based on a systematic review of both clinical and epidemiological evidence published through June 2024. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of recommendations.

Variations in practice will inevitably and appropriately occur when providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of a particular clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DOD policies. Further, inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 5.0 – 2025

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Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DOD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the Health Executive Committee (HEC) "…on the use of clinical and epidemiological evidence to improve the health of the population…" across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DOD populations.(1) This CPG is intended to provide health care providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with chronic kidney disease (CKD) in the primary care setting, thereby leading to improved clinical outcomes.

An effort to update the CKD CPG was initiated in 2024, using published data from September 2018 to June 2024. This guideline includes objective, evidence-based information on the primary care management of CKD intended to assist health care providers in all aspects of patient care, including, but not limited to, screening, assessment, treatment, and follow-up. The system-wide goal of evidence-based guidelines is to improve patient health and well-being by guiding providers who are caring for patients with CKD along management pathways that are supported by evidence. The expected outcome of the successful implementation of this guideline is to:

- Assess the patient's condition;
- Determine the most appropriate treatment plan in collaboration with the patient;
- Optimize each individual's functional independence, health outcomes, and quality of life;
- Minimize preventable complications and morbidity; and
- Emphasize the use of patient-centered care (PCC)

Recommendations

The following recommendations were made using a systematic approach that considered four domains per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications, as appropriate (e.g., resource use, equity, acceptability). GRADE is detailed in the full-text CKD CPG's Methods section and Appendix A.

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Diagnosis, Assessment and Lab Monitoring		1.	We suggest testing for chronic kidney disease (i.e., urine albumin/creatinine ratio and estimated glomerular filtration rate [eGFR]) in patients with one or more of the following associated risk factors: • Age over 60 years • Diabetes • Hypertension • Cardiovascular disease, including heart failure	Weak for	Reviewed, Amended
		2.	We recommend using urine albumin-to-creatinine ratio and estimated glomerular filtration rate for predicting chronic kidney disease progression.	Strong for	Reviewed, Amended
		3.	In patients with an estimated glomerular filtration rate <60 mL/minute/1.73 m², we suggest estimating glomerular filtration rate with a combined creatinine and cystatin C formula for risk prediction.	Weak for	Reviewed, Amended
		4.	We suggest the use of a validated end-stage kidney disease risk prediction model (e.g., kidney failure risk equation [KFRE]) for the management of stage G3-G5 chronic kidney disease.	Weak for	Reviewed, Amended
General Management Strategies	*Team Management and Education*	5.	When providing patient education about chronic kidney disease, there is insufficient evidence to recommend for or against any specific health education program or mode of delivery.	Neither for nor against	Reviewed Amended
		6.	We suggest interdisciplinary care (e.g., including dietitians, pharmacists, social workers, providers, nurses, and palliative care) for patients with chronic kidney disease.	Weak for	Not reviewed, Amended
		7.	For patients who need long-term venous access and are at high risk for requiring kidney replacement therapy, we suggest against peripherally inserted central catheter (PICC) lines to optimize success of future dialysis vascular access, while considering patient values and preferences.	Weak against	Not reviewed, Amended
	Indication for Referral to Nephrology for Kidney Replacement Therapy Including Dialysis and Kidney Transplant	8.	We suggest utilizing shared decision-making regarding kidney replacement therapy versus conservative management.	Weak for	Not reviewed, Not changed
		9.	In patients with high co-occurring conditions/low functional status, we suggest nephrology referral with sufficient time for comprehensive preparation for conservative management or dialysis for treatment of kidney failure, depending on patient values and preferences.	Weak for	Not reviewed, Amended
		10.	In patients with high co-occurring conditions/low functional status approaching the need for dialysis, there is insufficient evidence to recommend for or against dialysis to improve quality of life.	Neither for nor against	Not reviewed, Amended

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Pharmacologic Management of CKD and Associated Conditions	*Hypertension Medications*	11.	We suggest intensive blood pressure management to reduce mortality and major adverse cardiovascular events in patients with estimated glomerular filtration rate below 60 mL/minute/1.73 m².	Weak for	Reviewed, Amended
		12.	In patients with hypertension and albuminuria (i.e., urine albumin-to-creatinine ratio [UACR] >30 mg/g), we recommend the use of either an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker to slow the progression of chronic kidney disease.	Strong for	Reviewed, Amended
		13.	We suggest the addition of a thiazide diuretic or calcium channel blocker to reduce blood pressure in patients with chronic kidney disease and hypertension not controlled on an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker.	Weak for	Reviewed, New-added
	Other Medications to Decrease Cardiovascular Disease and Renal Outcomes	14.	In patients with advanced chronic kidney disease (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m^2) currently on an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, we suggest continuing therapy, unless there is drug intolerance or other adverse event.	Weak for	Reviewed, New-added
		15.	We recommend the addition of sodium-glucose co-transporter 2 inhibitors to maximally tolerated angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, in patients with chronic kidney disease who have one or more of the following: • Type 2 diabetes • Albuminuria (UACR >200 mg/g) • Heart failure to reduce the risk of major adverse cardiovascular events, heart failure, progression of kidney disease, and mortality, and continuing sodium-glucose co-transporter 2 inhibitors until start of dialysis.	Strong for	Reviewed, New-replaced
		16.	We recommend adding a glucagon-like peptide-1 receptor agonist to an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker in patients with type 2 diabetes and albuminuric chronic kidney disease to reduce the progression of chronic kidney disease, major adverse cardiovascular events, and all-cause mortality.	Strong for	Reviewed, New-replaced
		17.	In patients with chronic kidney disease and heart failure, we suggest sacubitril/valsartan as an alternative to monotherapy with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers.	Weak for	Reviewed, New-added

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Pharmacologic Management of CKD and Associated Conditions (continued)	*Other Medications to Decrease Cardiovascular Disease and Renal Outcomes (continued)*	18.	We suggest the addition of a non-steroidal mineralocorticoid receptor antagonist (e.g., finerenone) in individuals on maximally tolerated angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker who meet **all** the following criteria: • Type 2 diabetes • Albuminuria >30 mg/g • eGFR ≥25 mL/min/1.73 m^2 • Potassium <4.8 mEq/L for the purpose of decreasing major adverse cardiovascular events and slowing progression of chronic kidney disease.	Weak for	Reviewed, New-added
		19.	In patients with chronic kidney disease not on dialysis, we recommend the initiation of statins to reduce major adverse cardiovascular events and mortality.	Strong for	Reviewed, New-added
		20.	In patients with autosomal dominant polycystic kidney disease, we recommend referral to a nephrology provider for evaluation and assessment of appropriateness of treatment with tolvaptan.	Strong for	Reviewed, New-replaced
	Other Kidney Disease Related Complications	21.	In patients with chronic kidney disease, we suggest using potassium binders in the management of persistent, non-life-threatening hyperkalemia.	Weak for	Reviewed, New-added
Contrast-Associated Kidney Injury Management		22.	For patients with chronic kidney disease undergoing imaging utilizing iodinated contrast media who are at increased risk for iodinated contrast-associated acute kidney injury, we recommend intravenous volume expansion with isotonic crystalloid (see Algorithm Module E and Appendix Q for additional information).	Strong for	Reviewed, New-replaced
		23.	We recommend against the administration of N-acetylcysteine for prevention of iodinated contrast-associated acute kidney injury.	Strong against	Reviewed, Not changed

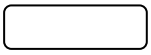
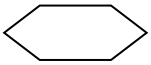
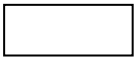
[a] For additional information, please refer to the section on Grading Recommendations in the full text CKD CPG.
[b] For additional information, please refer to Appendix A in the full text CKD CPG.

Algorithm

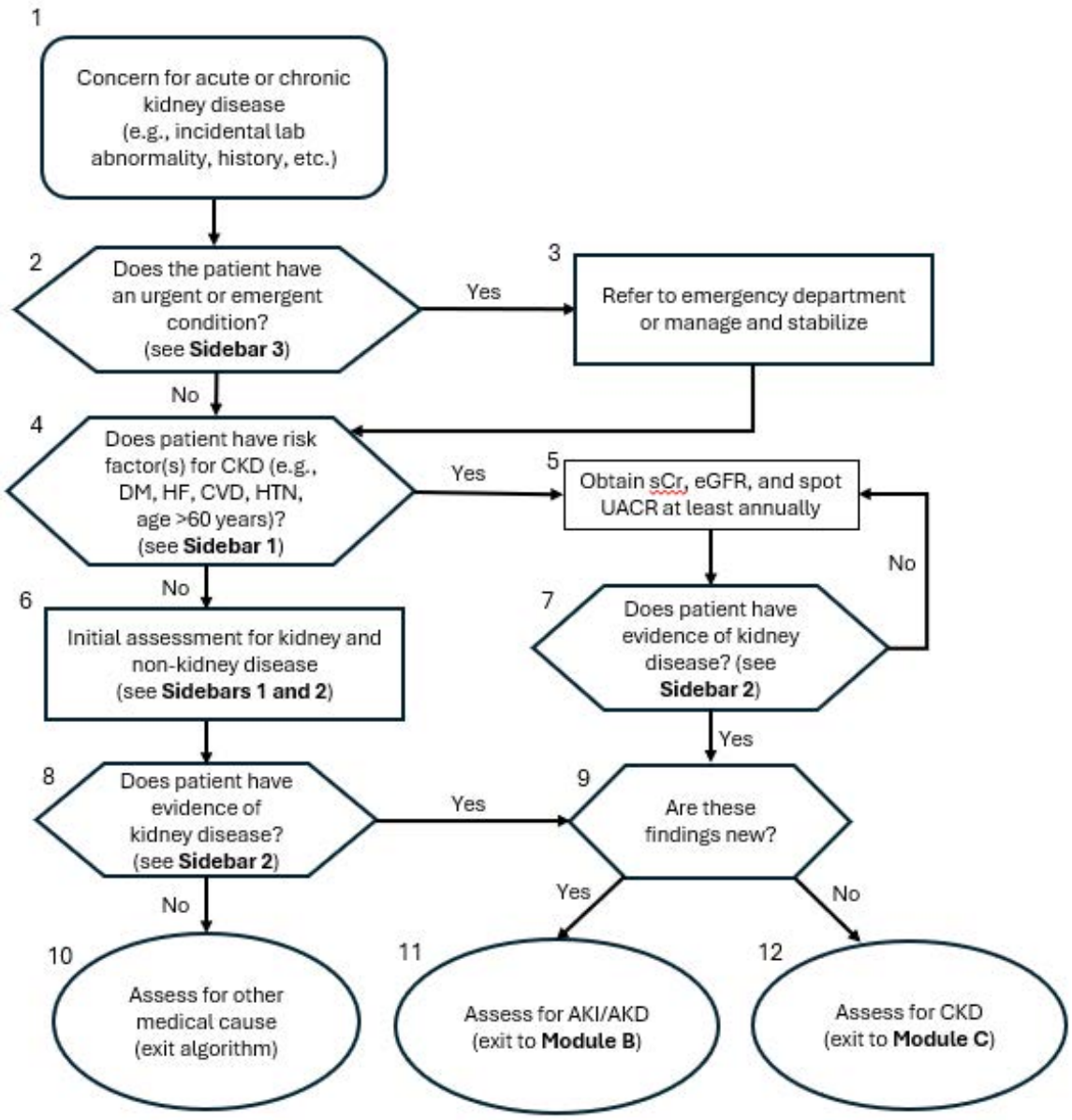
This algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in the primary care management of patients with CKD. The interventions included in the algorithm are paired with the corresponding recommendation in the CKD CPG where appropriate. The use of the algorithm format to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision-making and has the potential to change patterns of resource use. Although the Work Group recognizes that not all clinical practices are linear, the simplified linear approach depicted in the algorithm allows the provider to assess the critical information needed at major decision points in the clinical process. It includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

