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ESC GUIDELINES

2026 ESC Guidelines for the management of cardiovascular disease and chronic kidney disease, in collaboration with the European Renal Association (ERA)

Developed by the task force on the management of cardiovascular disease and chronic kidney disease of the European Society of Cardiology (ESC)

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Abbreviations and acronyms

A-HEFT	African-American Heart Failure Trial
AAA	Abdominal aortic aneurysm
AAD	Anti-arrhythmic drug
ABI	Ankle brachial index
ACEI	Angiotensin-converting enzyme inhibitor
ACHIEVE	Aldosterone Blockade for Health Improvement Evaluation in End-stage Renal Disease (trial)
ACS	Acute coronary syndrome
ADVOR	Acetazolamide in Decompensated Heart Failure with Volume Overload (trial)
AF	Atrial fibrillation
AF-CHF	Atrial Fibrillation and Congestive Heart Failure (trial)
AKI	Acute kidney injury
ALERT	Assessment of LEscol in Renal Transplantation (trial)
ARB	Angiotensin-II receptor blocker
ARNI	Angiotensin receptor/neprilysin inhibitor
ASCVD	Atherosclerotic cardiovascular disease
ATP	Anti-tachycardia pacing
ATTACK	Aspirin To Target Arterial events in Chronic Kidney disease (trial)
AUC	Area under the curve
BMI	Body mass index
BSA	Body surface area
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CARSK	Canadian Australasian Randomized Trial of Screening Kidney Transplant Candidates for CAD (trial)
CCB	Calcium channel blocker
CCS	Chronic coronary syndrome
CCTA	Coronary computed tomography angiography
CGA	Cause, GFR and Albuminuria (part of KDIGO CKD staging)
$CHADS_2$	Congestive heart failure, hypertension, age >75 years, diabetes; previous stroke (2 points) (maximum score = 6)
CHA_2DS_2-VA	Congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/ arterial thromboembolism (2 points), vascular disease, age 65–74 years (maximum score = 8)
CHA_2DS_2-VASc	Congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke or TIA or thromboembolism (2 points), vascular disease, age 65–74 years, sex category (female) (maximum score = 9)
CHANCE	Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (trial)
CI	Confidence interval
CI-AKI	Contrast-induced acute kidney injury
CIED	Cardiac implantable electronic device
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CKD-MBD	Chronic kidney disease – mineral bone disorder
CLOROTIC	Safety and Efficacy of the Combination of Loop with Thiazide-type Diuretics in Patients with Decompensated Heart Failure (trial)
CLTI	Chronic limb-threatening ischaemia
COAPT	Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (trial)
COMPASS	Cardiovascular Outcomes for People Using Anticoagulation Strategies (trial)
CONSENSUS	Cooperative North Scandinavian Enalapril Survival Study (trial)
COURAGE	Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (trial)
CREDENCE	Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (trial)
CRT	Cardiac resynchronization therapy
CT	Computed tomography
CVD	Cardiovascular disease
DanGerShock	Danish–German Cardiogenic Shock (trial)
DAPA-CKD	Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (trial)
DAPA-HF	Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (trial)
DAPA-MI	Dapagliflozin in patients with MI (trial)
DAPT	Dual antiplatelet therapy
DELIVER	Dapagliflozin Evaluation to Improve the Lives of Patients with Preserved Ejection Fraction Heart Failure (trial)
DHF	Decompensated heart failure
DIG	Digitalis Investigation Group
DIGIT-HF	DIGitoxin to Improve ouTcomes in patients with advanced chronic Heart Failure (trial)
DOAC	Direct oral anticoagulant
DOREMI	Dobutamine Compared with Milrinone (trial)
DOSE	Diuretic Optimization Strategies Evaluation (trial)
DPP-4	Dipeptidyl peptidase-4
DVT	Deep vein thrombosis
EAST-AFNET4	Early Treatment of Atrial Fibrillation for Stroke Prevention Trial
ECG	Electrocardiogram
ECLS-SHOCK	Extracorporeal Life Support in Infarct-Related Cardiogenic Shock (trial)
eGFR	Estimated glomerular filtration rate
EMPA-KIDNEY	The Study of Heart and Kidney Protection With Empagliflozin (trial)

EMPACT-MI	Study to Evaluate the Effect of Empagliflozin on Hospitalization for Heart Failure and Mortality in Patients with Acute Myocardial Infarction (trial)
EMPEROR-Preserved	Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction (trial)
EMPEROR-Reduced	Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction (trial)
EMPHASIS-HF	Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (trial)
EMPULSE	Multicentre, Randomised, Double-blind, 90-day Superiority Trial to Evaluate the Effect on Clinical Benefit, Safety and Tolerability of Once Daily Oral EMPagliflozin 10 mg Compared to Placebo, Initiated in Patients Hospitalised for acUte Heart faiLure Who Have Been StabilisEd (trial)
ENACT-HF	Efficacy of a Standardized Diuretic Protocol in Acute Heart Failure (trial)
EPHESUS	Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (trial)
ERA	European Renal Association
ESA	Erythropoiesis-stimulating agent
ESC	European Society of Cardiology
ESPIRIT	Effects of Intensive Systolic Blood Pressure Lowering Treatment in Reducing RIsk of Vascular Events (trial)
FIDELIO-DKD	Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (trial)
FIDELITY	The FInerenone in chronic kiDney diseasE and type 2 diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial programme analysis (trial meta-analysis)
FIND-CKD	FInerenone Non-Diabetic Chronic Kidney Disease (trial)
FINEARTS-HF	FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure (trial)
FLOW	Evaluate Renal Function with Semaglutide Once Weekly (trial)
FOURIER	Further cardiovascular Outcomes Research with PCSK9 Inhibition in subjects with Elevated Risk (trial)
GFR	Glomerular filtration rate
GLP-1RA	Glucagon-like peptide-1 receptor agonist
GRACE	Global Registry of Acute Coronary Events
GUSTO III	Global Use of Strategies To Open occluded coronary arteries (trial)
HbA1c	Haemoglobin A1c (glycated haemoglobin)
HF	Heart failure
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HIF-PHI	Hypoxia-inducible factor prolyl hydroxylase inhibitors
HOT	Hypertension Optimal Treatment (trial)
HR	Hazard ratio
Hs-cTn (I/T)	High-sensitivity cardiac troponin (I/T)
ICA	Invasive coronary angiography
ICD	Implantable cardioverter defibrillator
ICD2	Implantable Cardioverter-Defibrillator in Dialysis Patients (trial)
ISAR-REACT	Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment (trial)
ISCHEMIA-CKD	International Study of Comparative Health Effectiveness with Medical and Invasive Approaches–Chronic Kidney Disease (trial)
KCCQ	Kansas City Cardiomyopathy Questionnaire
KDIGO	Kidney Disease: Improving Global Outcomes
KFRE	Kidney Failure Risk Equation
KRT	Kidney replacement therapy
LAA-KIDNEY	Left Atrial Appendage closure in patients with non-valvular AF and end stage chronic KIDNEY disease (trial)
LAAO	Left atrial appendage occlusion
LDL-C	Low-density lipoprotein–cholesterol
LMWH	Low molecular weight heparin
Look-AHEAD	Action for HEAlth in Diabetes (trial)
LVAD	Left ventricular assist device
LVEF	Left ventricular ejection fraction
MCS	Mechanical circulatory support
MI	Myocardial infarction
MPS	Myocardial perfusion scintigraphy
MRA	Mineralocorticoid receptor antagonist
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NSTE-ACS	Non-ST-elevation acute coronary syndrome
NT-proBNP	N-terminal pro-B-type natriuretic peptide
ODYSSEY OUTCOMES	Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Effect of Alirocumab on the Occurrence of Cardiovascular Events in Patients Who Have Recently Experienced an Acute Coronary Syndrome (trial)
OR	Odds ratio
PAD	Peripheral arterial disease
PCI	Percutaneous coronary intervention
PCSK9	Proprotein convertase subtilisin/kexin type 9
PE	Pulmonary embolism
PET	Positron emission tomography
PIVOTAL	Proactive IV Iron Therapy in Haemodialysis Patients (trial)
PLATO	Study of Platelet Inhibition and Patient Outcomes (trial)

PROGRESS	Perindopril Protection Against Recurrent Stroke (trial)
PTH	Parathyroid hormone
PTRA	Percutaneous transluminal renal angioplasty
PUSH-AHF	Pragmatic Urinary Sodium-based algoritHm in Acute Heart Failure (trial)
RAAS	Renin-angiotensin-aldosterone system
RALES	Randomized Aldactone Evaluation Study
RAS	Renin-angiotensin system
RCT	Randomized controlled trial
RENAL-AF	Renal Hemodialysis Patients Allocated Apixaban Versus Warfarin in Atrial Fibrillation (trial)
RESHAPE-HF2	Randomized Investigation of the MitraClip Device in Heart Failure: Second Trial in Patients with Clinically Significant Functional Mitral Regurgitation (trial)
REVIVAL	Registry Evaluation of Vital Information for VADs in Ambulatory Life (trial)
RR	Relative risk
SCD	Sudden cardiac death
SCORE2	Systematic COronary Risk Evaluation 2
SCORE2-HF	SCORE2-Heart Failure
SCORE2-OP	SCORE2-Older Persons
SELECT	Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (trial)
SGLT2	Sodium glucose co-transporter-2
SHARP	Study of Heart And Renal Protection (trial)
SHIFT	Systolic Heart Failure Treatment with the If inhibitor Ivabradine Trial
SMART	SeMaglutide and Albuminuria Reduction Trial in Obese Individuals Without Diabetes (trial)
SMART2	Secondary Manifestations of ARTerial disease 2 (cohort)
SMART2-HF	Secondary Manifestations of ARTerial disease 2–heart failure
SOLVD	Studies of Left Ventricular Dysfunction (trial)
SOUL	Semaglutide cardiOvascular oUtcomes trial
SPECT	Single photon emission computed tomography
SPRINT	Systolic blood PRessure Intervention Trial
STAMP	Screening, Triage and staging of CKD, Addressing CKD risk, Modifying approaches to CVD management and Planning health services (guideline acronym)
STEMI	ST-elevation myocardial infarction
STRONG-HF	Safety, Tolerability, and Efficacy of Rapid Optimization, Helped by NT-proBNP Testing, of Heart Failure Therapies (trial)
SUMMIT	Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study Comparing the Efficacy and Safety of Tirzepatide Versus Placebo in Patients with Heart Failure with Preserved Ejection Fraction and Obesity (trial)
TEER	Transcatheter edge-to-edge repair
TIA	Transient ischaemic attack
TOPCAT	Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (trial)
TRILOGY ACS	Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (trial)
TRITON-TIMI	Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction (trial)
TSAT	Transferrin saturation
TTE	Transthoracic echocardiography
uACR	Urine albumin-to-creatinine ratio
US	United States
USRDS	Unites States Renal Data System
VICTOR	Vericiguat Global Study in Participants with Chronic Heart Failure (trial)
VICTORIA	Vericiguat Global Study in Subjects with Heart Failure with Reduced Ejection Fraction (trial)
VKA	Vitamin K antagonist
VTE	Venous thromboembolism
WRAP-IT	Worldwide Randomized Antibiotic Envelope Infection Prevention Trial
WRF	Worsening renal function

1. Preamble

Guidelines evaluate and summarize available evidence with the aim of assisting health professionals in proposing the best diagnostic or therapeutic approach for an individual patient with a given condition. ESC Guidelines are intended for use by health professionals but do not override their individual responsibility to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with the patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription and to respect the ethical rules of their profession.

ESC Guidelines represent the official position of the ESC on a given topic. Guideline topics are selected for updating after annual expert review of new evidence conducted by the ESC Clinical Practice Guidelines (CPG) Committee. ESC Policies and Procedures for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines). This Task Force was selected by the ESC to include professionals involved with the medical care of patients with this pathology and to include patient representatives and methodologists. The selection procedure included an open call for authors and aimed to include members from across the entire ESC region and from relevant ESC Subspecialty Communities. Consideration was given to diversity and inclusion.

Guidelines Task Forces perform a critical review and evaluation of the published literature on diagnostic and therapeutic approaches including assessment of the risk–benefit ratio. Recommendations are based on major randomized trials and relevant systematic reviews and meta-analyses, when available. Systematic literature searches are conducted in cases of controversy or uncertainty to ensure that all key studies are considered. For recommendations related to diagnosis and prognosis, additional types of evidence are included, such as diagnostic accuracy studies and studies focused on the development and validation of prognostic models. The strength of each recommendation and the level of evidence supporting it are weighed and scored according to predefined criteria. The criteria for grading the strength of recommendations are described in *Table 1*. A new system for grading levels of evidence for ESC Guidelines has been published[1,2] and utilized for the first time in the 2026 ESC Guidelines. For therapy and prevention, the framework includes consideration of study type and the number of studies supporting a recommendation, as well as whether a study is adequately powered, shows substantial evidence against the play of chance, and is free of major sources of bias. This is described in *Table 2*. A separate grading system has also been developed for diagnostic tests and prediction models, which is described in *Table 3*.

Patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) are also evaluated when available as the basis for recommendations and/or discussion in these guidelines.

Evidence tables summarizing key information from relevant studies are generated to facilitate the formulation of recommendations, to enhance comprehension of recommendations after publication, and to reinforce transparency in the guidelines development process. The tables are published in their own section of ESC Guidelines and reference specific recommendation tables.

After an iterative process of deliberations, a first Task Force vote on all recommendations is conducted prior to the initiation of rounds of review. A second Task Force vote on all recommendations is conducted after the final round of review and revision. For each vote, the Task Force follows ESC voting procedures: to achieve quorum, at least two thirds of the Task Force must vote agree or disagree, and to be approved all recommendations require at least 75% of votes in favour, excluding abstentions. Restrictions on voting and on participation in task force deliberations are applied as needed based on declarations of interest.

The writing and reviewing panels provide declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest are reviewed according to the ESC declaration of interest rules, which can be found on the ESC website (http://www.escardio.org/doi) and are compiled in a report published in a supplementary document with the guidelines. Funding for the development of ESC Guidelines is derived entirely from the ESC with no involvement of the healthcare industry.

The CPG Committee supervises and coordinates the preparation of new guidelines and approves their publication. In addition to review by the CPG Committee, ESC Guidelines undergo multiple rounds of double-blind peer review on a dedicated online review platform. The review is conducted by a panel of 70 or more topic experts including members from ESC National Cardiac Societies and from relevant ESC Subspecialty Communities. Reviewers critically assess and comment on the content of the Guidelines and grade their comments as major and minor. Guideline Task Forces consider all review comments and are required to respond on the online platform to all those classified as major. The review comments inform revisions after each round. After the final review round and the second Task Force vote on all recommendations, the Task Force and the CPG Committee members approve the final document for publication in the *European Heart Journal*.