For each VA/DOD CPG, there is a corresponding clinical algorithm that is depicted by a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(2) Sidebars 1-10 provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered “Yes” or “No”.
	Rectangles represent an action in the process of care.
	Ovals represent a link to another section within the algorithm

Module A: Initial Assessment of Kidney Disease



Abbreviations: AKD: acute kidney disease; AKI: acute kidney injury; BP: blood pressure; CKD: chronic kidney disease; CVD: cardiovascular disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; HF: heart failure; HTN: hypertension; sCr: serum creatinine; UACR: urine albumin-to-creatinine ratio

Sidebar 1. At-Risk Populations

- Diabetes mellitus, hypertension, cardiovascular disease, heart failure
- Patients aged 60 years and over
- Systemic illness (e.g., systemic lupus erythematosus, multiple myeloma, malignancy)
- Systemic infections (e.g., HIV, Hepatitis B or C)
- Structural kidney or urinary tract abnormalities
- History of AKI/AKD, recurrent pyelonephritis, or nephrolithiasis
- Family history of kidney disease (e.g., ADPKD, ApoL1-associated kidney disease)
- Obesity, Metabolic Syndrome, or Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)
- History of gout
- History of pregnancy complications (e.g., preeclampsia, pre-term delivery, gestational diabetes, small for gestational age, stillbirth)
- Nephrotoxins

Abbreviations: ADPKD: autosomal dominant polycystic kidney disease; AKD: acute kidney disease; AKI: acute kidney injury; ApoL1: Apolipoprotein L1; HIV: human immunodeficiency virus

Sidebar 2A. eGFR Calculation

- eGFR should be calculated using one of the CKD-EPI formulas without race
- For most individuals, the 2021 CKD-EPI creatinine formula is adequate for diagnosis and follow-up
- The 2021 CKD-EPI combined creatinine-cystatin C formula is more accurate and can be considered to confirm CKD, for dosing of medications with a narrow therapeutic window, or to better estimate risk of adverse outcomes (see CKD CPG Appendix J)
- Cystatin C formula alone should be used in patients with either:
  - Very low creatinine generation (e.g., neuromuscular disease, spinal cord injury, large lower extremity amputation, or severe muscle loss from malnutrition or disease)
  - Very high creatinine generation (e.g., body builders, anabolic steroid use, high muscle mass, or intake of creatine supplements)

Sidebar 2B. Assessment of Kidney Disease

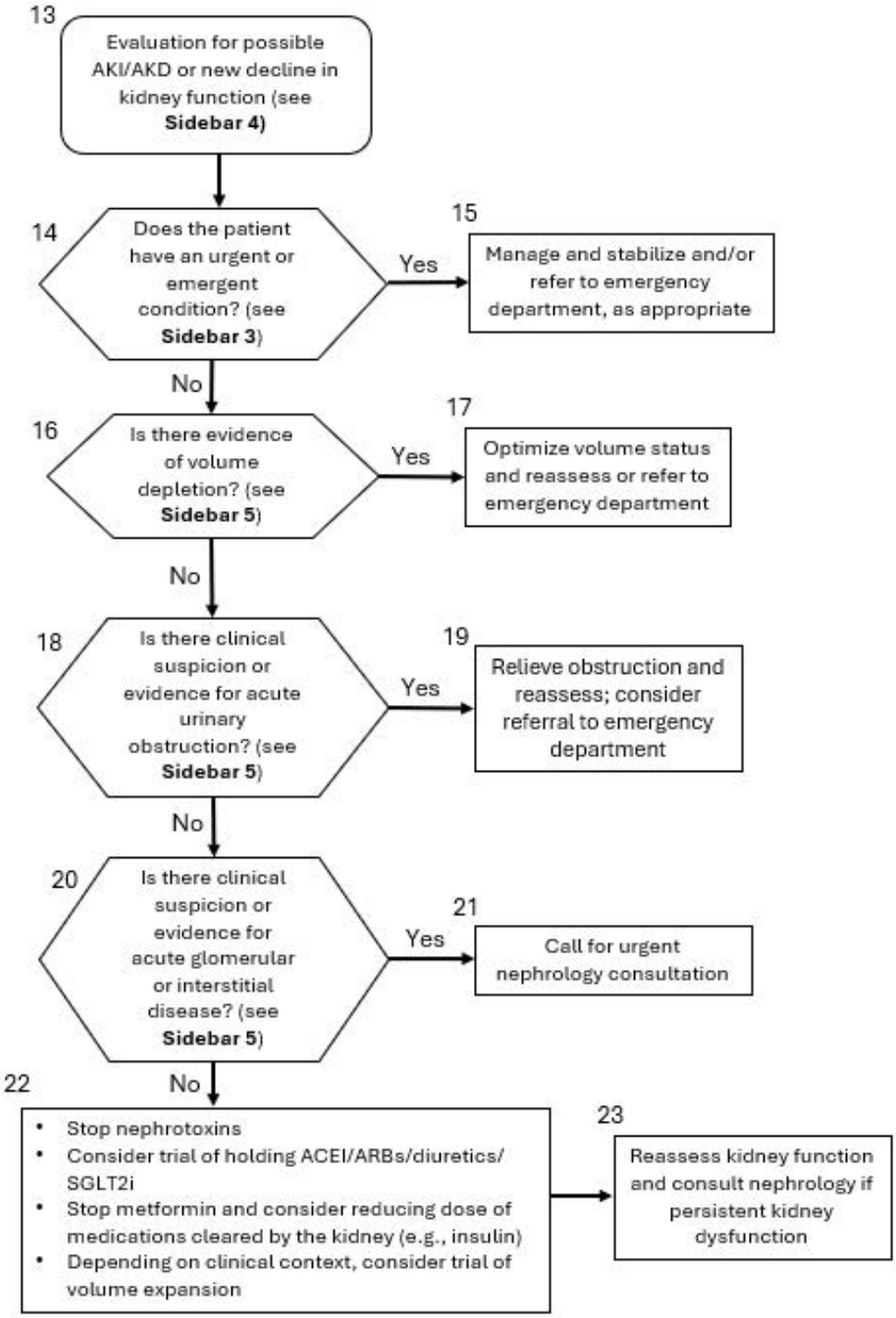
- History:
  - Symptoms of volume depletion (e.g., lightheadedness, dizziness) or overload (e.g., pedal edema, dyspnea)
  - Cause of volume depletion (e.g., diarrhea, vomiting, decreased oral intake, heat exposure)
  - Medications and supplements (e.g., NSAIDs, diuretics, SGLT2i therapy, BP medication changes)
  - Recent illnesses/infections (e.g., upper respiratory infection, osteomyelitis)
  - Urinary symptoms (e.g., hematuria, obstructive symptoms)
  - Constitutional or rheumatologic symptoms
- Physical: vital signs, assessment of volume status
- Labs: electrolytes, creatinine, urinalysis, urine albumin-to-creatinine ratio/urine protein-to-creatinine ratio - assess lab trends then repeat labs as clinically appropriate
  - Rule out AKI/AKD (see Module B)
  - Consider checking cystatin C (see Sidebar 2A and CKD CPG Appendix J)

Abbreviations: AKD: acute kidney disease; AKI: acute kidney injury; BP: blood pressure; CKD CPG: VA/DOD Chronic Kidney Disease Clinical Practice Guideline; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; eGFR: estimated glomerular filtration rate; NSAID: non-steroidal anti-inflammatory drug; SGLT2i: sodium-glucose cotransporter-2 inhibitor

Sidebar 3. Urgent/Emergent Conditions

- Clinical signs:
  - Unstable vital signs
  - Signs or symptoms of decompensated heart failure/symptomatic volume overload (e.g., shortness of breath, rales, jugular venous distention)
  - Signs or symptoms of uremia (e.g., nausea, vomiting, altered level of consciousness, pericarditis)
  - Anuria or oliguria
- Abnormal labs:
  - Significantly abnormal potassium
  - Acute unexplained decline in kidney function
  - Severe acid-base disturbance

Module B: Evaluation and Intervention for AKI/AKD or New Decline in Kidney Function



Abbreviations: ACEI: angiotensin converting enzyme Inhibitor; AKD: acute kidney disorder; AKI: acute kidney injury; ARB: Angiotensin II receptor blocker; SGLT2i: sodium-glucose cotransporter-2 inhibitor

Sidebar 4: Definition of AKI and AKD

- Definition of AKI (presence of any of the following):
  - Increase of sCr of >0.3 mg/dL over not more than 48 hours
  - Increase in sCr of >50% as compared to baseline, presumed to have occurred over not more than 7 days
  - Urine output of <0.5 mL/kg/hr over 6 hours
- Definition of AKD (presence of any of the following):
  - GFR <60 mL/min/1.73 m^2 for <3 months
  - Decrease in GFR by >35% or increase in sCr by >50% for <3 months
  - Kidney damage (structural) for <3 months

Definitions taken from Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int., Suppl. 2012; 2: 1-138. Chapters 2.1 and 2.5.

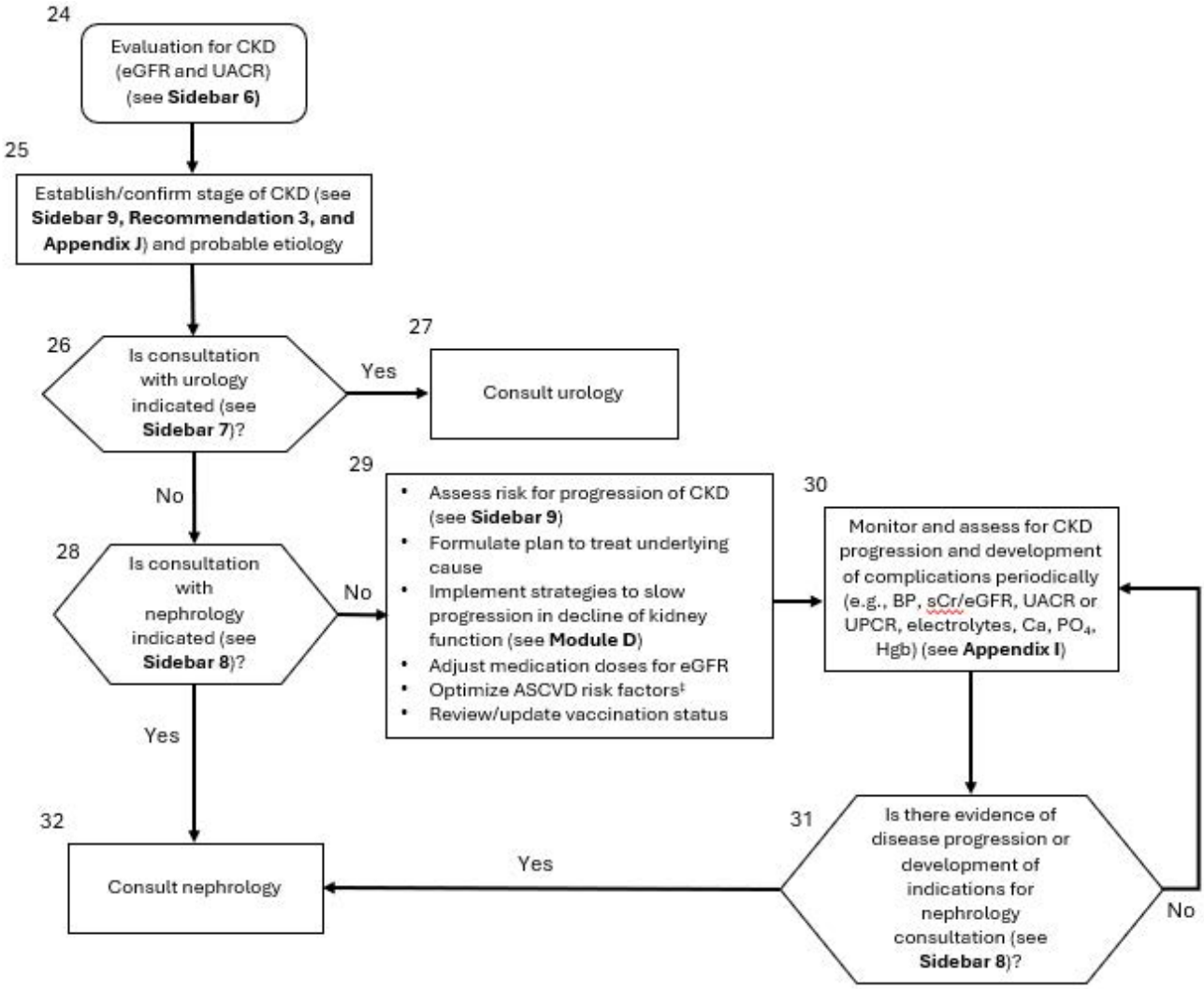
Abbreviations: AKD: acute kidney disorder; AKI: acute kidney injury; dL: deciliter; GFR: glomerular filtration rate; hr: hour; kg: kilogram; m: meter; mg: milligram; min: minute; mL: milliliter; sCr: serum creatinine

Sidebar 5: Assessment for AKD

- For volume depletion (e.g., lightheadedness or dizziness, hypotension, orthostasis)
- For urinary obstruction, e.g.:
  - Symptoms of voiding dysfunction, flank pain, or hematuria
  - Elevated post-void bladder volume
  - Evidence of obstruction on kidney imaging (e.g., hydronephrosis)
- For suspicion of acute glomerular or interstitial disease (e.g., hematuria, dysmorphic RBCs or RBC casts, new onset or acute increase in albuminuria) with:
  - Recent illness (e.g., infection)
  - Constitutional or rheumatologic symptoms
  - Rash
  - Edema
  - Hemoptysis

Abbreviations: AKD: acute kidney disorder; RBC: red blood cell

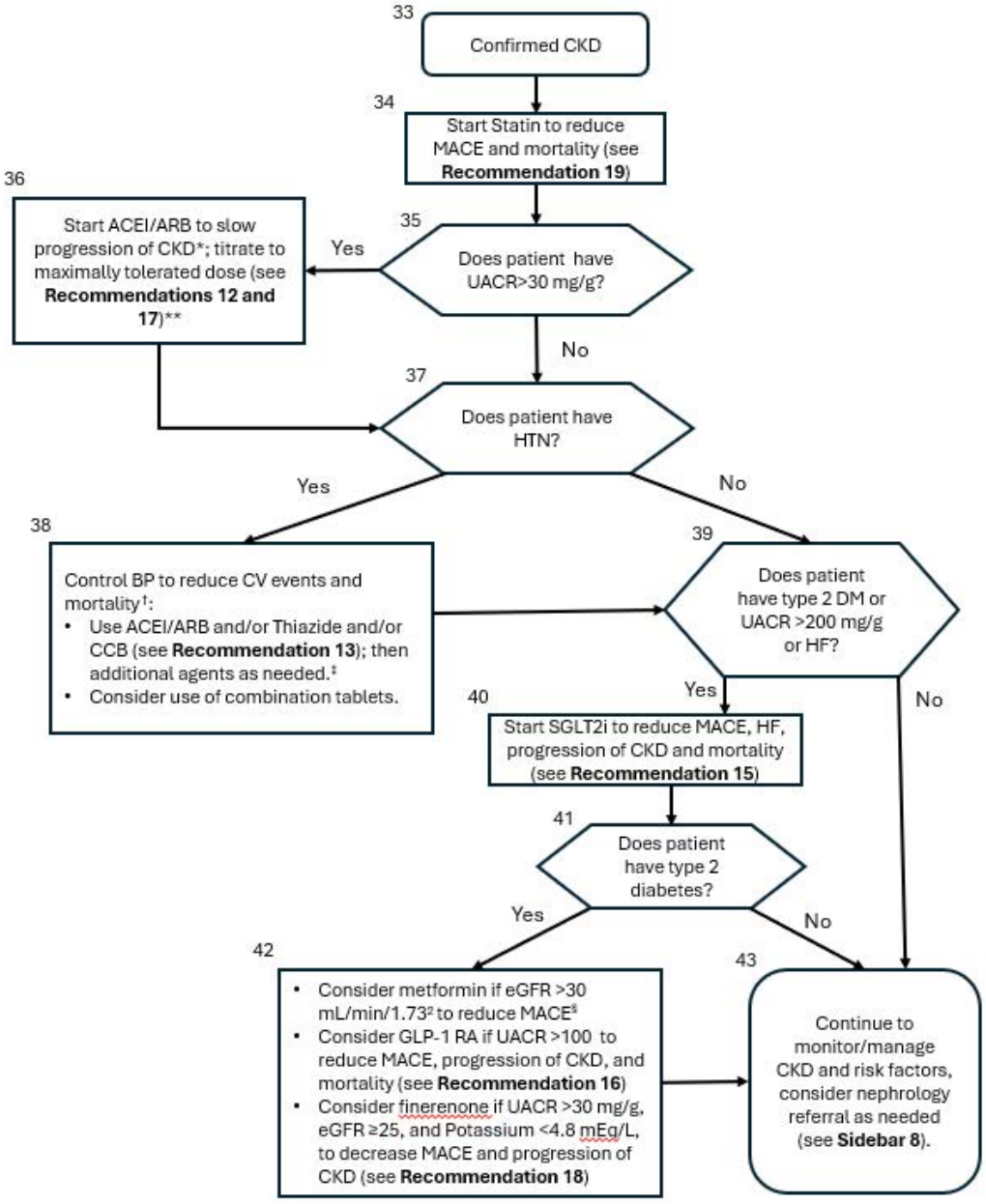
Module C: Evaluation and Management of CKD



‡As appropriate, refer to the following VA/DOD Clinical Practice Guidelines: Chronic Heart Failure, Diabetes, Hypertension, Dyslipidemia, Overweight and Obesity, and Tobacco Cessation

Abbreviations: ASCVD: atherosclerotic cardiovascular disease; BP: blood pressure; Ca: calcium; PO_4: orthophosphate; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; Hgb: hemoglobin; hr: hour; kg: kilogram; mL: milliliter; PO_4: orthophosphate; sCr: serum creatinine; UACR: urine albumin-to-creatinine ratio; UPCR: urine protein-to-creatinine ratio

Module D: Pharmacologic Management of CKD in Patients Not on Dialysis



The WG recommends stepwise addition of pharmacotherapies to slow progression of CKD and reduce MACE, noting that trials of SGLT2i, GLP-1 RA, and finerenone were each conducted on a background of ACEI/ARB therapy; however, the benefits of various combinations are unknown.