Table 1 **Classes of recommendations**

Class of recommendation	Definition	Wording to use
I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	*"is recommended"* or *"is indicated"*
II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	*"should be considered"*
IIb	Usefulness/efficacy is less well established by evidence/opinion.	*"may be considered"*
III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	*"is not recommended"*

Table 2 Levels of evidence—therapy and prevention

Level of evidence	Definition
A	Conclusive evidence, usually from at least two adequately powered randomized controlled trials[a] free of major bias, with substantial evidence against the play of chance when combined in a meta-analysis (e.g., P <0.005 for superiority).[b]
B1	Suggestive evidence from at least one adequately powered randomized controlled trial free of major bias, or a meta-analysis of such randomized controlled trials, with some evidence against the play of chance (e.g., P <0.05 for superiority).[c]
B2	Limited evidence from at least two adequately powered non-randomized studies with careful control of major sources of bias and substantial evidence against the play of chance (e.g., P <0.005 for superiority),[b] or from a meta-analysis of small, underpowered randomized controlled trials with some evidence against the play of chance (e.g., P <0.05 for superiority).[c]
C	Preliminary evidence from non-randomized studies without careful control of major sources of bias, a single small, underpowered randomized controlled trial, or expert consensus.

[a]Exceptionally, level of evidence A can be considered if (i) there is a single very large randomized controlled trial that provides convincing evidence across a wide range of patients that is already widely accepted by most practitioners; or (ii) the effects of the intervention are clinically obvious; in either case, over 90% of voting guideline task force members need to agree with level of evidence A.
[b]Studies do not need to individually show substantial evidence against the play of chance (e.g. a P-value of P < .005 for superiority) if a meta-analysis of these studies provides such evidence.
[c]Studies do not need to individually show some evidence against the play of chance (e.g. a P-value of <.05 for superiority) if a meta-analysis of these studies provides such evidence.

Table 3 Levels of evidence—diagnostic tests and prediction models

Level of evidence	Diagnostic test	Prediction model (including diagnostic and prognostic models)
A	Conclusive evidence of adequate diagnostic ability from at least two high-quality studies	Conclusive evidence of adequate predictive ability from at least one high-quality derivation study, and two or more external validation studies of at least moderate quality.
B	Suggestive evidence of adequate diagnostic ability from a single high-quality or at least two moderate-quality studies.	Suggestive evidence of adequate predictive ability from one or more derivation and one or more external validation studies of at least moderate quality.
C	Preliminary evidence of adequate diagnostic ability from a single moderate-quality study, any number of low-quality studies, or expert consensus.	Preliminary evidence of adequate predictive ability from a derivation study of at least moderate quality, but with external validation absent or in a low-quality study, or a derivation study of low quality (irrespective of external validation).

Unless otherwise stated, ESC Guidelines content refers to sex, understood as the biological condition of being male or female, defined by genes, hormones, and sexual organs. Off-label use of medication may be presented in this guideline if a sufficient level of evidence shows that it can be considered medically appropriate for a given condition. However, decisions on off-label use must be made by the responsible health professional giving special consideration to ethical rules concerning healthcare, the specific situation of the patient, patient consent, and country-specific health regulations.

2. Introduction

This Guideline was developed by a task force of clinicians, methodologists, patients, and other experts from the cardiology and

nephrology communities, including a collaboration with the European Renal Association (ERA). There were reviewers from across the European Society of Cardiology (ESC) membership, from the ERA and the ESC Clinical Practice Guidelines Committee. As such, it is an evidence-based consensus of the experts consulted in its development.

It has been estimated that there are ~100 million people in Europe with chronic kidney disease (CKD).[3] CKD is associated with a range of cardiovascular diseases (CVDs), including coronary artery disease (CAD), heart failure (HF), arrhythmias, stroke, peripheral arterial disease (PAD), and sudden cardiac death (SCD).[4] Decreased glomerular filtration rate (GFR) may also result from CVD, particularly HF. Consequently, CVD is common in patients with CKD. Recognizing the high prevalence and the close links between CVD and CKD, the World Health Organization adopted a resolution in May 2025 entitled 'Reducing the burden of noncommunicable diseases through the promotion of kidney health and strengthening prevention and control of kidney disease'.[5] The task force believes that active engagement in identifying CKD and timely initiation of cost-effective interventions by all clinicians, including the cardiology community, are required to reduce the global burden of CVD and CKD. This ESC Guideline is the first to be dedicated to CVD and CKD. The task force considered prevention, diagnosis, and treatment of patients with CVD and CKD. It covers the full range of CVDs in a single document, emphasizing where the presence of CKD necessitates changes in standard approaches and/or additional measures. This ESC Guideline aims to synthesize the best available evidence to facilitate:

- Early diagnosis of CKD in patients with CVD
- Appropriate use of kidney failure risk-modifying therapies in patients with CVD and CKD
- Early diagnosis of CVD in patients with CKD
- Prevention and treatment of CVD in the setting of CKD
- Approaches to changes in kidney function during medical and procedural treatments for CVD
- Multidisciplinary management of patients with CVD and CKD between specialities.

The guideline is primarily written for the cardiology community but is relevant to all members of clinical teams that care for patients with CVD and CKD. It therefore does not include details of nephrological specialist management (e.g. there are limited details on kidney replacement therapy [KRT] and treatment of specific metabolic complications, including renal anaemia). For nephrological details that are out of scope of this guideline, the task force has highlighted relevant Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for the interested reader. Furthermore, the guideline is not intended to act as a reference for specific drug dosing in CKD. The task force encourages use of Summary of Product Characteristics and relevant drug formularies—including the Renal Drug Handbook—as appropriate resources for such information.[6] Instead, the task force provides practical advice on approaches for estimating absolute GFR, includes doses tested in randomized controlled trials (RCTs), and highlights key situations where awareness of dosing is particularly important.

The Central illustration (*Figure 1* Central illustration) summarizes a "STAMP on CKD" approach, which includes Screening, Triage and staging of CKD, Addressing CKD risk, Modifying approaches to CVD management and Planning health services for the complexities of CKD.

This guideline recommends systematic screening for CKD by testing for estimated glomerular filtration rate (eGFR) and albuminuria in all patients with CVD. Important therapeutic considerations may be necessary when CVD and CKD coexist. eGFR and albuminuria should be used to estimate individualized absolute risk of CVD and of kidney failure using validated estimating formulae. Based on evidence from large RCTs, many patients with CKD should then have appropriate management (see *Figure 2*) of their risk of kidney failure with an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin-II receptor blocker (ARB), plus a sodium glucose cotransporter-2 (SGLT2) inhibitor. This should be added to a standard of care to manage cardiovascular risk featuring suitably intensive blood pressure management and consideration of a statin-based regimen. Some patients with diabetes and CKD are also recommended to be prescribed a non-steroidal mineralocorticoid receptor antagonist (MRA) and a glucagon-like peptide 1 receptor agonist (GLP-1RA).

Patients with chronic HF and CKD are recommended to be treated with a SGLT2 inhibitor independent of left ventricular ejection fraction (LVEF). In patients with HF with reduced ejection fraction (HFrEF), conventional treatment with an angiotensin receptor–neprilysin inhibitor (ARNI)—or single ACEI/ARB, beta-blocker, and MRA therapy—is recommended, and for HF with preserved ejection fraction (HFpEF), a non-steroidal MRA should be added. For patients with decompensated HF and CKD, higher doses of loop diuretics and early combination diuretic therapy should be considered, as diuretic resistance increases with worsening CKD stage.

For atherosclerotic cardiovascular disease (ASCVD, i.e. CAD, cerebrovascular disease, PAD), treatment in patients who have coexisting CKD should focus on the underlying condition and risk factors. There are strategies to minimize periprocedural acute kidney injury (AKI), and these should be implemented without delaying timely investigation and treatment. Supraventricular and ventricular arrhythmias and SCD become more common as eGFR decreases. There is sufficient evidence in patients with atrial fibrillation (AF), CKD, and eGFR $\geq$ 15 mL/min/1.73 m^2 to recommend direct oral anticoagulant therapy (and particularly factor Xa inhibitors at low GFR) over vitamin K antagonists to reduce the risk of stroke with lower bleeding risk. A similar approach may be considered for preventing recurrent venous thromboembolism (VTE) in patients with CKD.

This guideline provides a simple algorithm for cardiovascular assessment prior to kidney transplantation. More RCTs are needed in patients on KRT, and particularly in dialysis populations.[7,8]

Given the high risk associated with CVD among patients living with CKD, and the additional disease burdens that such patients face, it is important that health services are co-ordinated to support prompt and efficient care for complex presentations. Patients with CKD must avoid delays in receiving treatment for CVD. This will require an efficient interdisciplinary approach with shared decision-making processes to support good patient communication. Effective communication is critical to ensure personalized care, maintain adherence to treatments, and ensure both clinicians' and patients' care priorities are addressed.

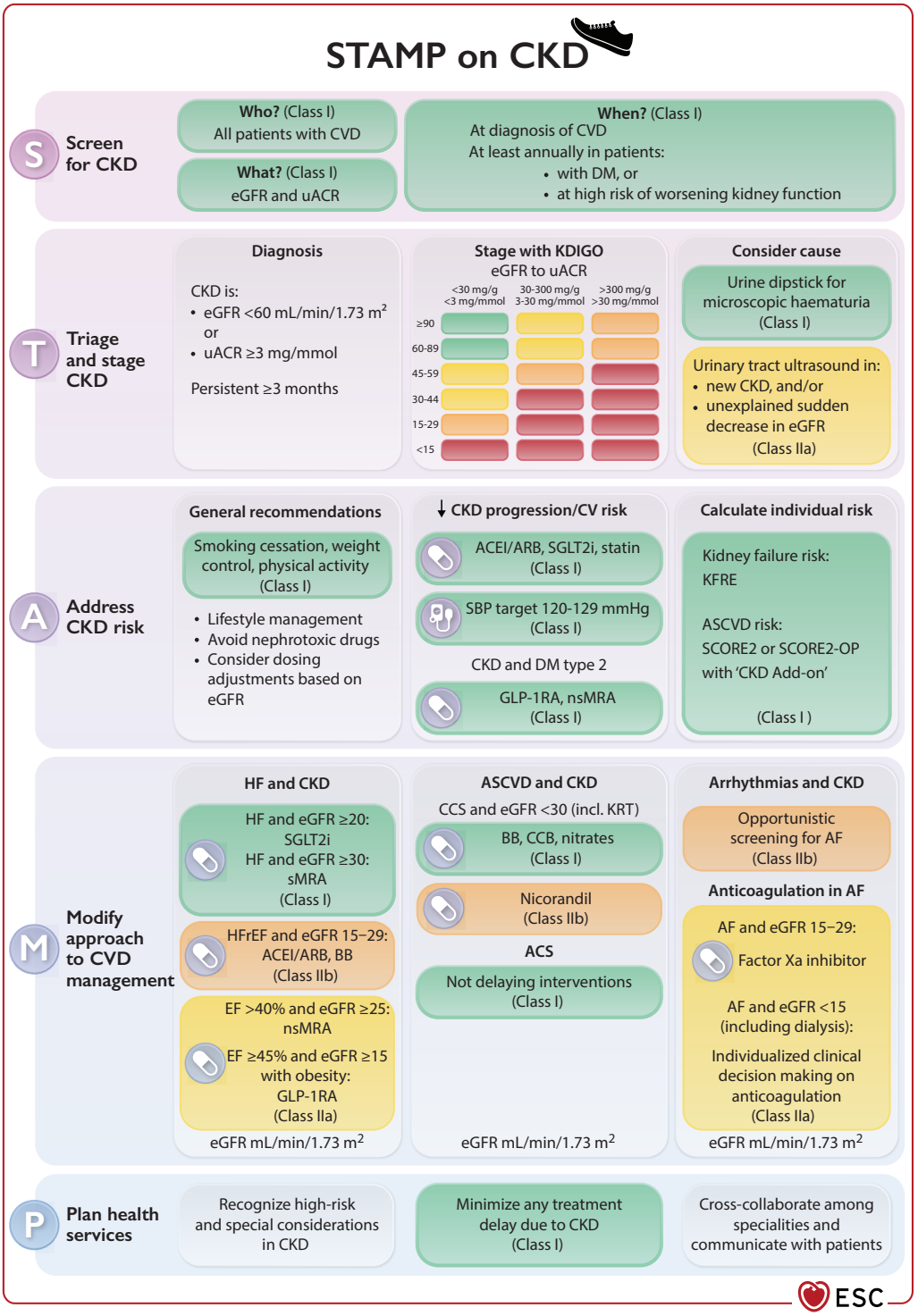

Figure 1 Central illustration. ACEI, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; AF, atrial fibrillation; ARB, angiotensin-II receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BB, beta-blocker; CCB, calcium channel blocker; CCS, chronic coronary syndrome; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; DM, diabetes mellitus; EF, ejection fraction; eGFR, estimated glomerular filtration rate (given in mL/min/1.73 m^2); GFR, glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; KDIGO, Kidney Disease: Improving Global Outcomes; KFRE, Kidney Failure Risk Equation; KRT, kidney replacement therapy; (n)sMRA, (non-)steroidal mineralocorticoid receptor antagonist; SBP, systolic blood pressure (given in mmHg); SCORE2 (-OP), Systematic COronary Risk Evaluation 2 (-Older Persons); SGLT2i, sodium glucose co-transporter 2 inhibitor; uACR, urine albumin-to-creatinine ratio (uACR ≥3 mg/mmol is approximately equivalent to ≥30 mg/g).

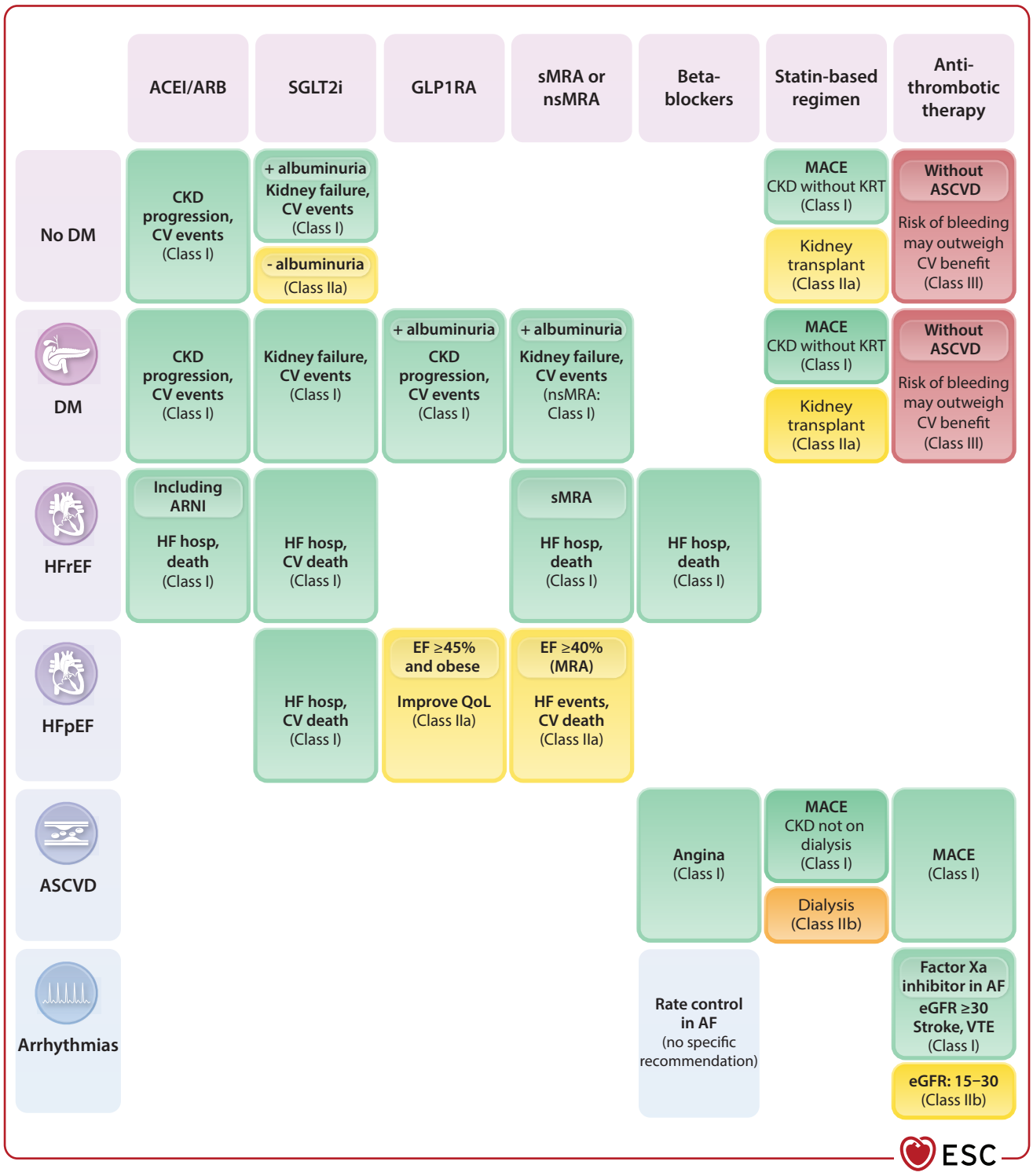

Figure 2 Recommended medical interventions by diabetes status and different cardiovascular diseases. ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CKD, chronic kidney disease; DM, diabetes mellitus; DOAC, direct oral anticoagulant; EF, ejection fraction; eGFR, estimated glomerular filtration rate (eGFR in mL/min/1.73 m^2); GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; hosp, hospitalization; KRT, kidney replacement therapy; MACE, major adverse cardiovascular events; (n)sMRA, (non-) steroidal mineralocorticoid receptor antagonist; SGLT2i, sodium glucose co-transporter 2 inhibitor; sMRA, steroidal mineralocorticoid receptor antagonist; QoL, quality of life; uACR, urine albumin-to-creatinine ratio; VTE, venous thromboembolism. The boxes for each underlying condition and medical intervention combination highlight class of recommendation and associated impacted outcome.

3. Chronic kidney disease

3.1. Chronic kidney disease definition and staging

Recommendation Table 1 — Recommendations for the diagnosis of chronic kidney disease (see Evidence Table 1)

Recommendations	Class[a]	Level[b]
Classifying CKD according to GFR and albuminuria into moderate, high, or very high-risk categories is recommended to assess increased likelihood for kidney failure and complications of CKD, including cardiovascular disease.[4,9]	I	A
Measurement of a creatinine-based eGFR using a validated estimating equation is recommended to assess kidney function and to stage CKD.[4,9,10]	I	A
Measuring uACR in a spot morning urine sample is recommended to assess albuminuria and classify CKD stage.[9]	I	A
Two measurements of eGFR and uACR over a period of at least 3 months are recommended to establish chronicity needed to confirm CKD.[9]	I	C
Measuring cystatin C-based eGFR should be considered in patients with likely sources of error[c] in creatinine-based eGFR when an accurate assessment of kidney function is needed for clinical decision-making.[9,11]	IIa	A

CKD, chronic kidney disease; (e)GFR, (estimated) glomerular filtration rate; uACR, urine albumin-to-creatinine ratio.
[a]Class of recommendation.
[b]Level of evidence.
[c]Abnormally high or low muscle mass (age and sex adjusted), or in the context of use of drugs that interfere with renal tubular creatinine secretion (see KDIGO 2024 guideline for full details).[9]

Chronic kidney disease is defined as the presence of abnormalities of kidney structure or function present for at least 3 months, with implications for health.[9] Although there are several markers that can denote such abnormalities, including abnormalities on imaging or urinary sediment, in clinical practice, GFR <60 mL/min/1.73 m^2 or urine albumin-to-creatinine ratio (uACR) ≥3 mg/mmol (≥30 mg/g) are most commonly used. Such a decrease in GFR or increase in albuminuria are independently associated with increased risk of kidney failure and a range of CVDs.[4]

3.1.1. Chronic kidney disease staging

Chronic kidney disease is staged based on Cause, GFR, and Albuminuria (the CGA system), with G and A categories formulated into a heatmap (*Figure 3*). This classification is based on individuals' increased relative risk of kidney failure and CKD-related complications including CVD, with category G5—a persistently low GFR of <15 mL/min/1.73 m^2—representing kidney failure. This term replaces the obsolete term 'end-stage kidney disease', and is the stage when KRT may become clinically necessary. The heatmap can also serve as a general guide to the frequency of kidney function monitoring and management strategies.[9]

3.1.2. Estimating glomerular filtration rate

The simplest method to estimate GFR is using blood—usually serum—creatinine and a validated estimated GFR (eGFR) equation.[4,9,10] The most commonly used equations do not require body weight and are instead indexed to 1.73 m^2 body surface area (BSA), enabling staging of individuals (see *Section 3.4* on drug dosing for details of when BSA de-indexed GFR [i.e. absolute GFR] needs to be considered). Historically, these equations incorporated age, sex, and race to explain between individual variation in serum creatinine concentrations that are unrelated to GFR (e.g. difference in rate of creatinine generation). They also account for the exponential relationship between serum creatinine and GFR.

Recently, there has been a move away from applying race in equations.[12,13] The 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR equation without the race coefficient appears to be an optimal compromise for European populations,[10] instead of the newer 2021 equation. The 2021 equation was developed for a United States (US) population and overestimates GFR in large parts of Europe.[12,14] Refining creatinine-based equations will continue (e.g. European Kidney Function Consortium [EKFC] equation), and any future changes will require careful justification before implementing, followed by education to ensure clinicians' and patients' understanding.[15,16]

Clinicians and patients should be aware that eGFR formulae are generally less precise above 60 mL/min/1.73 m^2 and there is natural within-person day-to-day biological variation.[17] Creatinine is a waste product produced by myocytes, meaning $eGFR_{creatinine}$ is inaccurate in patients with extremes of muscle mass (high or low). Cystatin C is synthesized by all nucleated cells and freely filtered by the kidneys, so eGFR calculated with cystatin C alone or equations combining it with serum creatinine are more reliable in such patients.[18–20] Measuring cystatin C may therefore be worthwhile in individuals with clearly abnormally high or low muscle mass for their age and sex, or in other scenarios where serum creatinine levels may not accurately reflect GFR (e.g. when using drugs that interfere with renal tubular creatinine secretion, such as trimethoprim). Non-GFR determinants of cystatin C also exist, so using it as alternative also has limitations (see KDIGO 2024 CKD guideline for more details).[9,11,21]

Routine clinical measurement of cystatin C in all individuals is not performed due to higher assay costs and less availability than for creatinine. For many individuals, kidney failure risk prediction is improved by obtaining information on albuminuria—which is frequently undermeasured—rather than by focusing resources on refining GFR estimation by measuring cystatin C alongside creatinine.

3.1.3. Measuring albuminuria

Albuminuria indicates primary glomerular disease and/or intraglomerular hyperfiltration with generalized endothelial damage. Hyperfiltration develops in obesity, hypertension, diabetes, or reduced nephron numbers (e.g. severe CKD).[22]

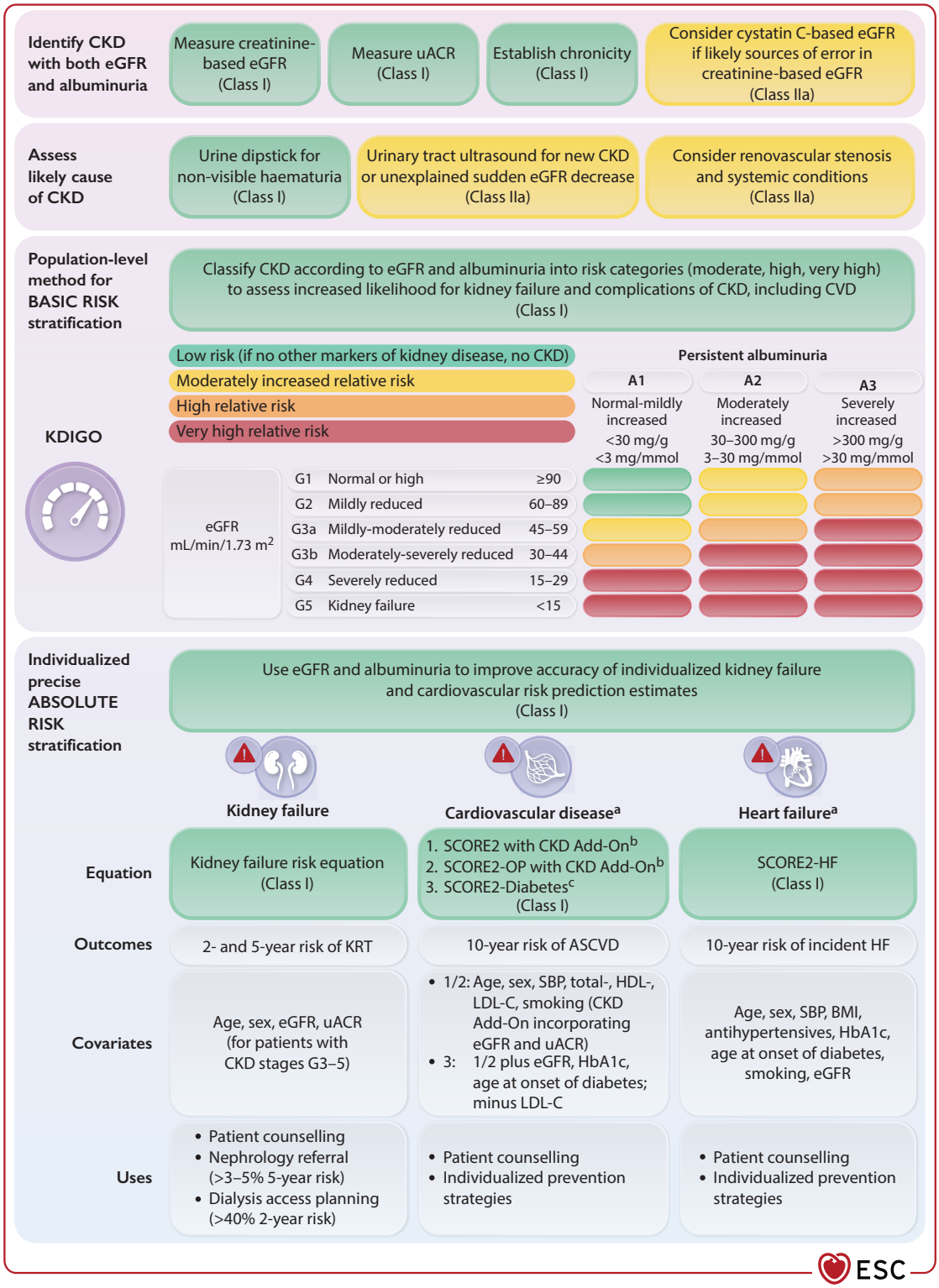

Figure 3 Chronic kidney disease classification and risk prediction approaches. ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA1c, haemoglobin A1c; HF, heart failure; HDL, high-density lipoprotein; KDIGO, Kidney Disease: Improving Global Outcomes; KRT, kidney replacement therapy; LDL-C, low-density lipoprotein–cholesterol; SBP, systolic blood pressure; SCORE2, Systematic COronary Risk Evaluation 2; uACR, urine albumin-to-creatinine ratio (uACR of 3 and 30 mg/mmol are approximately equivalent to 30 and 300 mg/g, and ~30 and 300 mg/day, respectively). [a]Predicts risk for incident events in people without pre-existing ASCVD. Not for use in patients who are already receiving maintenance KRT. [b]Not for use in patients with diabetes. The CKD Add-On improves risk stratification. [c]For use in patients with pre-existing type 2 diabetes. See *Table 4* for further details on choice of individual CVD risk prediction tools and references[4,9,25–29]

Albuminuria often precedes a decrease in GFR, meaning spot urine testing for uACR is ideal for screening for early CKD.[4] uACR is preferred to urine albumin alone, as it accounts for urine concentration (as creatinine is excreted at a relatively constant rate). The ratio to creatinine therefore accounts for variation in urine tonicity. A first morning void is optimal as it correlates most closely with 24 h timed urine albumin measurement, but random samples may be used for screening for patient convenience.[23] Arbitrarily, albuminuria is categorized as A1–A3 based on historical dipstick detection thresholds. A3 levels indicate severely increased albuminuria and equate to at least 0.3 g per day of albuminuria. A3 was previously referred to as macroalbuminuria.[9]

Urine dipstick testing is a rapid, inexpensive, and widely available method to screen for albumin in urine. Many standard dipsticks primarily detect albumin only at higher concentrations (A3 levels) and can be insensitive when urine is dilute, so ≥1+ albumin/protein should be considered abnormal.[9,24] Dipstick use should therefore be limited to initial testing in settings of limited resources, or when assessing for other urine abnormalities including red or white blood cells, or glycosuria.

Confirmation that albuminuria persists beyond 3 months using uACR assessment is recommended to confirm CKD diagnosis, as it can temporarily increase around the time of fever, strenuous exercise, and urinary tract infection.