* Strongest evidence for kidney protection with ACEI/ARB is in UACR>300 mg/g.
** In patients with HF, sacubitril/valsartan may be used as an alternative to ACEI/ARB.
† See VA/DOD Hypertension CPG
‡ Depending on co-occurring conditions
§ See VA/DOD Diabetes CPG

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; BP: blood pressure; CCB: calcium channel blocker; CKD: chronic kidney disease; CV: cardiovascular; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; g: gram; GLP-1 RA: glucagon-like peptide-1 receptor agonists; HF: heart failure; HTN: hypertension; L: liter; MACE: major adverse cardiovascular events; mEq: milliequivalent; mg: milligram; SGLT2i: sodium-glucose co-transporter-2 inhibitor; UACR: urine albumin-to-creatinine ratio

Sidebar 6: Criteria for CKD

- Markers of kidney damage (1 or more):
  - Albuminuria (UACR ≥30 mg/g) on at least two measurements separated by ≥3 months
  - Urine sediment abnormalities
  - Persistent hematuria
  - Evidence of kidney tubular disorders (e.g., renal tubular acidosis)
  - Abnormalities detected by histology or imaging
  - History of kidney transplantation

AND/OR

- Decreased eGFR <60 mL/min/1.73 m^2 (GFR categories G3a-G5) for ≥3 months

Source: CKD Evaluation and Management – KDIGO

Abbreviations: CKD: chronic kidney disease; GFR: glomerular filtration rate; UACR: urine albumin-to-creatinine ratio;

Sidebar 7: Indications for Urology Consultation

- Gross hematuria
- Microhematuria in the absence of albuminuria
- Kidney masses or complex kidney cysts
- Symptomatic or obstructing nephrolithiasis
- Hydronephrosis or bladder abnormalities
- Persistent urinary symptoms despite treatment (e.g., nocturia, hesitancy, urgency, incontinence)
- Urinary retention

Sidebar 8: Potential Indications for Nephrology Consultation

- eGFR <30 mL/min/1.73 m^2
- Rapid decline of eGFR (>5 mL/min/1.73 m^2 per year)
- 5-year risk of kidney failure >3-5% (see Risk Equations Table)
- Non-diabetics with confirmed heavy albuminuria (UACR >300 mg/g, 24-hr urine protein >500 mg, UPCR >0.5 g/g)
- Diabetes with persistent (>1000 mg/g) albuminuria despite RAASi/SGLT2i, or inability to use RAASi/SGLT2i
- Hematuria with albuminuria, glomerular hematuria (e.g., dysmorphic RBC, RBC casts), or hematuria after negative urologic work-up
- Polycystic kidney disease (PKD)
- Kidney transplant recipient
- CKD in a patient <45 years
- Suspected genetic cause of CKD
- Unclear origin of kidney dysfunction or albuminuria
- Metabolic management (prevention) of kidney stone disease
- Electrolyte abnormalities (e.g., hyperkalemia, hyponatremia)
- Complications of CKD (e.g., anemia, metabolic acidosis, hyperphosphatemia, hyperparathyroidism)
- Patient's level of disease exceeds the comfort level of the primary care provider

Abbreviations: CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; g: gram; hr: hour; m: meter; mg: milligram; min: minute; mL: milliliter; RAASi: renin-angiotensin-aldosterone system inhibitor; RBC: red blood cell; UACR: urine albumin-to-creatinine ratio; UPCR: urine protein-to-creatinine ratio

Sidebar 9: CKD Staging* and Prognosis

KDIGO: Prognosis of CKD by GFR and albuminuria categories

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

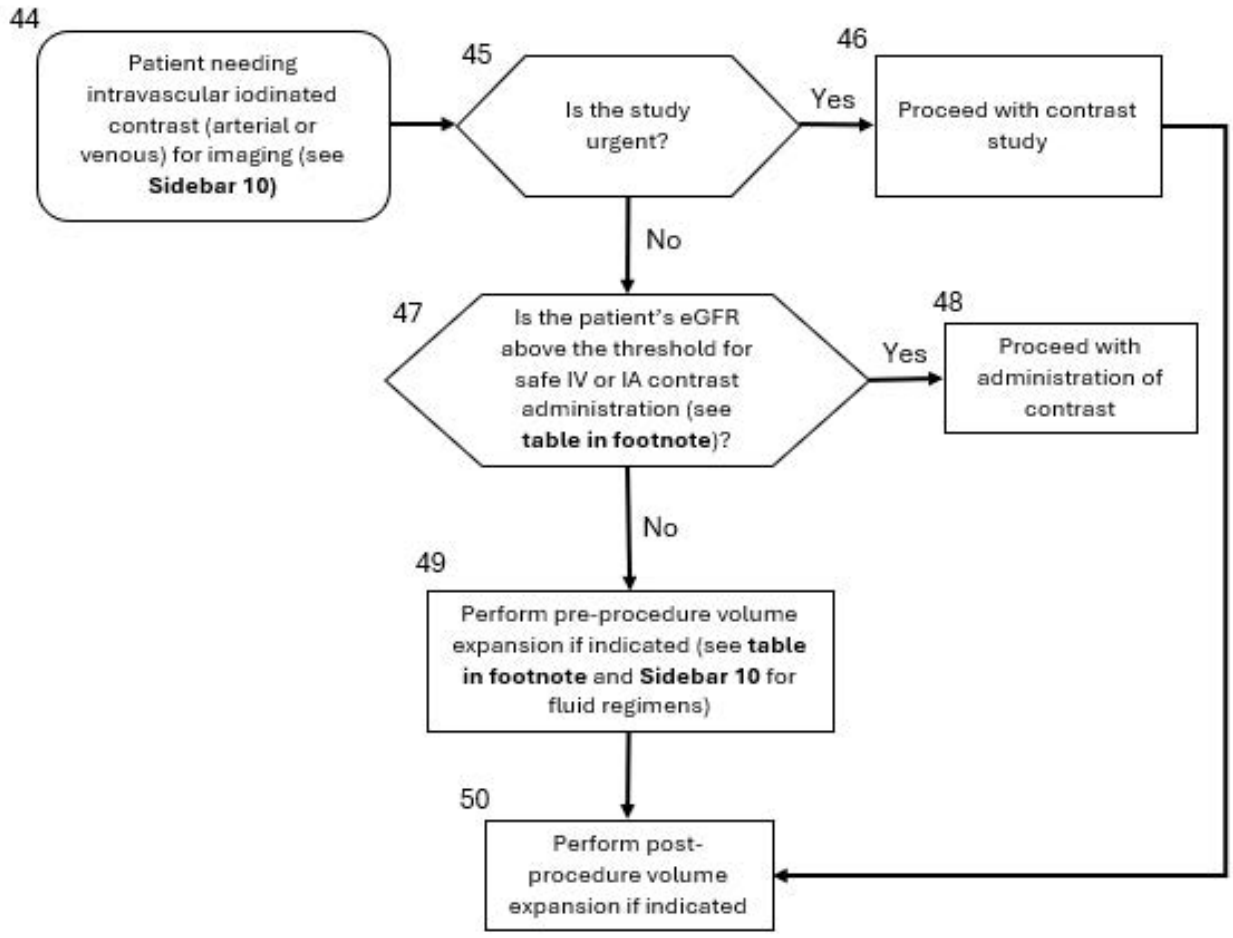
Reproduced from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S): S117–S314.

*ICD-10 codes for CKD stages: G1 (N18.1); G2 (N18.2); G3a (N18.31); G3b (N18.32); G4 (N18.4); G5 (N18.5); G5D (N18.6, dialysis dependent kidney failure)

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk

Abbreviations: CKD: chronic kidney disease; GFR: glomerular filtration rate ; mg: milligram; mmol: millimole

Module E: Management of Patients with CKD Requiring Iodinated Contrast



eGFR Threshold (mL/min/1.73 m^2)		Peri-Procedural Fluid Administration
CT (IV)	Angiography (IA)	
<30	<45	All patients
30-44	45-59	At discretion of ordering clinician in individuals with multiple risk factors (e.g., heavy albuminuria, high frequency NSAID administration)
>45	>60	Not indicated

Abbreviations: CT: computed tomography; eGFR: estimated glomerular filtration rate; IA: intra-arterial; IV: intravenous; NSAID: non-steroidal anti-inflammatory drug

Sidebar 10: Considerations for When Studies Requiring Iodinated Contrast Are Indicated

- Consider a non-iodinated contrast study as an alternative (e.g., CO_2, group 2 and 3 GBCM) (see Appendix Q)
- Use minimum amount of contrast necessary for appropriate testing
- Assess for risk factors for CA-AKI:
  - Decreased kidney function
  - Diabetes mellitus
  - Albuminuria
  - Heart failure
  - Volume depletion
  - Concomitant nephrotoxin exposure (especially NSAIDs)
- Fluid administration regimens (see Recommendation 22 and Appendix Q for additional information)
  - For outpatients or inpatients: isotonic electrolyte solution (e.g., 0.9% saline) infused as 3 mL/kg over one hour pre-procedure and 6 mL/kg over 2-4 hours post-procedure
  - For inpatients: 1 mL/kg per hour for 6-12 hours pre- and post-procedure

Abbreviations: CA-AKI: contrast associated acute kidney injury; CKD CPG: VA/DOD Chronic Kidney Disease Clinical Practice Guideline; CO_2: carbon dioxide; GBCM: gadolinium-based contrast media; kg: kilogram; mL: milliliter; NSAIDs: non-steroidal anti-inflammatory drugs

Scope of the CPG

Ideally, any patient in the healthcare system should have access to the interventions that are recommended in this guideline regardless of the setting and after taking into consideration the patient's specific circumstances.