3.2. Causes of chronic kidney disease

Recommendation Table 2 — Recommendations for the causes of chronic kidney disease (see Evidence Table 2)

Recommendations	Class[a]	Level[b]
Performing a urine dipstick test for microscopic haematuria is recommended in patients with newly identified CKD with the aim of detecting glomerular disease requiring nephrological or urological disease evaluation.	I	C
A urinary tract ultrasound should be considered in patients with newly diagnosed CKD and also in patients with an unexplained sudden decrease in eGFR to assess kidney size and symmetry, and to evaluate possible urinary tract obstruction, or other causes of decreased GFR.	IIa	C
Evaluation for renovascular stenosis with suitable imaging modality[c] should be considered in patients with: • Rapidly progressive CKD without clear cause • ≥30% change in eGFR upon starting or stopping a single renal haemodynamically active medication[d] • Recurrent flash pulmonary oedema, or • Treatment-resistant hypertension on ≥4 appropriately dosed blood pressure-lowering agents to identify patients with CKD with clinically relevant renal artery disease who may benefit from PTRA.[9]	IIa	C
Assessment for systemic conditions (e.g. amyloidosis or Fabry disease) should be considered in patients with unexplained heart failure and CKD to inform specific management.	IIa	C

Continued

CKD, chronic kidney disease; (e)GFR, (estimated) glomerular filtration rate; PTRA, percutaneous transluminal renal angioplasty.
[a]Class of recommendation.
[b]Level of evidence.
[c]Suitable modalities include Doppler ultrasound, CT angiogram or MR angiogram, with formal angiography reserved for when PTRA is to be considered.
[d]Such as ACEI, ARB, SGLT2 inhibitor, MRA.

Chronic kidney disease should not only be classified according to eGFR and albuminuria levels, but also according to cause (where possible). CKD has multiple primary causes, with a significant proportion of them related to chronic CVD. Understanding the underlying cause may influence management approaches. Early identification and treatment of certain causes can slow CKD progression and improve patient outcomes.[30–39]

Initial screening of individuals with newly identified CKD should include urinary dipstick testing for haematuria.[40–42] When present, especially when albuminuria coexists, glomerulonephritis should be suspected, triggering nephrology referral. Visible haematuria is usually urological in origin, necessitating urology referral.[43] A urinary tract ultrasound should be considered in patients with newly diagnosed CKD, especially when the decreased GFR is unexpected, and in patients with an unexplained sudden decrease in GFR.[44,45] Ultrasound can provide evidence for chronicity through measurement of kidney size (e.g. bipolar length). Ultrasound also diagnoses urinary tract obstruction. Renal asymmetry indicates a unilateral disease process, with Doppler ultrasound required to assess for renal artery stenosis as a potential cause. Although trials of renal artery stenting have been negative,[46,47] this guideline recommends a recommendation on when and how to investigate for renal artery stenosis. This is justified, as trials excluded patients among whom there was no uncertainty about the benefits of percutaneous transluminal renal angioplasty (PTRA).[46] More RCTs are needed to define more clearly which patients with renal artery stenosis could benefit from PTRA.[48,49]

Assessment of specific systemic conditions (e.g. amyloidosis or Fabry disease) should be considered in patients with unexplained HF as well as CKD, especially when they are relatively young.[50,51]

3.3. Screening for chronic kidney disease

Recommendation Table 3 — Recommendations for screening for chronic kidney disease (see Evidence Table 3)

Recommendations	Class[a]	Level[b]
Screening for CKD using eGFR and increased albuminuria is recommended in patients with CVD to enable adequate CVD and CKD risk prediction, to guide use of CVD and CKD risk-modifying treatment, for drug dosing considerations, and to allow timely nephrology referral.[4]	I	C

Continued

At least annual re-testing for eGFR is recommended in patients with diabetes or at high risk of worsening kidney function (e.g. presence of increased albuminuria or decreased eGFR) to detect CKD progression or re-classify CKD staging.	I	C
At least annual re-testing for albuminuria is recommended in patients with diabetes, hypertension, decreased eGFR, or haematuria on urine dipstick, or when presence or an increase in albuminuria would modify treatment, to re-classify CKD stage and optimize risk-modifying treatment.	I	C
Repeat measurement of eGFR and albuminuria within days to weeks is recommended in patients with newly detected unexpected decreased eGFR and/or increased albuminuria to allow a timely diagnosis of AKI for diagnostic evaluation and management.[9]	I	C
Re-testing for decreased eGFR more often should be considered for patients at risk of AKI and for patients using renally excreted drugs with a narrow therapeutic window to allow timely identification of AKI or progressive CKD and for drug dose adjustment.	IIa	C

AKI, acute kidney injury; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.
[a]Class of recommendation.
[b]Level of evidence.

Screening for CKD aims to improve early detection, risk stratification, and timely intervention. Initial screening should include both eGFR and albuminuria measurements and should be performed in all patients with newly established CVD, including hypertension, CAD, HF, PAD, and stroke. Because of improved sensitivity and specificity, quantitative measurement of uACR is preferred, but a qualitative dipstick test may be used as initial screening in lower resource settings. Ideally, chronicity of any decreased eGFR <60 mL/min/1.73 m^2 or an uACR ≥3 mg/mmol (≥30 mg/g) should be confirmed. When abnormalities are newly detected, severe, and unexpected, it is advised to re-test promptly (within days), to allow a timely diagnosis of AKI, which usually requires more urgent evaluation and management (*Figure 4*).

Guidance on frequency of CKD re-screening is based on consensus opinion.[9,52] Annual re-screening for increased albuminuria should especially be considered when its presence (or its change) would modify risk-modifying treatment (*Section 5*). The frequency of re-screening should be individualized based on the patient's risk profile and the progression of underlying CVD. For lower-risk individuals, re-screening every 2–3 years may be sufficient.

3.4. Drug dosing in chronic kidney disease

Recommendation Table 4 — Recommendations for drug dosing in chronic kidney disease (see Evidence Table 4)

Recommendations	Class[a]	Level[b]
Assessment of the benefits vs potential harms when prescribing medications which are potentially nephrotoxic is recommended in patients with CKD with the aim of minimizing the risk of AKI or accelerating CKD progression.[53]	I	C
Monitoring eGFR, relevant electrolytes, QT interval on electrocardiography (when indicated), and therapeutic medication levels (where possible) is recommended in patients with CKD who are receiving medications which are renally excreted and have narrow therapeutic windows or potential adverse effects when eGFR is decreased, with the aim of preventing adverse drug reactions and ensuring safe and effective treatment.	I	C

AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.
[a]Class of recommendation.
[b]Level of evidence.

Adjusting doses of renally excreted drugs based on the level of GFR to avoid toxicity and to ensure therapeutic efficacy is recommended in patients with CKD.[54–57] CKD is a risk factor for QT prolongation; therefore, electrocardiography monitoring is particularly important when prescribed QT-prolonging drugs.[58,59] This guideline encourages use of Summary of Product Characteristics (or regional equivalents) and relevant drug formularies as appropriate resources for drug dose adjustment information. It should be emphasized that the eGFR value calculated by clinical chemistry laboratories is expressed indexed to 1.73 m^2 of BSA to mL/min/1.73 m^2. Where BSA is notably higher or much lower than this 1.73 m^2, absolute GFR should be calculated by correcting for estimated BSA. For example, use a suitable BSA estimating formula and then multiply eGFR by a factor of BSA/1.73.[60] Such adjustment is most important when using renally excreted drugs with a narrow therapeutic window (see *Section 3.1.2* for details of eGFR considerations).[61] Where precise quantification is required (e.g. chemotherapy prescription), GFR can be directly measured using clearance of exogenous markers (e.g. iohexol, iothalamate, ^{51}Cr-EDTA, and ^{99}mTc-DTPA).[9] Creatinine clearance (e.g. estimated by Cockcroft-Gault or 24 h urine collections) are alternative methods to estimate absolute GFR, but are vulnerable to overestimating GFR due to renal tubular creatinine secretion (especially at low GFR).

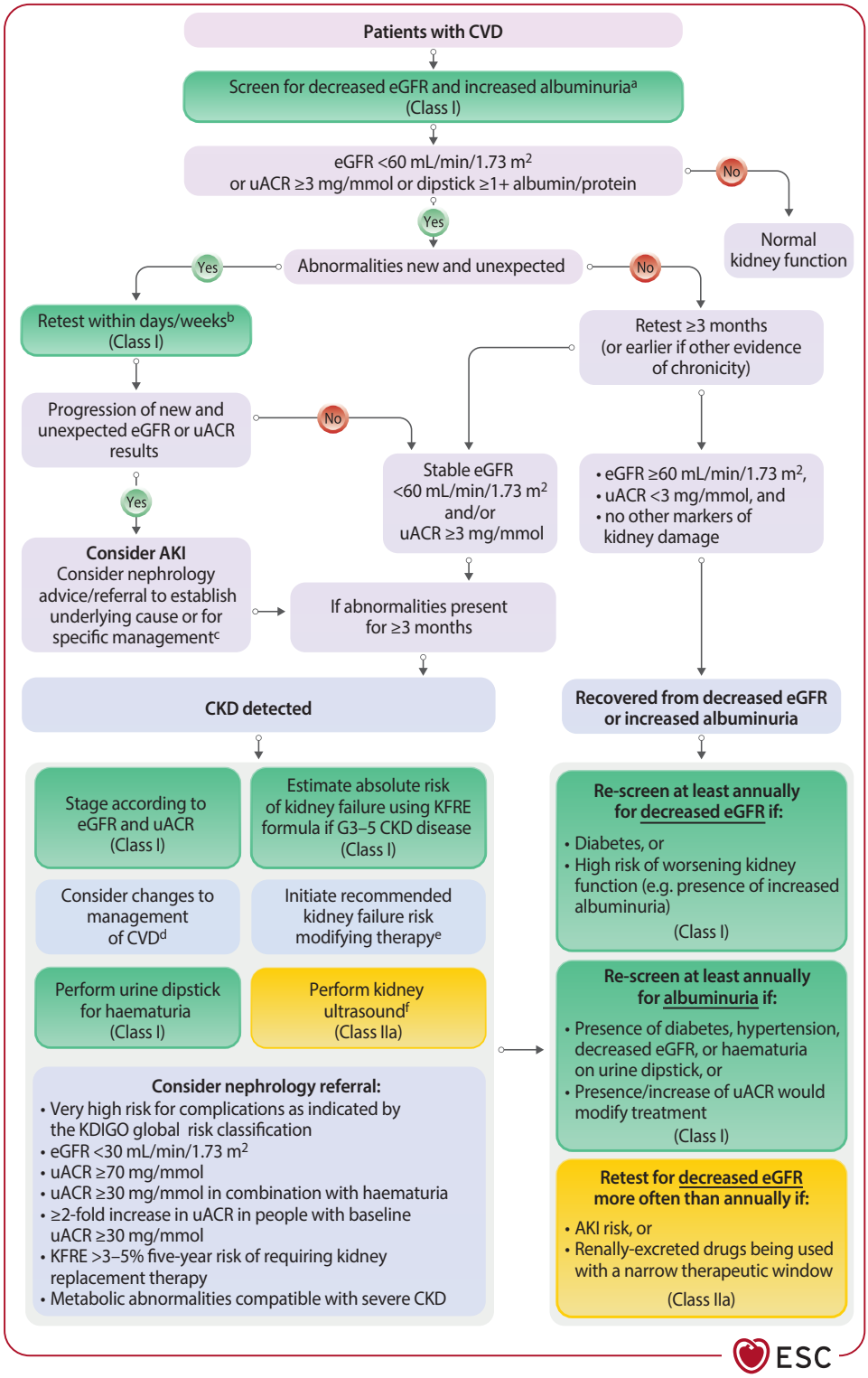

Figure 4 Screening algorithm for diagnosis and staging of chronic kidney disease in cardiovascular disease. AKI, acute kidney injury; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; KFRE, Kidney Failure Risk Equation; uACR, urine albumin-to-creatinine ratio. Multiply uACR in mg/mmol by 10 to approximately convert uACR to mg/g. 300 mg/g equates to approximately 300 mg/24 h. [a]Screening ideally by assessing uACR, but by dipstick as initial test dependent on local resource. [b]Dependent on the severity of findings. [c]Nephrology referral for suspected glomerular disease, unknown cause of AKI, high risk of need for kidney replacement therapy, kidney transplant recipients (urology referral for obstructive disease). [d]See *Sections 6–10* for management of CVD. [e]See *Section 5.5* and *Figure 7* for management of kidney failure risk. [f]Newly diagnosed CKD and when unexplained sudden decrease in eGFR

3.5. Assessing kidney failure risk in chronic kidney disease

Recommendation Table 5 — Recommendations for assessing kidney failure risk in chronic kidney disease (see Evidence Table 5)

Recommendations	Class[a]	Level[b]
Using a validated Kidney Failure Risk Equation (KFRE), is recommended in patients with CKD categories G3–5 when assessing an individual's absolute risk for progression to require KRT to allow timely referral for nephrology evaluation and management.[25,26]	I	A

CKD, chronic kidney disease; KFRE, Kidney Failure Risk Equation; KRT, kidney replacement therapy. A web-based calculator suitable for use in Europe is available: https://kidneyfailurerisk.co.uk/
[a]Class of recommendation.
[b]Level of evidence.

In patients with CKD, it is recommended to regularly assess an individual's risk of kidney failure using validated risk-prediction tools and clinical markers to guide management decisions and timing of interventions. Predicting risk of kidney failure is particularly useful for:

Risk stratification: Identifying high-risk patients who may benefit from early referral to nephrology, closer monitoring, or more intensive interventions (including more rapid introduction and dose escalation of risk-modifying therapy).

Clinical decision-making: Guiding decisions about timing for interventions such as dialysis preparation or kidney transplant evaluation.

Patient counselling (see *Section 14*).

Risk of kidney failure in patients with CKD can be estimated by different approaches (*Figure 3*):

1. Simple population approach: the KDIGO global risk classification system

The KDIGO CKD classification and heatmap (see *Section 3.1*) subdivides people with CKD according to three global classes of *relative* risk. People with moderately increased risk (yellow) have a 3–20-fold increased risk of developing kidney failure, whereas people at high risk (orange) and very high risk (red) have a 20–70-fold and >70-fold increased risk, respectively. This risk is independent of age and sex.[9] Very high risk is one accepted referral criterion for nephrology evaluation and management.[4]

2. Individualized approach: use a validated absolute risk prediction tool, such as the Kidney Failure Risk Equation (KFRE)

At CKD stages G3–5, the alternative is to use equations incorporating eGFR, uACR, age, and sex, to estimate an individual's *absolute* risk of needing treatment for kidney failure (i.e. maintenance dialysis or transplantation).[62,63] A KFRE estimate of >3%–5% 5-year risk is the proposed referral criterion for nephrology evaluation and management (https://kidneyfailurerisk.co.uk/).[64] The KDIGO CKD classification allows for simple risk stratification to guide earlier prevention and intervention, whereas the KFRE is preferable to ensure timely referral of patients to start preparations for KRT.

3.6. Impact of cardiovascular disease on chronic kidney disease

Incident CVD is strongly associated with increased risk of kidney failure. A pooled analysis of observational cohort studies that included data from ∼25 million people showed that the risk of kidney failure for which KRT is started is highest in the first 3 months after presentation with CVD, being 2–4-fold higher after incident CAD, stroke, or AF, and even 45-fold higher after incident HF (*Figure 5*).[65] Beyond this initial period, CVD remains a significant contributor to the development and progression of CKD.