Guideline recommendations are intended to be patient-centered. Thus, treatment and care should account for a patient's needs and preferences. Good communication between health care professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to demographic, cultural, and other differences. The information that patients are provided about treatment and care should be culturally appropriate and available to people with limited literacy skills. It should also be accessible to people with additional needs, such as physical, sensory, or learning disabilities. Family involvement should be considered, if appropriate.

This CPG is intended for use by VA and DOD primary care providers and others on the health care team involved in assessing and managing patients who have or are at risk for CKD. The patient population of interest for this CPG is adult patients (18 years or older) who have or are at risk for CKD, are eligible for care in the VA and DOD healthcare delivery systems, and who are being treated in an ambulatory or clinical setting. This includes Veterans and Service Members as well as their eligible adult dependents. This CPG does not provide recommendations for management of CKD in children or adolescents. Recommendations in this CPG are applicable for any adult patients of VA or DOD, inclusive of all care locations (VA, DOD, or community-based care).

Methods

The methodology used in developing the 2025 CKD CPG follows the *Guideline for Guidelines*, an internal document of the VA and DOD EBPWG updated in July 2019 that outlines procedures for developing and submitting VA/DOD CPGs.(3) The *Guideline for Guidelines* is available at http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, the management of potential conflicts of interest [COI],(4) interdisciplinary stakeholder involvement, use of SR and external review).(5) Appendix A of the full CPG provides a detailed description of the CPG development methodology.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations and writing and publishing a guideline document to be used by providers within the VA/DOD healthcare systems as well as those within the community who treat military personnel or Veterans. Specifically, the Champions and Work Group members for this guideline were responsible for identifying the key questions (KQs) of the most clinical relevance, importance, and interest for the management of patients with or at risk for CKD. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group,
- Directing and coordinating the Work Group, and
- Participating throughout the guideline development and review processes.

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency, identified the following four providers to serve as Champions (i.e., leaders) of this CPG's Work Group: Linda Fried, MD, MPH, and Amy R. Schwartz, MD, from VA; and Mai T. Nguyen, MD, FACP, FASN, and Jonathan Sosnov, MD, from DOD.

The Sigma Team, including Sigma Health Consulting and Duty First Consulting, was contracted by the VA and DOD to support the development of this CPG and conduct the evidence review. The first conference call was held in February 2024, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value, the DOD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review (SR) about the management of patients with or at risk for CKD. The group also identified a list of clinical specialties and areas of expertise important and relevant to the management of CKD, from which Work Group members were recruited. The specialties and clinical areas of interest included: nephrology, internal medicine, renal social work, clinical pharmacy, primary care, family medicine, renal dietetics, and ambulatory care.

The guideline development process for the 2025 CKD CPG consisted of the following steps:

1. Determining the scope of the CPG;
2. Crafting clinically relevant KQs to guide the systematic evidence review;
3. Identifying discussion topics for the Patient Focus Group and considering the patient perspective;
4. Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
5. Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

A. Grading Recommendations

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (6):

- Confidence in the quality of the evidence
- Balance of desirable and undesirable outcomes
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.,
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

Using these four domains, the Work Group determined the relative strength of each

recommendation (Strong or Weak). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(7) A Strong recommendation generally indicates High or Moderate confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility). A recommendation's strength (i.e., Strong versus Weak) does not reference its clinical importance (e.g., a Weak recommendation is evidence-based and still important to clinical care).

In some instances, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for a particular therapy or intervention. The way this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for or against an intervention that might be in common practice that is unsupported by clinical evidence, particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence …")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option …")

The grade of each recommendation made in the 2025 CKD CPG can be found in the section on Recommendations. Additional information regarding the use of the GRADE system can be found in Appendix A in the full 2025 CKD CPG.

Guideline Work Group

Organization	Names*
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Department of Defense	**Mai T. Nguyen, MD, FACP, FASN (Champion)**
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Patient-Centered Care

VA and DOD encourage providers to be sensitive to demographic, cultural, and other differences that affect patients' values, needs, and preferences aimed at treating the condition while also optimizing the individual's overall health and well-being. Regardless of the care setting, all patients should have access to individualized evidence-based care.(8,9) A holistic health approach (https:/www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and well-being goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. Guideline recommendations should be applied in a holistic approach to care that is patient-centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities.

Shared Decision-Making

This CPG encourages providers to practice shared decision-making, a process in which providers, patients, and patient care partners (e.g., family, friends, caregivers) consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(10) Shared decision-making is emphasized in Crossing the Quality Chasm, an Institute of Medicine (IOM), now NAM, report in 2001 (11) and is a core component of a patient-centered, whole health approach. Moreover, the unique role of SDM in nephrology care has been previously recognized in CPGs published by the Renal Physicians Association. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, possible outcomes, and levels or settings of care or both, especially where patient heterogeneity in weighing risks and benefits might exist. The VA and DOD have embraced shared decision-making. Providers are encouraged to use shared decision-making to individualize treatment goals and plans based on patient capabilities, needs, and preferences (see Recommendations 8-10).

Appendices in the 2025 VA/DOD CKD CPG

Select appendices from the full 2025 CKD CPG appear below, including the Management of CKD (Appendix H), Monitoring of CKD (Appendix I), Pain Management (Appendix N**, partial**), Gadolinium and Iodinated Contrast (Appendix Q), and General Medical and Lifestyle Management Recommendations to Improve Standard of Care in CKD Patients (Appendix R). Refer to the full guideline for these additional appendices: Approaches for eGFR Calculation (**Appendix J**), Nephrotoxic Agents (**Appendix K**), List of Pharmacotherapies (**Appendix L**),

Management of Hyperkalemia (**Appendix M**), Military Occupational Exposure (**Appendix O**), and Special Considerations when Caring for Older Patients (**Appendix P**). The full guideline can be found at: *https://www.healthquality.va.gov/guidelines/cd/ckd/*.

Management of CKD

Concerns:	Interventions:
Medications	• Adjust medication dose based on eGFR or CrCl if indicated • Eliminate/avoid nephrotoxic agents (see **Appendix K** in the full CPG) • Assess medication adherence • Assess for medication side effects since drug clearance may be reduced in patients with kidney dysfunction and side effects may contribute to non-adherence

Diabetes	• Optimize glycemic control
	  • Target HbA1c 7-8.5% in most patients with diabetes and CKD
	  • HbA1c <7% is appropriate for patients with life expectancy greater than 10-15 years and mild microvascular complications, if it can be safely done
	  • Target HbA1c 8-9% for patients with type 2 diabetes with life expectancy <5 years, significant comorbid conditions, advanced complications of diabetes, or difficulties in self-management attributable to e.g., mental status, disability, or other factors such as food insecurity and insufficient social support
	  • Metformin can be used if eGFR >30 mL/min/1.73m^2
	• Recommend participation in a Diabetes Self-Management Education and Support Program (see VA/DOD Diabetes CPG).
	• Recommend use of ACEI or ARB at maximally tolerated dose if UCR >30 mg/g – continue ACEI or ARB unless drug intolerance or other adverse events (see Recommendation 14)
	• Recommend use of SGLT2i or GLP-1 RA (see Recommendations 15 and 16, Module D, and VA/DOD Diabetes CPG[a]) to slow progression of kidney disease
	• Recommend finerenone if UACR >30 mg/g despite maximal ACEI or ARB and potassium <4.8 mmol/L (see Recommendation 18)
	• Recommend avoiding sulfonylureas
	• Suggest more frequent blood sugar monitoring and/or use of continuous glucose monitor for patients at risk for hypoglycemia (e.g., those on insulin)

Hypertension	• Optimize blood pressure control (see Recommendations 11-13, Module D, and VA/DOD Hypertension CPG[b]) • Recommend use of ACEI or ARB as first-line especially in patients with albuminuria - continue ACEI or ARB unless drug intolerance or other adverse events (see Recommendation 12 and 14) • Recommend adding thiazide diuretics and/or calcium channel blockers, if blood pressure not controlled on ACEI or ARB (Recommendation 13) • Restrict dietary sodium to 2,300 mg/day (see VA/DOD Hypertension CPG) • Optimize volume status • Consider nephrology referral for resistant hypertension, defined as BP >140/90 mmHg despite optimal dose of 3 anti-hypertensives that include a diuretic
Albuminuria (urine albumin/creatinine	• Recommend use of ACEI or ARB at maximally tolerated dose – continue ACEI or ARB unless drug intolerance or other adverse events (see

Concerns:	Interventions:
>200mg/g in individuals without diabetes)	Recommendation 14) • Decrease other antihypertensives to maximize use of ACEI or ARB • Recommend adding SGLT2i for persistent proteinuria despite maximally tolerated dose of ACEI or ARB (see Recommendation 15 and Module D)
Vaccination	• Assess Hepatitis B status and vaccinate, if non-immune • Update pneumococcal vaccines • Update influenza and COVID vaccination annually • Provide age-appropriate vaccination (e.g., MMR, VZV, Tdap/Td, RSV) • Do not administer live vaccines (e.g., MMR, Zostavax) to kidney transplant recipients.
CV health	• Recommend placing a referral to an RD and/or a comprehensive lifestyle intervention program for weight management to achieve/maintain ideal body weight/BMI (e.g., VHA's MOVE! Weight Management). See the VA/DOD CPG for Management of Overweight and Obesity for further guidance on weight management. • Assess and treat dyslipidemia (see VA/DOD Dyslipidemia CPG[c]) • Recommend use of a statin (see Recommendation 19) • Assess risks/benefits of aspirin therapy • Recommend tobacco cessation • Encourage physical activity, considering the guidance of 150 min/week of moderate aerobic activity as appropriate
Pain	• Avoid NSAID use, including OTC and prescription (oral/topical), if possible • Use of Buprenorphine is preferred over other opiates for chronic pain (see **Appendix N** in the full CPG and VA/DOD Opioid Therapy for Chronic Pain CPG[d])
Education/behavior change support	• Review dietary habits and refer patient to an RD for individualized nutrition counseling on sodium, potassium, phosphorus, and fluid intake as indicated. • Offer education on diagnosis and prognosis of CKD, as well as measures to prevent progression to kidney failure • Develop sick day planning specifically addressing temporary cessation of sulfonylureas, ACEI, diuretics/direct renin inhibitors, metformin, ARBs, NSAIDs, and SGLT2i's (i.e., SADMANS) • Educate on KRT options to include dialysis, vascular access, and transplant when eGFR <20 mL/min/1.73 m^2 • Screen for depression or health-related mental illness
Anemia	• Evaluate for underlying cause of anemia • Assess for nutritional deficiency and replete iron, vitamin B12, and folate stores if levels low • Refer to nephrology if patient has CKD stage 3b or higher and persistent hemoglobin <10 for consideration of ESA • Refer for IV iron, if patient has persistent iron deficiency (transferrin saturation <20%, ferritin <100 mg/dl) despite trial of oral iron (after age-appropriate evaluation for etiology or if patient unable to tolerate oral iron)
Electrolytes	• Dietary management for hyperphosphatemia or hyperkalemia – consider referral to medical nutrition therapy • Manage persistent hyperkalemia with bicarbonate, adjustment of diuretics and potassium binders as indicated (see **Appendix M** in the full CPG). • Treat metabolic acidosis with bicarbonate
Mineral Bone Disease	• Modify diet for hyperphosphatemia (e.g., plant-based diet, avoidance of phosphorus additives/preservatives) • Consider vitamin D and active vitamin D