3.7. Other complications of chronic kidney disease

Decreased GFR leads to various metabolic abnormalities that can contribute to increased CVD risk. CVD risk increases in early CKD, but measurable abnormalities like anaemia, hyperphosphataemia, hyperparathyroidism, and acidosis usually do not occur until GFR decreases to <30 mL/min/1.73 m^2.[9] Hyperkalaemia is also more common in CKD.[66] This section outlines the major metabolic abnormalities seen in CKD, focusing on their impact on cardiovascular health and highlighting when to seek specialist advice. More detailed information can be found in specific nephrology guidelines developed by KDIGO.[9]

3.7.1. Electrolyte abnormalities

3.7.1.1. Potassium

Patients with CKD are at an increased risk of hyperkalaemia due to reduced urinary potassium excretion.[66,67] Metabolic acidosis may further increase serum potassium due to intra- and extracellular shifts.[9] Severe hyperkalaemia can result in life-threatening arrhythmias, particularly when serum potassium is >6.5 mmol/L.[67] Decisions on management should be individualized and take account of changes from an individual's usual serum potassium levels. A conservative threshold for action is recurrent serum potassium values >5.5 mmol/L. Hyperkalaemia should trigger review of co-medication, correcting any metabolic acidosis, improving glycaemic control, and then considering need for loop diuretics and potassium-restricted diets. Higher thresholds for action (e.g. >5.7 mmol/L) are often justified in CKD due to chronic hyperkalaemia, aiming to avoid serum potassium levels of 6.0 mmol/L or above. Modern potassium binders (e.g. patiromer, sodium zirconium cyclosilicate) are available for refractory hyperkalaemia.[9,68] Importantly, insulin-dextrose infusions do not result in any potassium excretion, so severe and refractory hyperkalaemia in patients with severely decreased GFR or low urine output may need emergent dialysis.[67]

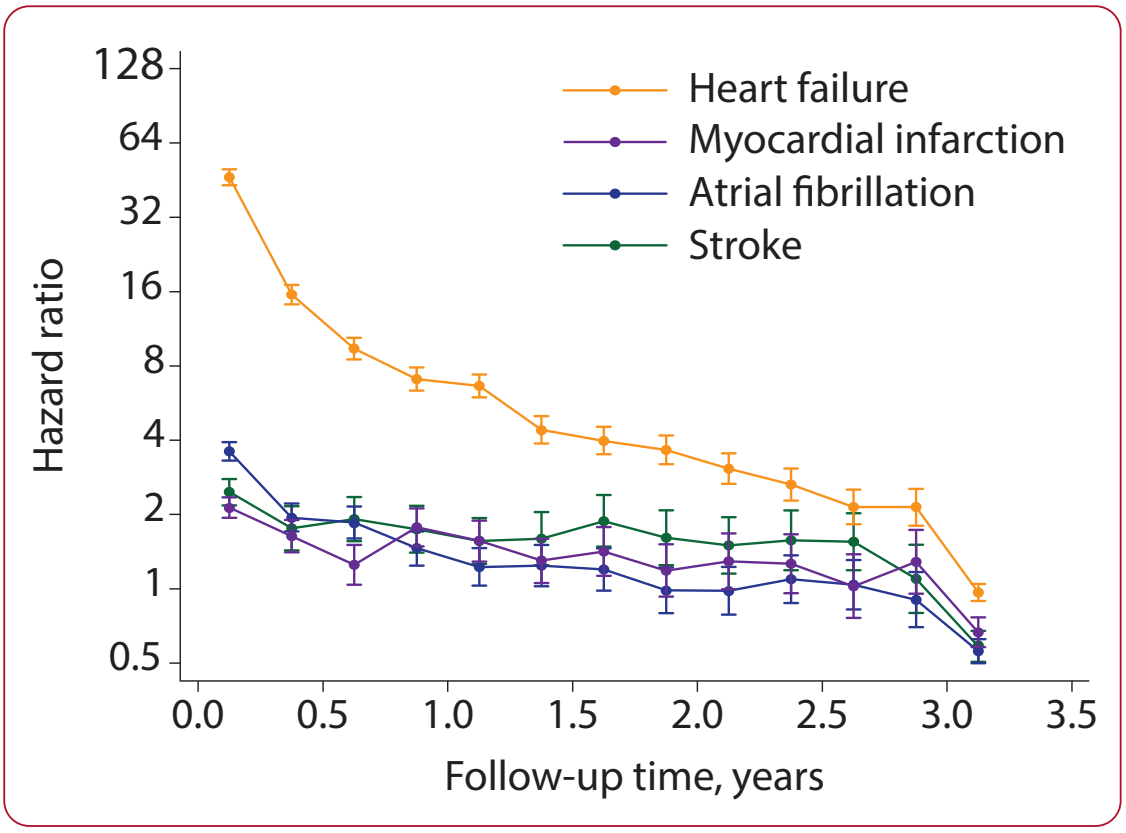

Figure 5 Risk of kidney replacement therapy by time since incident cardiovascular disease. CVD, cardiovascular disease; Adjusted hazard ratios and 95% confidence intervals are associations between different types of incident CVD with subsequent risk of KRT. Hazard ratios are adjusted for cardiovascular risk factors and CVD subtypes vs participants without the relevant CVD. Reproduced from Mark *et al.*, 2023, *EHJ* with permission[65]

3.7.2. Anaemia and iron

Renal anaemia begins to develop at moderate-to-severely decreased GFR.[66] It is primarily caused by a deficiency in renal erythropoietin, leading to normocytic anaemia with a low reticulocyte count. Additionally, CKD often results in absolute or functional iron deficiency due to impaired iron absorption, chronic inflammation, and blood loss during haemodialysis. The management of anaemia in CKD typically involves the use of erythropoiesis-stimulating agents (ESAs) to increase red blood cell production after oral or intravenous iron supplementation to support erythropoiesis. Although observational studies showed a strong continuous association between the level of anaemia and cardiovascular outcomes, RCTs did not find improvement in cardiovascular event rates or mortality with full anaemia correction with ESAs,[69,70] while stroke risk appears increased.[71] Nephrologists therefore treat renal anaemia to tight haemoglobin targets to reduce the need for blood transfusions and improve symptoms of anaemia safely. There are differences between guidelines, but one approach is to initiate ESA therapy when haemoglobin concentration falls below 9.0–10.0 g/dL, with a target not to correct beyond 11.5 g/dL. The range allows for individualized thresholds (see *Section 7.4* for recommendation statement encouraging avoidance of full correction of anaemia). In contrast, oral iron may be encouraged earlier, e.g. when haemoglobin falls below 13 g/dL in men and below 12 g/dL in women. Iron supplementation in patients with CKD not on dialysis is reasonable when ferritin is <100 µg/L and transferrin saturation (TSAT) <40%, or ferritin 100–300 µg/L with TSAT <25% (see also *Section 12.2* and in a dedicated KDIGO guideline[72]).

3.7.3. Chronic kidney disease-related mineral and bone disorder

Decreased GFR contributes to disturbances in mineral metabolism, including elevated phosphate levels and abnormalities in calcium and parathyroid hormone (PTH) regulation.[66] These disorders are collectively referred to as CKD-related mineral and bone disorder (CKD-MBD).[73,74] Hyperphosphataemia generally appears in severe CKD. It contributes to endothelial dysfunction, and phosphate precipitates together with calcium, accelerating vascular and valve calcification.[74] Decreased GFR is also associated with decreased renal activation of vitamin D, and eventually low serum calcium levels. These processes result in homeostatic increases in PTH levels, promoting stored calcium release from the bones. When low GFR persists, PTH production can become autonomous (tertiary hyperparathyroidism).[75]

Although not definitely demonstrated to modify CVD risk in RCTs, hyperphosphataemia is intensively managed by nephrology services by dietary phosphate restriction and the use of phosphate binders.[73,76] Additionally, vitamin D analogues or calcimimetics (e.g. cinacalcet) can be used to control secondary hyperparathyroidism.[9] Nephrology specialist advice should be sought in managing a raised serum phosphate (e.g. when >1.7 mmol/L).

3.7.4. Acid–base imbalance: metabolic acidosis

Metabolic acidosis is a common finding in patients with CKD when the kidneys' ability to excrete hydrogen ions and regenerate bicarbonate diminishes. Metabolic acidosis may have several adverse effects on cardiovascular health, including exacerbating phosphate retention that contributes to the precipitation of calcium–phosphate complexes in the vasculature. Acidosis may also negatively affect myocardial function, including reducing contractility.[9] The management of metabolic acidosis typically involves oral alkali therapy with sodium bicarbonate[77] despite limited evidence from RCTs of definitive clinical benefit. Oral alkali therapy is considered only when serum bicarbonate decreases <18 mmol/L, with monitoring for adverse effects on blood pressure and fluid balance, particularly in severe CKD or HF.[9]

4. Patterns of cardiovascular diseases in chronic kidney disease

4.1. Epidemiology of different cardiovascular diseases in chronic kidney disease

4.1.1. Primary cardiovascular events

In a meta-analysis of 114 global cohorts including ~28 million individuals, an eGFR <60 mL/min/1.73 m^2 and/or albuminuria were independently associated with higher risks of myocardial infarction (MI), stroke, HF, AF, PAD, and cardiovascular mortality compared with individuals without CKD (*Figure 3* and *Figure 6*).[4] Risk progressively increases at lower eGFR or at higher levels of albuminuria, with highest risks among those with severely decreased eGFR (<30 mL/min/1.73 m^2) and severely increased levels of albuminuria [A3 levels >30 mg/mmol (>300 mg/g)].[4] Absolute risk of CVD varies substantially by patient characteristics (e.g. age), but the relative risk increases resulting from decreased eGFR and increased albuminuria are qualitatively similar irrespective of age, sex, race, and diabetes status, supporting the homogeneous KDIGO heatmap approach in stratifying risk for CVD by CKD stage.[4,78,79] Beyond assessments at single time points, and even among people without pre-existing CKD, steeper eGFR decline and/or greater increases in albuminuria over time are associated with higher risks of CVD.[80–83]

4.1.2. Recurrent cardiovascular events

Following a first cardiovascular event, patients with CKD are more likely to have a subsequent cardiovascular event than individuals without CKD.[84,85] Due to the high likelihood of primary and recurrent CVD among patients with CKD, it is important to assess opportunistically for symptoms and signs of established ASCVD, HF, arrhythmias, and valvular heart disease at each clinical encounter to achieve early diagnosis and management.

Recommendation Table 6 — Recommendation for cardiovascular disease assessment in chronic kidney disease (see Evidence Table 6)

Recommendations	Class[a]	Level[b]
Assessment for symptoms and signs of hypertension, ASCVD, HF, arrhythmias, and valvular heart disease is recommended for patients with CKD at each clinical encounter to help achieve early diagnosis and management of these cardiovascular diseases.[4,80]	I	C

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; HF, heart failure.
[a]Class of recommendation.
[b]Level of evidence.

4.2. Assessing cardiovascular risk in chronic kidney disease

Traditional risk factors for CVD including older age, hypertension, dyslipidaemia, smoking, and diabetes are included in risk-prediction tools. Additional risk is conferred by obesity, physical inactivity, psychosocial factors, and family history (referred to as risk modifiers in recent ESC guidelines).[86] These risk factors are useful for predicting CVD risk among patients with CKD.[4,27,28] However, the combination of eGFR and albuminuria outperforms most other single predictors of CVD, particularly among those with pre-existing diabetes or hypertension.[27] In the absence of other major risk factors for CVD, and where accurate individual risk estimation is not required, eGFR and albuminuria criteria using KDIGO heatmap approaches can be used as simple risk-stratification tools to identify those at relatively increased risk. KDIGO high or very high risk categories identify patients who should have intensive active risk factor management and follow-up (*Figure 3*).[28]

4.2.1. Cardiovascular disease risk-estimating equations

Although not mandatory when assessing patients with CKD, accurately estimating an individual's absolute cardiovascular risk can guide the intensity of therapy, improve risk stratification following therapy, and guide monitoring frequency and screening for *de novo* and/or subclinical disease (*Figure 3*). It may be particularly useful to quantify risk more precisely in patients who are in the moderate KDIGO risk category. The ESC has developed and validated several Systematic COronary Risk Evaluation-2 (SCORE2) tools to estimate absolute 10-year fatal and non-fatal CVD risk in individuals without pre-existing CVD. *Table 4* summarizes tools that incorporate eGFR within risk assessments.

4.2.1.1. Individuals without type 2 diabetes and without atherosclerotic cardiovascular disease

SCORE2 and SCORE2 Older Persons (SCORE2-OP) were developed (45 European cohorts; 677 684 individuals) and validated

(25 European cohorts; 1 133 181 individuals) using sex-stratified models with adjustment for competing risks and relevant covariates.[87] They underestimate CVD risk in patients with CKD.[28,29] Risk stratification for ASCVD and cardiovascular mortality can be quantitatively enhanced by incorporating eGFR and albuminuria into these cardiovascular risk-prediction tools.[28] The validated SCORE2 CKD Add-On (https://ckdpcrisk.org/ckdpatchscore/) identifies the additional risk associated with eGFR and albuminuria categories (*Figure 6*). See Supplementary data online for Evidence Tables that accompany *Recommendation Table 7* for details of the validation of each risk-prediction tool. In the 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice, individuals with moderate or severe CKD were considered to be at high and very high CVD risk, respectively, and SCORE2 or SCORE2-OP estimations were recommended for use in mild CKD (i.e. eGFR 45–59 mL/min/1.73 m^2 without albuminuria). This helps optimize primary prevention strategies. More precise estimation of absolute risk may be required. In patients with CKD without ASCVD or type 2 diabetes, the CKD Add-On is recommended as it improves classification of CVD risk estimated using SCORE2/SCORE2-OP, re-classifying around 14% of individuals upward into a higher risk category, and 15% downward into a lower risk category.[27–29]

4.2.1.2. Individuals with type 2 diabetes without atherosclerotic cardiovascular disease

Among patients with type 2 diabetes without symptomatic ASCVD, the SCORE2-Diabetes risk score is recommended in patients with CKD to estimate 10-year ASCVD risk.[88] SCORE2-Diabetes was developed using a similar methodology to SCORE2 and SCORE2-OP. Compared with SCORE2, SCORE2-Diabetes improved risk discrimination in these populations with diabetes. A key limitation is the lack of albuminuria in this risk score due to suboptimal availability in the development and validation cohorts. In some individuals, and particularly those with A3 levels, risk is likely higher than predicted by the tool, and clinical judgment and an individualized approach is required.

4.2.1.3. Individuals with pre-existing cardiovascular disease

Individuals with pre-existing CVD are at high risk of recurrent cardiovascular events, but this risk can still vary widely between individuals from low (<10% 10-year risk) to extremely high (>40%) risk.[89] If an accurate estimation of risk is required, the use of the Secondary Manifestations of ARTerial disease-2 (SMART2) risk score is recommended in patients who have CKD and pre-existing atherosclerotic vascular disease to estimate the risk of recurrent vascular events.[89,90] Baseline eGFR was well preserved in the original study (median 77 mL/min/1.73 m^2 in the derivation cohort), but the score performs well in CKD.[90]

4.2.1.4. Individuals at risk of heart failure

Prediction of non-fatal HF was not included in earlier SCORE tools. SCORE2-HF[91] and SMART2-HF[92] can be used to predict incident HF in individuals without and with pre-existing ASCVD, respectively. Both scores incorporate eGFR into risk-prediction algorithms but were developed in populations with generally preserved kidney function. Albuminuria was not included due to suboptimal availability in development and validation cohorts. An evidence base for when knowledge of ASCVD and HF risk modifies management and improves outcomes is now required.[93]

Recommendation Table 7 — Recommendations for assessing cardiovascular risk in chronic kidney disease (see Evidence Table 7)

Recommendations	Class[a]	Level[b]
Where available, risk scores incorporating eGFR and albuminuria are recommended for cardiovascular risk assessment in patients with CKD to provide an accurate estimate.[27,28]	I	B
Patients with severe CKD (eGFR <30 mL/min/1.73 m^2 with any level of albuminuria; eGFR 30–44 mL/min/1.73 m^2 and uACR 3–30 mg/mmol; uACR >30 mg/mmol with any level of eGFR) are recommended to be considered at relatively very high CVD risk to optimize implementation of primary prevention strategies.[4,27,28]	I	B
Patients with moderate CKD (eGFR 30–44 mL/min/1.73 m^2 and uACR <3 mg/mmol; eGFR 45–59 mL/min/1.73 m^2 and uACR 3–30 mg/mmol) without other major risk factors are recommended to be considered at relatively high CVD risk to optimize implementation of primary prevention strategies.[4,27,28]	I	B
When an accurate estimation of an individual's absolute risk is required, the use of the SCORE2 (aged <70 years) or SCORE2-OP (age ≥70 years) risk calculators with the CKD Add-On is recommended in patients who have CKD without type 2 diabetes and without symptomatic ASCVD to estimate 10-year ASCVD risk.[27–29]	I	B
When an accurate estimation of an individual's absolute risk is required, the use of the SCORE2-Diabetes risk score is recommended in patients with both CKD and type 2 diabetes but without symptomatic ASCVD to estimate 10-year ASCVD risk.[27,28,88]	I	B
When an accurate estimation of an individual's absolute risk is required, the use of the SMART2 risk score is recommended in patients who have CKD and pre-existing atherosclerotic vascular disease to estimate the risk of recurrent vascular events.[89]	I	B

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; SCORE2, Systematic COronary Risk Evaluation 2; SCORE2-OP, Systematic COronary Risk Evaluation 2-Older Persons; SMART2, Secondary Manifestations of ARTerial disease; uACR, urine albumin-to-creatinine ratio.
uACR 3 and 30 mg/mmol are approximately equivalent to 30 and 300 mg/g, respectively.
[a]Class of recommendation.
[b]Level of evidence.

Table 4 Scores for estimating risk of cardiovascular disease incorporating estimated glomerular filtration rate

Risk score	Diabetes status	Age criteria	Outcome
Without pre-existing ASCVD			
SCORE2 + CKD Add-On [27–29]	Without type 2 diabetes	<70 years	10-year risk of ASCVD
SCORE2-OP + CKD Add-On [27–29]	Without type 2 diabetes	≥70 years	10-year risk of ASCVD
SCORE2-Diabetes[88]	With type 2 diabetes	≥40 years	10-year risk of ASCVD
SCORE2-HF[91]	Any diabetes status	≥40 years	Incident HF
With pre-existing ASCVD and without HF			
SMART2[89]	Any diabetes status	≥40 years	Recurrent vascular events
SMART2-HF[92]	Any diabetes status	≥40 years	Incident HF
With pre-existing HFpEF			
LIFE-Preserved[94]	Any diabetes status	≥40 years	Any-year or lifetime risk of HF hospitalization or CV death

Scores not for use in patients with kidney failure. Risk of ASCVD and HF from separate equations should not be summed as combined estimates could be inflated. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; SCORE2, Systematic COronary Risk Evaluation 2; SCORE2-OP, Systematic COronary Risk Evaluation 2-Older Persons; SMART2, Secondary Manifestations of ARTerial disease (trial). Only scores using the CKD Add-On incorporate albuminuria.

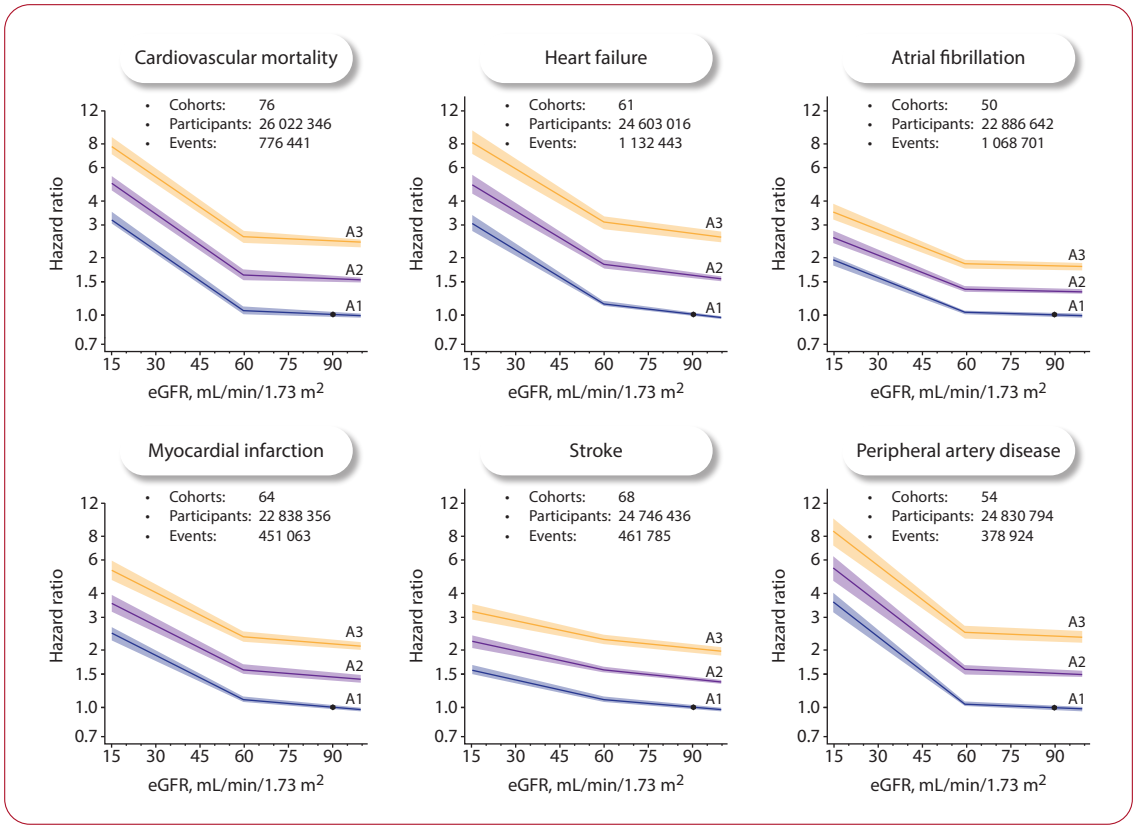

Figure 6 Associations between estimated glomerular filtration rate and albuminuria categories with subsequent risk of cardiovascular disease. eGFR, estimated glomerular filtration rate; uACR, urinary albumin-to-creatinine ratio. A1, A2, and A3 are represented by the median level of albuminuria within A-stage in the NHANES cohort: uACR 0.6 mg/mmol, 6 mg/mmol, 70 mg/mmol. Models are linear splines with a knot at eGFR 60 mL/min/1.73 m^2 and linear on natural log transformed uACR. Reference at eGFR 90 mL/min/1.73 m^2 and uACR 0.6 mg/mmol. Hazard ratios represent a specific eGFR value and uACR value. Models were adjusted for age, sex, cardiovascular risk factors, and comorbidities. The dataset was based on studies from *JAMA* 2023 Oct 3;330(13):1266–77. To convert uACR approximately to mg/g, multiple mg/mmol by 10.[4] (Figure adapted with permission from the CKD Prognosis Consortium (CKD-PC). (copyright: www.ckdpc.org/main-figures)

5. Kidney failure and cardiovascular risk reduction in chronic kidney disease

5.1. Lifestyle factors in chronic kidney disease

5.1.1. Smoking cessation

Observational studies have highlighted the harmful cardiovascular effects associated with tobacco smoking in CKD.[95,96] This guideline aligns with the previous ESC Guidelines,[32,86,97] and recommends people with CKD stop smoking tobacco to reduce cardiovascular risk and mortality.[98–100] Intensive smoking cessation programmes including combining nicotine-replacement products with behavioural interventions are superior to brief advice in supporting smoking abstinence.[101] Note that decreased GFR necessitates dose reduction of the partial nicotine agonist varenicline.[102,103] Similar to tobacco products (smoked or heated), there have been reports of lung disease and risk of CVD with tobacco-free e-cigarettes in non-CKD populations.

5.1.2. Weight management, physical activity, and diet

Obesity is an independent risk factor for CVD and progression of CKD. Current evidence suggests that intentional weight loss improves blood pressure and lipid profile in patients with CKD.[104] In a secondary analysis of the Look-AHEAD (Action for HEAlth in Diabetes) trial, a long-term intensive weight loss intervention was shown to reduce the risk of worsening CKD category in overweight or obese patients with type 2 diabetes.[105] Clinicians should recommend intentional weight loss by increasing physical activity and appropriate dietary modifications in patients who are overweight or obese [i.e. body mass index (BMI) ≥25 kg/m^2, or ≥23 kg/m^2 in Asian populations], particularly in those with eGFR ≥30 mL/min/1.73 m^2.[9] Weight loss in obese individuals awaiting kidney transplantation is important, as high BMI (≥30 kg/m^2) has been associated with increased surgical peri-operative risk, new-onset diabetes after transplantation, and lower patient and graft survival compared with patients with lower BMI.[106,107]

Despite well-known associations between physical inactivity and cardiovascular risk,[108–113] there are no RCTs examining the impact of different exercise programmes with adequate power to assess effects on clinical CVD outcomes in people with CKD.[114–116] Until more data on individualized exercise advice and associated improvement of cardiovascular outcomes in patients with CKD are available, the principles of physical activity advice and muscle-strengthening activity in CKD should be orientated towards the general recommendations of current ESC Guidelines on cardiovascular disease prevention and exercise[86,117,118] and the World Health Organization.[119] Advice to patients should be tailored to their severity of CVD and any physical limitations.

Controlling sodium intake is important in patients with CKD who are commonly salt-sensitive and have reduced homeostatic regulation of blood pressure and extracellular fluid status. In RCTs, restricted sodium intake led to lower blood pressure, lower albuminuria, and improved cardiovascular outcomes.[120–122] Clinical studies have also demonstrated that restricting dietary sodium might enhance the effectiveness of diuretics in CKD.[123] A recent meta-analysis of cohorts and RCTs suggested that lower dietary sodium intake reduces the risk of composite kidney outcomes.[124] In a subgroup analysis in patients with eGFR >30 mL/min/1.73 m^2, lower sodium intake was associated with a lower risk of cardiovascular events.[124] Dietary modification can be challenging for patients, nevertheless, given the evidence that dietary sodium restriction improves blood pressure and albuminuria, it is reasonable to recommend restriction to <2 g sodium per day (equivalent to <5 g sodium chloride) to people with CKD alongside a diet that emphasizes vegetables, plus pharmacological strategies to reduce risk of kidney failure and cardiovascular outcomes.[120] Better RCT data on the safety of potassium-based salt substitutes would be valuable in CKD, due to risk of hyperkalaemia.[125]

Recommendation Table 8 — Recommendations for lifestyle factors in chronic kidney disease (see Evidence Table 8)

Recommendations	Class[a]	Level[b]
Smoking cessation, supportive care, and referral to providers and programmes for smoking cessation are recommended in patients with CKD who smoke tobacco, to reduce the risk of cardiovascular events and mortality.[98–101]	I	B1
An individualized diet with low sodium intake (<2 g sodium per day, equivalent to <5 g sodium chloride), and high intake of vegetables is recommended in patients with CKD, to reduce blood pressure, albuminuria, and cardiovascular events, and slow CKD progression.[120–122,124]	I	B1
Weight loss through individualized lifestyle modification with or without weight loss medication is recommended in patients with CKD who are overweight or obese (BMI ≥25 kg/m^2) to achieve a BMI 18.5–25 kg/m^2 to reduce blood pressure, improve lipid profile, and reduce risk of worsening of CKD category.[104,105,126]	I	B2
Physical activity (e.g. ≥150 minutes of moderate-intensity physical activity throughout the week, where possible) is recommended in patients with CKD to reduce blood pressure and cardiovascular risk.[108,109,116]	I	B2

BMI, body mass index; CKD, chronic kidney disease.
[a]Class of recommendation.
[b]Level of evidence.