Concerns:	Interventions:
Iodinated contrast agents	• Use isotonic IVF to prevent CA-AKI, if indicated and time allows (see Recommendations 22-23 and Algorithm Module E)
Gadolinium	• Do not use group 1 gadolinium agents if eGFR <30 mL/min/1.73 m^2 or current AKI (see Appendix Q)
Nuclear medicine contrast	• No concerns for kidney toxicity so may use as clinically indicated
Kidney stones	• Recommend low-sodium diet and sufficient fluid intake to produce urine output >2.2 L/day • Dietary calcium restriction is not recommended even for calcium stones • Send stones for analysis when available • Manage symptomatic stones with analgesics, hydration, and alpha-blockers initially and refer to urology for persistent symptoms or obstructive nephrolithiasis • Refer to nephrology for metabolic evaluation/management of recurrent nephrolithiasis

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; AKI: acute kidney injury; ARB: angiotensin II receptor blockers; BMI: body mass index; BP: blood pressure; CPG: clinical practice guideline; CrCl: creatinine clearance; CV: cardiovascular; DM: diabetes mellitus; DOD: Department of Defense; eGFR: estimated glomerular filtration rate; ESA: erythropoiesis-stimulating agent; GLP-1 RA: glucagon-like peptide-1 receptor agonist; IVF: intravenous fluids; KRT: kidney replacement therapy; MMR: measles, mumps, and rubella; NSAID: non-steroidal anti-inflammatory drug; OTC: over-the-counter; RD: registered dietitian; RSV: respiratory syncytial virus; SGLT2i: sodium-glucose cotransporter-2 inhibitor; Td: tetanus and diphtheria; Tdap: tetanus, diphtheria, and pertussis; VA: Department of Veteran Affairs; VZV: varicella zoster virus

[a] See the VA/DOD Clinical Practice Guideline for the Management of Diabetes Mellitus in Primary Care. Available at: https://www.healthquality.va.gov/guidelines/cd/diabetes/index.asp

[b] See the VA/DOD Clinical Practice Guideline for the Management of Hypertension in Primary Care. Available at: https://www.healthquality.va.gov/guidelines/cd/htn/index.asp

[c] See the VA/DOD Clinical Practice Guideline for the Management of Dyslipidemia in Primary Care. Available at: https://www.healthquality.va.gov/guidelines/cd/lipids/index.asp

[d] See the VA/DOD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: https://www.healthquality.va.gov/guidelines/pain/cot/index.asp

[e] Practice Point 4.3.2 -- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024 Apr;105(4S):S117-S314. doi: 10.1016/j.kint.2023.10.018. PMID: 38490803.

Monitoring of CKD

Assessment	Frequency
Serum creatinine to estimate GFR, using the 2021 CKD-EPI creatinine equation	• At diagnosis and at least annually in patients at low or moderate risk of progression, at least 2-3x/year in those at high risk of progression and at least 4x/year in those at very high risk of progression (see Sidebar 9); more often when measurement will impact therapeutic decision-making. For example, within 2-4 weeks of initiation or increase in the dose of a RAASi.
Cystatin C	• At least once; repeat if more accurate assessment than can be provided by eGFRcr is needed (e.g., in extremes of creatinine generation such as high muscle mass, spinal cord injury, neuromuscular disease, or malnutrition; see **Appendix J** in full CPG).
Spot urine ACR	• At diagnosis and at least annually; more often in patients at higher risk of progression (consider 2-3x/year in those at high risk of progression and 4x/year in those at very high risk of progression; see Sidebar 9) or when measurement will impact therapeutic decision-making.
Blood Pressure	• At diagnosis, at each visit, and as needed to ensure blood pressure is

Assessment	Frequency
	controlled to goal. • Strongly consider home blood pressure monitoring.
Potassium	• At diagnosis and at least annually; more often in patients with a history of hyperkalemia or at risk due to stage of CKD or medications. • Within 2-4 weeks of initiation or increase in the dose of a RAASi, depending on the current eGFR and serum potassium. • One month after initiation of a nonsteroidal MRA and then at least every 4 months.
Bicarbonate	• When measurement will impact therapeutic decision-making. Practically, bicarbonate is likely to be reported when eGFR or potassium are monitored.
Calcium, Phosphate, PTH, and 25-hydroxyvitamin D	• When measurement will impact therapeutic decision-making. Routine monitoring is unlikely to be needed in CKD G1-G3A. Practically, monitoring of calcium/phosphate/PTH is unlikely to impact therapeutic decision-making in patients who do not have an indication for nephrology consultation.
Hemoglobin	• At least annually in patients with CKD3, at least twice per year in CKD 4, and at least 4x/year in CKD 5.
Kidney Failure Risk Prediction Calculation	• In CKD G3-G5, at diagnosis and periodically as eGFR and ACR change.
Cardiovascular Risk Prediction	• At diagnosis and when prediction will impact therapeutic decision-making (e.g., use of statins).
Medication reconciliation and review	• At diagnosis and each clinic visit or transition of care. • Assess the need for adjustments in drug dosing, for nephrotoxins (prescribed and over the counter medications and supplements), and for indicated medications that may have been held due to acute events.

Abbreviations: ACR: albumin-to-creatinine ratio; CKD: chronic kidney disease; CKD-EPI: CKD Epidemiology Collaboration; eGFR: estimated glomerular filtration rate; eGFRcr: eGFR using creatinine; MRA: mineralocorticoid receptor antagonist; PTH: parathyroid hormone; RAASi: renin-angiotensin system inhibitor

Useful Equations in CKD Diagnosis, Staging, and Risk Assessment

Clinical Utility	Useful for	Equation (calculator website)	Required patient data	Comments
Predicts 2- and 5-yr risk of kidney failure in patients with CKD stage G3-G5	Patients with eGFR <60	Kidney Failure Risk Equation (KFRE) (12) (https://www.kidneyfailurerisk.com/)	Four-variable equation: age, sex, eGFR, UACR Eight-variable equation: age, sex, eGFR, UACR, serum calcium, phosphate, bicarbonate, albumin	• Validated in >2 million in >30 countries • Validated in pediatric, transplant and ethnically diverse populations • Incorporated in national/international guidelines including KDIGO CPG • Included in Clinical Decision Support Console in CPRS (VAMC)

Clinical Utility	Useful for	Equation (calculator website)	Required patient data	Comments
Estimates 2- and 4-yr risk of ESKD, CVD, and death	Patients with eGFR <30	CKD G4+ (CKD-PC) risk calculator (13) (https://ckdpcrisk.org/lowgfrevents/)	Age, sex, race, eGFR, SBP, history of CVD, DM, UACR, smoking status	• Calculates competing risks of ESKD, CVD and death • May be useful in SDM since risk of CVD and mortality is higher than risk of ESKD in most older/frail patients
Predicts risk of 40% decline in kidney function or kidney failure	Patient with eGFR >60	40% decline in kidney function in 3-years (14) (https://ckdpcrisk.org/gfrdecline40/)	Age, sex, eGFR, UACR, SBP, antihypertensive medication use, diabetes, history of heart failure, history of coronary heart disease, history of atrial fibrillation, smoking status, BMI In diabetics: hemoglobin A1c, insulin use, use of oral diabetes medication	• 40% decline in kidney function is more applicable in those with early CKD • Used as surrogate marker for FDA/clinical trials • Overall lower C-statistic in Grams model (compared to Ferguson model) but Grams model developed/validated in larger population and Ferguson model developed/validated in Canadian patients; no online calculator available for Ferguson model
Estimates 5-year probability of eGFR <60 mL/min/1.73 m^2	Patients with CKD	Risk of Developing Reduced Kidney Function (15) (http://ckdpcrisk.org/ckdrisk)	Diabetes status, age, sex, race, eGFR, MCVD, BMI, smoking history, DM treatment, HgbA1c, UACR, HTN	
Estimates probability of having eGFR <60 mL/min/ 1.73 m^2	Patient without known CKD	Screening for Occult Renal Disease (SCORED) score (16) (https://nccd.cdc.gov/ckd/Calculators.aspx)	Age, sex, anemia, HTN, DM, history CVD, history of CHF, PVD	
Conversion of UPCR or dipstick to UACR	Patients with or at-risk for CKD	Conversion of UPCR and dipstick to UACR (17) (http://ckdpcrisk.org/pcr2acr)	Crude equation: UPCR (mg/g) or urine dipstick protein Adjusted equation: sex, hypertension, and diabetes	• Many risk calculators include UACR but UACR data is not always available, so conversion enables clinicians to estimate UACR from other readily available measures of albuminuria • Urine dipsticks are low-cost and rapidly available, even in resource-restricted locations • Albuminuria is subject to intra-individual

Clinical Utility	Useful for	Equation (calculator website)	Required patient data	Comments
				biological variability (first morning void thought to be most accurate) • Caution in non-albumin proteinuria (e.g., multiple myeloma, amyloidosis). • Similar estimates for KFRE calculated when using predicted vs. observed ACR (17)
Estimates 10-year and 30-year risk of CVD (composite CVD risk and individual risk of ASCVD and HF)	Patients without known CVD or HF, aged 30-79 years	AHA Predicting Risk of Cardiovascular Disease Events (PREVENT) equations (18) (https://professional.heart.org/en/guidelines-and-statements/prevent-calculator)	Age, sex, total cholesterol, HDL, SBP, BMI, eGFR, DM status, smoking status, use of antihypertensive medication, use of lipid-lowering medication Optional factors: UACR, A1C, zip code (for estimating SDI)	• Performed better than PCE (18,19) • 1% increase in PREVENT risk estimate associated with increased CVD mortality (HR: 1.09) (19)

Abbreviations: A1C: glycated hemoglobin; ACR: albumin-to-creatinine ratio; ASCVD: atherosclerotic CVD; BMI: body mass index; CHF: congestive heart failure; CKD: chronic kidney disease; CKD-PC: Chronic Kidney Disease Prognosis Consortium; CPG: clinical practice guideline; CPRS: computerized patient record system; CVD: cardiovascular disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; ESKD: end-stage kidney disease; HgbA1c: hemoglobin A1c; HDL: high density lipoprotein; HF: heart failure; HR: hazard ratio; HTN: hypertension; KDIGO: Kidney Disease: Improving Global Outcomes; MCVD: monogenic CVD; PCE: pooled cohort equation; PVD: peripheral vascular disease; SBP: systolic blood pressure; SDI: Social Determinants of Health Index; UACR: urine ACR; UPCR: urine protein-to-creatinine ratio; VAMC: Veterans Affairs medical center

Chronic Pain Management in CKD

Refer to **Appendix N** in the full CPG for additional guidance on pain management in individuals with CKD: *https://www.healthquality.va.gov/guidelines/cd/ckd/*

Conceptual Approach to Chronic Pain Management in Patients with CKD

Concept	Strategies
Focus on function as primary target of intervention	• Emphasize functional outcomes (rather than pain scores) when assessing therapeutic interventions • Help patients identify self-management strategies that gradually increase engagement with both physical and social activities WITH their baseline level of pain • Promote restorative sleep (20) • Educate patients about stress reduction techniques (e.g., mindfulness, deep breathing, imagery)(21)
Address co-occurring conditions	• Treat co-occurring mental health conditions (e.g., PTSD, depression, anxiety) that impair patient engagement in a functional recovery plan - pain may improve as symptoms of depression, anxiety, or insomnia abate (22) • Optimize medical conditions that hinder patient participation in functional activities • Identify OUD or physiologic opioid dependence and treat with MUOD (e.g., buprenorphine, or referral for methadone)

	• Encourage functional activities that are meaningful to the patient since participation may improve both pain and mental health conditions.
Try non-pharmacologic interventions	• Add psychosocial or behavioral interventions (e.g., Cognitive Behavioral Therapy,(23) Acceptance and Commitment Therapy,(24) Pain Reprocessing Therapy,(25) Cognitive Functional Therapy (26) based on availability and patient preference if self-management strategies are insufficient. • Consider acupuncture and chiropractic care if available and indicated • Be familiar with local resources for non-pharmacologic interventions
Prescribe pharmacologic intervention to increase engagement in functional recovery activities, when appropriate	• Select medications based on risk of nephrotoxicity, side effects, overdose and potential drug interactions • Assess risks and benefits of treatments on co-occurring conditions • Adjust dose of medication for patient's kidney function, optimally assessed using eGFR or using manufacturer's dose guidance, if available (see **Appendix K** in full CPG) • Consider starting at lower dose and titrating slowly to mitigate risks • Use analgesics judiciously, short-term, to support functional activities • De-prescribe if no benefit is observed in the near-term (e.g., 3 months) to prevent polypharmacy • Consider patient-directed deprescribing if functional benefit has been achieved and stabilized (e.g., 9-12 months). • Assess risk of fall and fracture given possibility of underlying bone disease in patients with CKD and use caution when co-prescribing sedating medications (e.g., opioids, benzodiazepines, gabapentenoids)
Refer to pain specialist	• Consider referral when there is diagnostic uncertainty, limited uptake in functional aspects of the treatment plan, limited gains, or difficulties with medication management • Employ multidisciplinary/interdisciplinary approach (e.g., VA Pain Management Team) especially for patients with complex pain syndromes • Offer virtual options for patients who have barriers to travel (e.g., distance, appointment burden), when available

Abbreviations: CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; MOUD: medication for OUD; OUD: opioid use disorder; PTSD: post-traumatic stress disorder; VA: Veterans Affairs

Gadolinium and Iodinated Contrast

A. Iodinated Radiocontrast Media

Iodinated radiocontrast media are used for contrast-enhanced computed tomography (CT) and coronary and non-coronary angiography. Historically, iodinated contrast was one of the most common causes of nephrotoxic AKI, accounting for 11-12% of episodes of hospital-acquired AKI in two series, one published more than 40 years ago.(27, 28) More recently, epidemiologic studies comparing the development of AKI in individuals undergoing contrast-enhanced CT with those undergoing non-contrast CT have suggested that the risk of contrast-associated AKI (CA-AKI) is low. In one analysis of more than 10,000 individuals undergoing contrast-enhanced CT to an equal number of individuals undergoing non-contrast CT at the Mayo Clinic who were matched based on propensity for development of AKI, McDonald and colleagues found no increased risk for development of AKI associated with use of iodinated contrast.(29) However, in a similar analysis of over 17,500 propensity-matched individuals undergoing CT with or without contrast administration at the University of Michigan, Davenport and colleagues found a progressive risk of CA-AKI associated with reduced kidney function, with an odds ratio increasing from 1.1 among individuals with an eGFR of 45-59 mL/min/1.73 m^2 to an odds ratio of 3.0 among those with an eGFR <30 mL/min/1.73 m^2.(30) Multiple factors have likely contributed to the decreasing risk of

CA-AKI including decreased toxicity associated with the currently used contrast agents (i.e., iso-osmolal and low osmolality agents as compared to the older high osmolality agents) and the need for lower volumes of contrast given improved imaging technology.

Based on current data, the American College of Radiology (ACR) and the National Kidney Foundation (NKF) have concluded that the risk of CA-AKI associated with IV contrast in individuals with an eGFR ≥45 mL/min/1.73 m^2 is minimal and prophylactic strategies to mitigate AKI risk are not indicated, but that such strategies should be used for individuals with an eGFR <30 mL/min/1.73 m^2.(31) Among individuals with an eGFR 30-44 mL/min/1.73 m^2, the ACR/NKF consensus suggests use of prophylaxis if patients have co-occurring conditions associated with heightened AKI risk, including diabetic nephropathy and heart failure.

The risk of CA-AKI following intra-arterial contrast administration/angiography is higher than after IV administration. Whether this is due to greater toxicity of iodinated contrast media when administered intra-arterially or due to other factors, including the potential risk of atheroembolic disease associated with vascular manipulation, is uncertain. There is evidence, however, of a dose-response relationship between the volume of contrast administered and the incidence of CA-AKI.(32) Because of the higher risk of CA-AKI associated with intra-arterial contrast administration, the threshold for utilizing prophylaxis to mitigate the risk of CA-AKI is generally higher than for IV contrast administration, with eGFR thresholds of 45 mL/min/1.73 m^2 for the majority of individuals and 60 mL/min/1.73 m^2 for higher-risk individuals, including those with diabetic nephropathy or heart failure.

Strategies to mitigate the risk of CA-AKI include use of the least nephrotoxic iodinated contrast media available (i.e., use of low osmolal or iso-osmolal contrast media), using the minimal volume of contrast media necessary to provide adequate imaging, and administering periprocedural IV isotonic crystalloid. No single regimen for periprocedural IVF administration has been demonstrated to be superior; however, administration of isotonic crystalloid at a rate of 1 mL/kg per hour for 6 to 12 hours pre- and post-procedure for hospitalized patients while administration of 3 mL/kg of isotonic crystalloid over one hour pre-procedure followed by 6 mL/kg over 2 to 6 hours post procedure for outpatients is often suggested.(33) Higher rates or larger volumes of fluid administration, protocols that use left-ventricular end diastolic pressure (34) and devices to match fluid administration to urine flow rate (e.g., Renal Guard® device)(35) have been utilized but are not clearly superior to simple fixed-volume fluid administration as suggested above. Similarly, the optimal IVF to be administered is also uncertain; while initially thought to be superior to 0.9% saline, the PRESERVE trial demonstrated that 1.26% sodium bicarbonate is not superior to 0.9% saline,(33) and other isotonic crystalloid solutions, such as lactated Ringer's solution, are likely equivalent to 0.9% saline but have not been rigorously evaluated. A variety of pharmacologic agents have been evaluated for potential benefits in mitigating the risk of CA-AKI including N-acetylcysteine,(33,36) dopamine,(37,38) fenoldopam,(39) mannitol,(40,41) furosemide,(40,41) ascorbic acid, and statins (42-44) have been evaluated, but none have been shown to be beneficial. Periprocedural hemodialysis or hemofiltration is also not effective.(45) The WG therefore recommends administration of 0.9% saline in high-risk patients but do not recommend administration of other agents for prophylactic purposes.