5.2. Blood pressure in chronic kidney disease

5.2.1. Blood pressure targets

In patients with CKD, elevated blood pressure is associated with increased risk of cardiovascular morbidity and mortality, and progression to kidney failure.[127–129] Regular serial measurements of blood pressure are recommended in all patients with CKD. Diagnosis and monitoring of elevated blood pressure in CKD should be based on ESC-recommended blood pressure measurement approaches. Out-of-office (home and/or ambulatory) blood pressure is recommended for diagnosis to identify

masked hypertension and elevated night-time blood pressure.[97,130–132] Such monitoring may also identify when office-based blood pressure measurement overestimates an individual's usual blood pressure (i.e. white-coat hypertension). Adults with moderate CKD are considered at high cardiovascular risk, and adults with severe CKD at very high cardiovascular risk (see *Section 4*).[97,130–132] A confirmed standardized office blood pressure ≥130/80 mmHg is therefore recommended to be considered elevated blood pressure necessitating lifestyle optimization and blood pressure-lowering medications to reduce cardiovascular risk in CKD.[97,130–132] This recommendation is supported by trials of intensive vs standard blood pressure lowering, which have demonstrated reduced risk of major adverse cardiovascular outcomes with intensive regimens. Although there are no clear benefits on incident CKD or risk of kidney failure,[133,134] meta-analyses have raised a hypothesis that, in the presence of proteinuria, intensive blood pressure-lowering therapy may reduce the risk of CKD progression.[135,136]

Interpreting RCT data on blood pressure targets in patients with CKD is complicated due to limited numbers of patients with CKD in the definitive trials and difference between trials on how blood pressure measurements were collected.[137] The 2021 KDIGO Guideline suggests that adults with elevated blood pressure and CKD should be treated to a target systolic blood pressure <120 mmHg, when tolerated, using a standardized office blood pressure measurement approach.[138] This recommendation was justified by the Systolic blood Pressure Intervention Trial (SPRINT) results, where automated readings may have been largely measured in unattended participants. This approach tends to lead to lower recordings than attended standardized blood pressure measurement.[139,140] SPRINT deliberately sought to include large numbers of patients with an eGFR 20–60 mL/min/1.73 m^2, and 28% of the trial population (*n/N* = 2645/9361) had CKD at recruitment.[141] The beneficial effect of intensive blood pressure lowering on cardiovascular outcomes in SPRINT was similar in participants with and without CKD. Intensive blood pressure lowering reduced the risk of incident albuminuria but did, however, increase the risk of a 30% decrease in eGFR to a value <60 mL/min/1.73 m^2 in participants without CKD (a finding replicated in the more recent ESPRIT trial).[142] This finding raises some uncertainty about the renal safety and efficacy of further lowering systolic blood pressure to <120 mmHg.[143] This effect may reflect the haemodynamic effects of the blood pressure-lowering treatments needed to achieve a lower blood pressure target.[144] Reassuringly, there was no difference in risk of dialysis or risk of kidney progression outcomes (defined by a ≥50% decline in eGFR from baseline) between the intensive and standard blood pressure target groups. Despite enriching the SPRINT population for patients with CKD, there were too few kidney outcomes to assess whether there were long-term benefits (or perhaps even harms) on progression to kidney failure.[145] Findings from SPRINT are generally consistent with systematic reviews and meta-analyses examining the effect of intensive blood pressure control in patients with CKD considered in isolation.[133,146–149] Based on the current evidence, it is recommended that systolic blood pressure should be targeted to 120–129 mmHg in patients with CKD and eGFR ≥30 mL/min/1.73 m^2, if tolerated. The 2024 ESC Guidelines for the management of elevated blood pressure and hypertension recommend out-of-office blood pressure measurement for ongoing management to quantify the effects of treatment and guide blood pressure-lowering medication titration (level of evidence B),[97] but the large trials of intensive blood pressure lowering were based on office-based measurements. If the KDIGO recommended target of ≤120 mmHg is followed instead, then out-of-office blood pressure measurements or the unattended office blood pressure measurement protocol implemented in the SPRINT trial should be considered to avoid risk of hypotension or kidney adverse events.[143] Below eGFR 30 mL/min/1.73 m^2, a Class I recommendation supporting this target is not possible in this guideline because such patients were not represented in SPRINT and there are limited other RCT data. Blood pressure targets for patients with eGFR <30 mL/min/1.73 m^2 should be individualized, with a systolic blood pressure target of 120–129 mmHg appearing reasonable for many such patients. Blood pressure targets for patients on dialysis are discussed in *Section 12* and after kidney transplantation in *Section 13*. Individuals' frailty, comorbidities, and tolerability should inform an individualized approach.

5.2.2. Pharmacotherapy and interventional management

Achieving blood pressure targets in CKD should prioritize use of interventions shown to reduce risk of CVD and/or kidney failure in populations with CKD, including inhibitors of the renin-angiotensin-aldosterone system (RAAS) and SGLT2 inhibitors, where indicated (see *Section 5.5* and *Figure 7*). Where additional blood pressure pharmacotherapy is required, the 2024 ESC Guidelines on the management of elevated blood pressure and hypertension and the 2023 ESH Guidelines on arterial hypertension provide guidance,[97,131,150] and encourage dihydropyridine calcium channel blocker (CCB) and/or diuretic therapy to be added. Thiazides/thiazide-like diuretics are generally preferred over loop diuretics if eGFR is ≥30 mL/min/1.73 m^2, and can augment the albuminuria-lowering effect of ACEI/ARB treatment.[151] Below this level, loop diuretics are generally preferred although thiazides/thiazide-like diuretics can still safely be used.[152,153] In patients not on finerenone with resistant hypertension and an eGFR ≥30 mL/min/1.73 m^2, spironolactone can be used where serum potassium allows. Beta-blockers and alpha-blockers can be prescribed although have not been tested in dedicated CKD trials.[131,150] Aldosterone synthase inhibitors are in development.[154]

Recommendation Table 9 — Recommendations for blood pressure management in chronic kidney disease (see Evidence Table 9)

Recommendations	Class[a]	Level[b]
Screening by attended standardized office BP measurement[c] is recommended in all patients with CKD for early identification and confirmation of elevated BP/hypertension.[128,129]	I	A

Continued

Intensified BP control by lifestyle optimization and BP-lowering medications is recommended in patients with CKD and eGFR ≥30 mL/min/1.73 m^2, who have confirmed standardized office BP ≥130/80 mmHg to reduce the risk of CVD.[127,147,155]	I	A
A systolic BP target of 120–129 mmHg, if tolerated, is recommended in patients with CKD and eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of CVD and reduce albuminuria.[127,132,133,143,146,156,157]	I	A
Performing out-of-office (i.e. ABPM or HBPM) is recommended in patients with CKD to identify white-coat hypertension, masked hypertension, or elevated night-time BP.[143,147,158–160]	I	C
Individualized BP targets are recommended in patients with eGFR <30 mL/min/1.73 m^2 to reduce risk of CVD.[146,161]	I	C

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HBPM, home blood pressure monitoring.
[a]Class of recommendation.
[b]Level of evidence.
[c]Attended standardized office-based BP measurements should be collected following the 2024 ESC Guidelines for the management of elevated blood pressure and hypertension.[97]

5.3. Dyslipidaemia in chronic kidney disease

5.3.1. Characteristics of chronic kidney disease-associated dyslipidaemia

Dyslipidaemia is common in CKD, generally progressing to be more atherogenic as GFR decreases. Reduced levels of high-density lipoprotein cholesterol (HDL-C) and higher levels of triglycerides are a feature. Low-density lipoprotein cholesterol (LDL-C) concentration often remains within the normal range but with an increased proportion of LDL particles, which are small and dense, and hence, potentially more atherogenic.[162–164] Lipid profiles in CKD can also vary by level of albuminuria (e.g. nephrotic syndrome), type of KRT, or use of immunosuppressant therapy.[165,166]

It is recommended to perform a baseline lipid panel, including total cholesterol, LDL-C, HDL-C, and triglycerides, in patients with newly identified CKD and in those on maintenance KRT to identify lipid abnormalities (including those that could require specialist referral or specific additional treatment), and allow risk prediction (*Section 4.2.1*).[86,167] In patients with high triglyceride levels, non-HDL-C or apolipoprotein B measurement (where available) should be considered, as LDL-C alone may not fully represent the atherogenic lipoprotein burden, which includes triglyceride-rich lipoproteins and their remnants.[168]

Elevated lipoprotein(a) levels are associated with increased risks of ASCVD and aortic stenosis.[169,170] While lipoprotein(a) levels are primarily genetically determined, levels appear to increase as GFR declines, in part due to reduced renal clearance.[171] Lipoprotein(a) assessment may be considered as part of baseline lipid evaluation. However, its addition to SCORE2 tools does not importantly improve risk prediction, and trials of interventions that substantially lower lipoprotein(a) are still ongoing.[172]

Re-assessment of lipid parameters may be considered after beginning or modifying lipid-lowering therapy if the results would alter management (e.g. in a patient with CKD and prior ASCVD where a specific LDL-C target is desirable). However, a 'fire-and-forget' strategy[173] after initiating appropriately intensive lipid-modification therapy (i.e. a regimen shown to be safe in CKD that maximizes absolute reductions in LDL-C) is justified in many patients with CKD without prior ASCVD as part of a low-cost and scalable population approach to ensure equitable and effective primary prevention for the tens of millions of people with CKD in Europe. Currently about half of patients with CKD categories G3–5 in large European countries is untreated, and when treated, intensive regimens are under-utilized.[86,167,174]

5.3.2. Pharmacotherapy

The relative risk reductions on major vascular events per 1.0 mmol/L lower LDL-C achieved with statin-based therapy are irrespective of baseline LDL-C,[175] and such treatment is low cost.[86,176] Patients with CKD are typically at moderate, high, or very high cardiovascular risk relative to the general population and therefore, to simplify implementation, a statin-based regimen (i.e. a statin alone or in combination with ezetimibe) is recommended in patients with CKD and eGFR 15–60 mL/min/1.73 m^2, irrespective of lipid levels, to reduce the risk of major atherosclerotic events.

Randomized controlled trial evidence in CKD is provided by the Study of Heart And Renal Protection (SHARP) trial, which randomized 9270 patients with CKD aged ≥40 years (including about one-third on dialysis at recruitment). It demonstrated a 17% relative risk reduction in major atherosclerotic events (defined as coronary death, non-fatal MI, non-haemorrhagic stroke, or arterial revascularization excluding dialysis access procedures) with simvastatin 20 mg plus ezetimibe 10 mg vs matching placebo.[177] Major trials involving patients with CKD have tested the following statin-based regimens: fluvastatin 40 mg (transplantation),[178] pravastatin 20–40 mg (CKD),[179,180] atorvastatin 20 mg (dialysis),[181] rosuvastatin 10–20 mg (dialysis),[182,183] and simvastatin 20 mg plus ezetimibe 10 mg (CKD and dialysis),[177] all of which were safe. On an individual basis, a high-intensity regimen (e.g. atorvastatin 40 mg plus ezetimibe 10 mg or rosuvastatin 40 mg) may be considered when there is a decision to target LDL-C <1.8 mmol/L (<70 mg/dL) (see *Section 7*). A meta-analysis of 26 lipid-lowering treatment clinical trials has demonstrated that the reduction in CVD risk is directly proportional to the achieved absolute decrease in LDL-C levels, irrespective of the specific therapy used.[175] In patients with CKD, the relative reductions in risk of major vascular events per mmol/L reduction in LDL-C appear to begin to attenuate as eGFR declines below ~30 mL/min/1.73 m^2; therefore, an intensive lipid-lowering treatment should be considered from the outset in patients with CKD to maximize the absolute reduction in LDL-C and hence maximize treatment benefit.[175,184]

The recommendation to offer lipid-lowering treatment at the first evidence of CKD (i.e. an eGFR of <60 mL/min/1.73 m^2) irrespective of age is justified, as CKD is a lifelong condition, and so offering statin-based regimens to young patients with

mild-to-moderately decreased eGFR (i.e. 45–60 mL/min/1.73 m^2) ensures maximal benefits from safe, low-cost, LDL-C-lowering regimens can be realized.

Kidney transplant recipients are at high CVD risk, and statin therapy is recommended to reduce major atherosclerotic cardiovascular events. ALERT (Assessment of LEscol in Renal Transplantation) is the only large, dedicated, placebo-controlled trial with lipid-lowering therapy in adult kidney transplant recipients ($n = 1787$). It reported effects on its primary major adverse cardiac event composite outcome, which were consistent with other trials, albeit statistically non-significant [relative risk 0.83, 95% confidence interval (CI) 0.64–1.06].[185,186] An extension of ALERT and meta-analysis including 3465 kidney transplant patients further supported the potential benefit of statins in reducing cardiovascular events in this population.[186,187] This is consistent with the totality of the evidence on use of statins in patients with CKD.[184] Statins and ezetimibe can be used in all doses with steroids, mycophenolate mofetil, and azathioprine.[188] Some caution is needed when using high-intensity doses in patients treated with tacrolimus or sirolimus, but there is no absolute contraindication. Risk of myopathy, however, could be unacceptably high with some statins or with high-dose regimens in patients receiving ciclosporin due to drug interactions. Suggested maximum daily doses when receiving ciclosporin are atorvastatin 10 mg, fluvastatin 40 mg, pravastatin 20 mg, and rosuvastatin 5 mg (avoid lovastatin, pitavastatin, and simvastatin).[189] Ciclosporin and tacrolimus exposure may slightly increase when ezetimibe is initiated.[188]

When to prescribe statins in dialysis-dependent patients remains uncertain. Dedicated trials did not demonstrate a significant reduction in cardiovascular events with atorvastatin or rosuvastatin in haemodialysis patients.[181,182] However, in SHARP, effects were consistent between patients on dialysis and those not on dialysis after accounting for between-subgroup differences in achieved LDL-C.[177,190] A definitive meta-analysis that unified outcome definitions found a statistical trend towards diminishing effects on major vascular events (major coronary event, coronary revascularization, or stroke) per 1.0 mmol/L lower LDL-C as eGFR decreased below 30 mL/min/1.73 m^2. This included no clear effect in patients who were dialysis dependent, when considered in isolation (relative risk 0.94, 99% CI 0.79–1.11).[184] Nevertheless, initiating statin-based regimens may still be reasonable in dialysis patients not on lipid-lowering therapy, especially if kidney transplant is a consideration, or if they have a history of ASCVD (those with prior MI or coronary revascularization were excluded from SHARP due to insufficient clinical equipoise).[167] This is further justified by the clear benefit of LDL-C lowering in the secondary prevention setting in general populations, and as the large CKD trials have demonstrated the safety of statins in patients with CKD with severely decreased GFR. Even small relative benefits among those at exceedingly high risk may be important.[185,186,190,191]

More recent lipid-lowering agents such as bempedoic acid and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, such as monoclonal antibodies (evolocumab and alirocumab) and small interfering RNAs (inclisiran), are promising.[192] In the Further cardiovascular OUtcomes Research with PCSK9 Inhibition in subjects with Elevated Risk (FOURIER) trial, LDL-C lowering and relative clinical efficacy and safety of evolocumab vs placebo were consistent in secondary prevention across CKD groups, although patients with eGFR <20 mL/min/1.73 m^2 or a history of kidney transplantation were excluded.[193] See *Sections 7.1.2.2* and *7.4.1* for recommendations for use of PCSK9 inhibitors in patients with CKD with chronic coronary syndrome or history of ischaemic stroke.

Recommendation Table 10 — Recommendations for the management of dyslipidaemia in patients with chronic kidney disease (see Evidence Table 10)

Recommendations	Class[a]	Level[b]
Lipid evaluation		
Assessment of a baseline extended lipid panel, including total cholesterol, LDL-C, HDL-C, and triglycerides is recommended in patients with newly diagnosed CKD to identify lipid abnormalities and support cardiovascular risk prediction.[29]	I	C
Assessment of non-HDL cholesterol (or apolipoprotein B, if available) should be considered in people with CKD for cardiovascular risk prediction and in those with high triglycerides or diabetes as an alternative treatment goal to LDL-C.[164]	IIa	C
CKD without KRT		
Irrespective of lipid levels, an intensive statin-based regimen shown to be safe in CKD[c] is recommended in patients with CKD with an eGFR <60 mL/min/1.73 m^2 not on KRT to reduce risk of major atherosclerotic events.[184,194,195]	I	A
Kidney transplant recipients		
A statin-based regimen should be considered in kidney transplant recipients to reduce the risk of major atherosclerotic events.[185–187]	IIa	B1
CKD treated by dialysis		
Continuation of a statin-based regimen may be considered on dialysis initiation to ensure ongoing cardiovascular protection.	IIb	C
Initiating a statin-based regimen may be considered in patients on dialysis with a history of ASCVD to reduce the risk of recurrent atherosclerotic events.[177]	IIb	C
A statin-based regimen may be considered in patients on dialysis in whom kidney transplantation is planned to reduce the long-term risk of major atherosclerotic events.	IIb	C

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy (dialysis or kidney transplant); RCT, randomized controlled trial.
[a]Class of recommendation.
[b]Level of evidence.
[c]For example, a moderate- or high-intensity statin with or without ezetimibe (see *Section 5.3.2* for details on RCTs in different CKD populations).