The failure to perform indicated medical procedures due to excessive concern regarding the development of iatrogenic AKI has been termed "renalism".(46) Studies have demonstrated that failure to perform otherwise indicated coronary angiograms and percutaneous coronary angiography (PCI) are associated with an increased mortality risk.(46-48) Similarly, it has been suggested that failure to utilize iodinated contrast for imaging, when indicated, can lead to

underdiagnosis of malignancies, aortic aneurysms, pulmonary emboli and other critical findings. **It is therefore recommended that indicated procedures be performed regardless of level of kidney function, with appropriate prophylactic interventions implemented to mitigate risks when possible.**

B. Gadolinium-Based Contrast Media

Gadolinium-based contrast media (GBCM) are used to enhance magnetic resonance imaging (MRI). Gadolinium (Gd) is a rare earth metal in the lanthanide series that is strongly paramagnetic, enhancing discrimination between tissues during an MRI. Gd as a free ion (Gd^{3+}) is highly toxic since it competes with ionized calcium (Ca^{2+}) in biological systems, leading to competitive inhibition of a range of biological processes, including inhibition of Ca^{2+}-binding enzymes and affecting voltage-gated calcium channels.(49,50) In addition, Gd^{3+} may have been demonstrated to be deposited in a variety of tissues, including brain, bone, and skin, even in individuals with preserved kidney function.

To mitigate the toxicity of gadolinium and enhance its solubility, GBCM complexes the Gd^{3+} ion with a carrier molecule. Before 2006, GBCM were thought to be entirely safe so high doses of GBCM were used for MRI studies and GBCM were also used in place of iodinated contrast agents for radiocontrast enhancement to prevent CA-AKI in patients with CKD. In 2006, Grobner reported the association of gadolinium-based contrast agents (GBCAs) with nephrogenic systemic fibrosis (NSF), an irreversible systemic fibrotic disease, in dialysis patients.(51) NSF is a systemic fibrotic disease seen only in patients with kidney dysfunction who received GBCM.

The predominant risk factors for NSF are reduced kidney function (including dialysis dependence and severe acute or chronic kidney dysfunction) and the type and dose of GBCM. Advanced liver disease, including individuals post liver transplant, have also been considered to be at increased risk, however it is likely that this reflects concomitant kidney dysfunction, often masked due to reduced generation resulting in blunted elevations in serum creatinine. The exact pathobiology of NSF is poorly understood as older data are limited to retrospective observational studies, animal models are limited, and there are no new cases with use of newer GBCMs. It is hypothesized that the initiating factor in the development of NSF is dissociation of Gd^{3+} ions from the carrier molecules in exchange for endogenous metal ions, such as Fe^{3+}, Cu^{2+}, and Zn^{2+}, through a process of transmetallation. Since GBCM are normally rapidly excreted by the kidney, reduced kidney function results in increased retention of the GBCM in the body, giving Gd^{3+} time to dissociate from the carrier molecule.

The risk of NSF increases with cumulative doses of GBCM and is associated with variation in the affinity between the Gd^{3+} ion and the carrier molecule. GBCM are now categorized into three groups: Group 1 GBCM (e.g., gadpdiamide, gadopentate dimeglumine, and gadoversetamide) are linear non-ionic molecules that have the lowest binding affinity and the highest association with development of NSF. Group 2 GBCM (e.g., gadobenate dimeglumine, gadobutrol, gadoteric acid, and gadoteridol) are linear ionic or macrocyclic agents with much higher binding affinity than the Group 1 GBCM. Gadoxetate disodium, the sole Group 3 GBCM, is an ionic linear molecule with both hepatic and renal excretion that has higher binding affinity than the Group 1 agents.

In an analysis of 4,931 patients with stage G4 or G5 CKD or ESKD on dialysis who underwent MRI with Group 2 GBCM, there were no cases of NSF. Across this entire population, the upper

bound of the 95% confidence interval of the risk of NSF was 0.07%.(52) In a subsequent analysis, breaking the risk down based on CKD stage and dialysis dependence, the upper bound of the 95% confidence interval for the risk of NSF was 0.2% for stage G5 CKD on dialysis (n=1,849), 0.5% for stage G5 CKD not on dialysis (n=732), and 0.19% for stage G4 CKD (n=1,955).(53) Based on these data, a workgroup convened by the ACR and NKF concluded that the risk of NSF is very low for standard dose (0.1 mmol/kg) of group 2 GBCM, even in patients with eGFR <30mL/min/1.73 m^2 or AKI.(54) They further recommend that dialysis should not be initiated nor should dialysis schedule or frequency be altered following administration of group 2 GBCM.

An analysis done by the VA Evidence Synthesis Program identified no reported cases of NSF associated with use of Group 2 or Group 3 GBCM.(55) Across 12 studies that included over 18,000 patients with any degree of kidney disease, the upper 95% confidence interval for the risk of NSF occurrence per exposure using Group 2 and Group 3 GBCM ranged between 0.0002 and 0.3085, with the highest bound associated with a study that only included 10 patients.(56) While they did not calculate a pooled upper bound of the 95% confidence limit, based on zero cases of NSF among more than 18,000 individuals with kidney disease, the value would be 0.0002, corresponding to a 97.5% probability that the risk of NSF is less than 1 in 5,000 exposures. In a second analysis of 12 studies that included 118,844 patients exposed to either Group 1 or Group 2 GBCM there were 41 cases of NSF, 37 associated with exposure to only Group 1 GBCM, and 4 with exposure to Group 2 GBCM, although 3 of the 4 had likely confounding with prior exposure to Group 1 agents. In addition, they identified 18 cases of NSF after exposure to Group 2 or Group 3 GBCM in 10 case reports or small case series. Of the 18 cases, 9 described confounding with prior exposure to a Group 1 GBCM. Overall, they concluded that there are very few reported cases of NSF after exposure to Group 2 or Group 3 GBCM and most reported cases are of uncertain value since they occurred in patients who had been exposed to Group 1 GBCM around the same time. Generally, they found little data to inform the care of patients who are at risk for developing CKD or those with AKI and concluded that rare cases of NSF cannot be excluded in patients with significant kidney disease.

Based on these data, a precise risk of NSF after exposure to Group 2 or Group 3 GBCM cannot be given but is likely extremely low. While potential risks should be discussed with the patient, and they should be included in shared decision-making, Group 2 GBCM can be utilized in individuals with an eGFR <30 mL/min/1.73 m^2 if other imaging techniques will not be adequate. The dose of GBCM used should be the minimum required to obtain satisfactory imaging. No prophylactic interventions are of benefit in minimizing the risk of NSF; for patients on hemodialysis, the procedure should be timed to immediately precede a dialysis session. However, dialysis should otherwise not be altered or initiated based on use of group 2 GBCM.

General Medical and Lifestyle Management Recommendations to Improve Standard of Care in CKD Patients

Patients with CKD along with other advanced chronic disease patient populations benefit from lifestyle modification, which includes smoking cessation, improving sleep quality, increased physical activity, weight management, and diet modification. Outlined below are additional considerations for the CKD patient population.

A. Exercise

Patients with CKD are typically less active than sedentary individuals without CKD.(57-59) O'Hare

et al. reported that sedentary dialysis patients had a higher risk of death within one year than those who reported participation in some form of physical activity.(60) Physical inactivity is also a strong predictor of CV mortality in patients with earlier stages of CKD (61) and represents a potentially modifiable risk factor. In addition to CV risks associated with physical inactivity, several studies have also highlighted the link between inactivity and poor physical functioning and fitness in patients with CKD.(57,60,62) Recent studies have shown that exercise is feasible and safe to perform among patients with CKD, including among patients with ESKD during dialysis. Both intradialytic exercise (IDE) and home-based exercise (HBE) enhance physical function, cardiopulmonary capacity, health-related quality of life (HRQoL), and cognitive well-being. Some research proposed an indirect link between IDE and survival rates.(63-66) Given the strong association between physical inactivity and mortality in dialysis patients (60,67) and the potential improvements in physical functioning associated with increasing activity,(68) it is reasonable to recommend exercise among patients with CKD. Trecommends at least 150 minutes of moderate intensity physical activity every week (i.e., 30 minutes on at least 5 days), aligning with the same recommendation from the Surgeon General,(70) the Centers for Disease Control and Prevention,(71) and American Heart Association. For individuals who may be frail or for whom safety is a concern with exercise, a physical therapy referral prior to the discussion of implementing exercise is reasonable.

B. Dietary Management of CKD

Recommending a generally healthy well-balanced diet, rich in fruits and vegetables is reasonable for all patients with chronic disease burden. The dietary evaluation and management of patients with CKD should be individualized with support from a registered dietitian to avoid a one size fits all approach to dietary education. For example, sodium restricted diet may mitigate proteinuria in patients with proteinuric CKD;(73) however, among CKD patients in whom salt wasting is a feature of the disease, these recommendations may not apply.

Additionally, the Dietary Approaches to Stop Hypertension (DASH) and Mediterranean diets are recommended in the management of hypertension (see VA/DOD Hypertension CPG, and both are generally higher in potassium. However, fresh fruits and vegetables are typically higher in potassium,(74) which may be problematic in some patients who develop hyperkalemia as a result of their CKD; thus, adjustments may be needed. An unintended consequence of this advice may be a shift toward less healthful diets. In the early stages of CKD, a high intake of foods naturally rich in potassium appears to be protective against disease progression, and dietary restriction of foods naturally containing potassium, such as fruits and vegetables, may be harmful to health.(69) Multiple observational reports in CKD have explored the association between dietary potassium intake and outcomes; in a majority, surrogates of high potassium intake were associated with a lower risk of death or progression of kidney disease. In addition, observational studies in persons with CKD or ESKD report weak associations between dietary potassium intake and potassium concentration.(75)

Finally, given the association of cardiovascular outcomes with CKD related bone mineral disease, it is also reasonable to recommend a low inorganic phosphorus (i.e., phosphorus additives in processed packaged foods) diet for patients with evidence of progressive CKD.

Individuals with multiple co-occurring conditions are at a higher risk for malnutrition particularly with pharmacologic treatment. The use of GLP-1 RA combined with SGLT2i in individuals with CKD may require careful monitoring for muscle wasting and the need for additional protein consumption.(76) Conversely, protein restriction may be reasonable for individuals whose protein

consumption is deemed to be more than nutritional needs. Consider a referral to a renal dietitian for assessment and education regarding appropriate protein intake. Patients should be screened frequently for evidence of acute and/or chronic malnutrition using the six Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition (ASPEN) clinical criteria and further assessed and treated if screening is positive.(77,78)

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