5.4. Antithrombotic therapy in chronic kidney disease without symptomatic atherosclerotic cardiovascular disease

Randomized controlled trials mainly in general populations have shown that while antiplatelet therapy offers modest benefits in primary cardiovascular prevention, it also increases the risk of bleeding.[196] For patients with CKD (including those on KRT) in whom platelet dysfunction is common, the absolute cardiovascular benefit of antiplatelet therapy may be greater than in lower-risk patient populations, but the absolute bleeding risk may also be increased.[197,198,199]

Pilot RCTs in dedicated CKD populations compared 100 mg aspirin with placebo or usual care but were small and underpowered to assess effects on cardiovascular outcomes.[200,201] *Post hoc* analyses of larger non-CKD primary prevention trials in populations with diabetes or hypertension, and older populations, found that baseline risk of both cardiovascular outcomes and bleeding outcomes increased progressively with decreasing eGFR. The trials found that relative benefits of aspirin on cardiovascular outcomes were similar in patients with CKD compared with those without CKD,[202–205] with one trial raising a hypothesis that relative benefits may increase at eGFR <45 mL/min/1.73 m^2.[203,205] Meta-analyses of RCTs evaluating aspirin for use in patients with CKD without symptomatic ASCVD (i.e. primary prevention) concluded that a possible reduction in cardiovascular events is offset by an increased risk of major bleeding.[206–208] Data on hard clinical outcomes will need individual participant level meta-analysis combined with the Aspirin To Target Arterial events in Chronic Kidney disease (ATTACK) trial data (once reported) to establish which patients with CKD may receive net benefits on clinical outcomes in the context of primary CVD prevention.[209]

Recommendation Table 11 — Recommendations for the use of antiplatelet therapy in chronic kidney disease without symptomatic atherosclerotic cardiovascular disease (see Evidence Table 11)

Recommendations	Class[a]	Level[b]
Routine use of antiplatelet therapy is not recommended in patients with CKD with eGFR <60 mL/min/1.73 m^2 without symptomatic ASCVD because increased risk of major bleeding may outweigh any reduction in risk of cardiovascular events.[201,204,206,207]	III	B1

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.
[a]Class of recommendation.
[b]Level of evidence.

5.5. Specific pharmacological interventions to reduce cardiovascular and/or kidney failure risk in chronic kidney disease

Several drugs reduce the risk of progression of CKD to kidney failure and/or reduce cardiovascular risk in large trials that recruited patients with CKD. Early initiation and long-term continuation are recommended to prevent end-organ damage in patients at risk. Guidance on implementation is provided in *Section 5.5.5*. Recommendations in this section apply to patients with CKD not requiring KRT. Please refer to *Sections 12* and *13* for KRT considerations.

5.5.1. Angiotensin-converting enzyme inhibitors/angiotensin receptor blockers

Angiotensin-converting enzyme inhibitors or ARBs are recommended for most patients with CKD. One might consider not prescribing an ACEI/ARB in patients with normal/low blood pressure without albuminuria (unless there is another indication for use). Dedicated clinical outcome trials have shown that ACEI and ARB therapy both reduced the risk of kidney failure in patients with diabetes and overt nephropathy and prevented worsening of albuminuria in those with earlier diabetic kidney disease.[210–214] There is less evidence in patients with CKD without diabetes, although ACEI/ARB use is still recommended to lower blood pressure, albuminuria, and kidney failure risk based on trials showing that ACEIs reduced risk of kidney failure in patients with proteinuric non-diabetic CKD.[215–218] Trials with sufficiently large sample sizes and sufficiently long follow-up to assess the effects of ACEI/ARBs on the risk of kidney failure in patients with CKD without albuminuria have not been conducted. Our simple, practical, and broad ACEI/ARB recommendation therefore excludes patients without albuminuria with normal/low blood pressure who do not have HF.

Kidney protective effects of ACEI/ARBs are considered class effects due to consistent safety and efficacy results in RCTs. The combined use of both an ACEI and ARB in patients with CKD is not recommended, due to the increased risk of side effects (mainly biochemical changes: hyperkalaemia and AKI) and the lack of evidence of benefit on kidney, cardiovascular, or mortality outcomes in the reported trials that have been sufficiently large to exclude moderate benefits.[219–223] With potassium monitoring, ACEI/ARBs can safely be continued as kidney function declines to severe CKD and kidney failure to manage blood pressure and cardiovascular risk.[224,225]

5.5.2. Sodium glucose co-transporter 2 inhibitors

Several large trials have demonstrated the safety and efficacy of SGLT2 inhibitors in reducing the risk of kidney failure and CVD in patients with type 2 diabetes and increased cardiovascular risk, patients with HF, and specifically in CKD populations. Benefits of SGLT2 inhibition on CKD progression are apparent irrespective of diabetes status and irrespective of use of ACEI/ARBs.[226]

The Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE), Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trials, and The Study of Heart and Kidney Protection With Empagliflozin (EMPA-KIDNEY) demonstrated that canagliflozin, dapagliflozin, and empagliflozin, respectively, consistently reduced the risk of kidney disease progression (based on a ≥50% decline in eGFR) by ~40% overall, irrespective of each trial's mean baseline eGFR.[226–229] Based on these trials, initiating an SGLT2 inhibitor alongside ACEI/ARB is therefore recommended in patients with type 2 diabetes at the first clinical evidence of CKD.[226–229] In patients without

diabetes who have CKD, SGLT2 inhibition is recommended if eGFR is ≥20 mL/min/1.73 m^2 and uACR is ≥20 mg/mmol (≥200 mg/g).[226,228] Below this level of albuminuria in those without diabetes, an SGLT2 inhibitor should be considered if eGFR is 20–44 mL/min/1.73 m^2.[226] SGLT2 inhibitors are indicated down to an eGFR of 20 mL/min/1.73 m^2. EMPA-KIDNEY recruited patients with the lowest levels of eGFR down to 20 mL/min/1.73 m^2 at screening and included 254 patients with an eGFR 15–20 mL/min/1.73 m^2 at randomization. Exploratory analyses suggest preserved benefits of SGLT2 inhibitors even at these low levels of eGFR.[226,] Off-label initiation below this threshold is reasonable to consider given the safety of SGLT2 inhibition and since such patients are at the highest absolute risk of kidney failure.[230] Once initiated, therapy should be continued long term and reviewed around the time of needing KRT. For guidance in patients with a kidney transplant, see *Section 13*. The effects of SGLT2 inhibition at lower eGFR than studied in the reported trials and in patients requiring KRT are being assessed in the ongoing RENAL LIFECYCLE trial (NCT05374291).

Serial replication of findings suggests a class effect of SGLT2 inhibitors on both kidney disease progression and HF outcomes.[227,231] In support of a class effect, SGLT2 inhibitors have similar mechanisms of action, and meta-analyses standardizing outcomes demonstrate consistency across drugs, supported by biological plausibility. Use of any SGLT2 inhibitor in CKD across the spectrum in which treatment is indicated is therefore reasonable based on established safety profiles and broad CKD populations covered by licensed indications. Specific eGFR and uACR thresholds applied in these recommendations (see *Recommendation Table 12*) reflect trial eligibility criteria and are also supported by health economic analyses.[232,233]

No definitive recommendations can be given for use of SGLT2 inhibitors in patients without diabetes without HF who are at moderately increased relative risk of kidney failure and CVD based on an eGFR 45–59 mL/min/1.73 m^2 or uACR 3–19 mg/mmol (30–199 mg/g) as they have not been studied in large RCTs. Net benefits of SGLT2 inhibitors on risk of CKD progression, cardiovascular death, and HF complications and hospitalization may be predicted by extrapolating results of the existing RCTs. However, defining criteria for selecting which of these patients to treat is challenging without being able to estimate an individual's absolute risk for these outcomes. Such patients may still have significant lifetime absolute risk of kidney failure, as they are at moderate or high relative risk according to KDIGO heatmaps, and so early and long-term treatment could result in important benefits. Better relevant risk scores and more health economic analyses addressing this uncertainty are needed.

Individual trials lacked statistical power to precisely quantify the cardiovascular benefits of SGLT2 inhibition in CKD. However, pooled results and long-term follow-up studies demonstrate reductions in risk of cardiovascular death.[227,234] SGLT2 inhibitors reduced the risk of the composite outcome of hospitalizations for HF or cardiovascular death, largely due to reductions in deaths attributed to HF and SCD in patients with CKD.[231] Perhaps related to effects on HF hospitalizations, SGLT2 inhibitors have been shown to reduce body water.[235] Meta-analysis suggests SGLT2 inhibitors do not modify the risk of MI or stroke.[231] In addition to reducing kidney failure and cardiovascular risk, SGLT2 inhibitors reduce the risk of reported AKI by around one-quarter overall in the studied populations.[227,236]

It should be noted that their glucose-lowering effects are markedly attenuated at low eGFR and, therefore, SGLT2 inhibitors should not be expected to modify glycaemia importantly in patients with CKD, particularly when eGFR is <30 mL/min/1.73 m^2.[226] In patients with type 1 diabetes and CKD, there is insufficient RCT evidence to determine whether the absolute benefits of SGLT2 inhibitors are outweighed by the increased absolute risk of ketoacidosis, but their use (with ketone meters) safely slowed annual rate of eGFR decline in 68 participants in EMPA-KIDNEY.[230]

5.5.3. Mineralocorticoid receptor antagonists

5.5.3.1. Non-steroidal mineralocorticoid receptor antagonists

The non-steroidal MRA finerenone reduces the risk of kidney failure and CVD in patients with CKD, albuminuria, and type 2 diabetes. Efficacy and safety data were generated by two complementary placebo-controlled trials, Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) and Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) testing finerenone in about 13 000 patients with type 2 diabetes and different, overlapping stages of CKD, already on maximal tolerated ACEI/ARB.[237,238]

Both trials demonstrated that finerenone reduces the risk of kidney failure in patients with type 2 diabetes. In the FInerenone in chronic kiDney diseasE and type 2 diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial programme analYsis (FIDELITY), allocation to finerenone reduced the risk of the kidney composite outcome (time to kidney failure, sustained ≥57% decrease in eGFR or renal death) by 23% compared with placebo [hazard ratio (HR) 0.77, 95% CI 0.67–0.88].[239] Pooled analysis from both trials also demonstrated a 14% relative risk reduction in the composite cardiovascular outcome of cardiovascular death, non-fatal MI, non-fatal stroke, or hospitalization for HF (HR 0.86, 95% CI 0.78–0.95), which was largely driven by reduced risk of hospitalization for HF (HR 0.78, 95% CI 0.66–0.92). Cardiovascular findings were generally consistent in the FINE-HEART pooled analysis overall including FIDELIO-DKD and FIGARO-DKD with the FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure (FINEARTS-HF) population with HF (LVEF ≥40%) with and without diabetes.[240] Across the trials, ~40% of patients had an eGFR >60 mL/min/1.73 m^2 and were therefore eligible for FIDELIO-DKD and FIGARO-DKD based upon albuminuria measurement, highlighting the importance of uACR testing in at-risk patients (see *Section 3.1.3*).

Investigator-reported AKI occurred in similar proportions in both the finerenone and placebo groups of these trials.[239,240] Due to its mechanism of mineralocorticoid receptor antagonism, finerenone increases serum potassium. FIDELIO-DKD and FIGARO-DKD used restricted potassium thresholds requiring potentially eligible patients to have serum potassium values ≤4.8 mmol/L at screening (limiting generalizability of the safety results). Hyperkalaemia-related adverse events did occur more

commonly with finerenone vs placebo (14.0% vs 6.9%, respectively); however, none were fatal, and hyperkalaemia rarely led to discontinuation of study treatment (1.7% vs 0.6%, respectively) or hospitalization (0.9% vs 0.2%, respectively). These data support initiating finerenone when serum potassium is ≤5.0 mmol/L.[237–239]

At the time these ESC Guidelines were formulated, there were no large RCTs to support the use of non-steroidal MRAs in patients with CKD without diabetes or albuminuria, and without HF. The FInerenone Non-Diabetic Chronic Kidney Disease (FIND-CKD) trial (NCT05047263) was ongoing. Additionally, trials of aldosterone synthase inhibitors (NCT06531824, NCT06268873, NCT06742723) in combination with SGLT2 inhibition are under way in patients with CKD with and without diabetes across a broad range of kidney function, and can be expected to provide new evidence on targeting the aldosterone pathway in CKD.

5.5.3.2. Steroidal mineralocorticoid receptor antagonists

The effects of steroidal MRAs (e.g. spironolactone, eplerenone) on kidney failure and cardiovascular outcomes in patients with CKD specifically are uncertain and they increase hyperkalaemia vs placebo.[241] Steroidal MRAs are therefore not routinely recommended in CKD but can serve as an alternative to non-steroidal MRAs, if serum potassium can be managed, for treatment of HF, resistant hypertension, or hyperaldosteronism in CKD. See *Section 11* for details of RCTs of steroidal MRAs in dialysis.

5.5.4. Glucagon-like peptide-1 receptor agonists

The GLP-1RA semaglutide has also been shown to reduce kidney disease progression and cardiovascular risk in 3533 patients with type 2 diabetes and CKD with an eGFR 25–75 mL/min/1.73 m^2 and albuminuria in the Evaluate Renal Function with Semaglutide Once Weekly (FLOW) trial (BMI 32.0 ± 6.3 kg/m^2).[242,243] Allocation to weekly subcutaneous semaglutide 1 mg reduced the risk of the primary composite kidney outcome of kidney failure (dialysis, transplantation, or eGFR <15 mL/min/1.73 m^2), ≥50% eGFR decline from baseline, or death from kidney-related or cardiovascular causes by 24% compared with placebo (HR 0.76, 95% CI 0.66–0.88). There were consistent effects across subgroups by BMI (≤30 vs >30 kg/m^2), baseline haemoglobin A1c (HbA1c), eGFR, and uACR. The rate of eGFR decline was reduced by about one-third, and although FLOW was not powered to assess kidney failure alone, when results are combined with other large GLP-1RA trials (8 trials, 57 830 participants), evidence of a benefit emerges (HR 0.84, 95% CI 0.72–0.99).[243] The secondary composite cardiovascular outcome of non-fatal MI, non-fatal stroke, or cardiovascular death was significantly reduced by semaglutide by 18% (HR 0.82, 95% CI 0.68–0.98).[242] In the more recent Semaglutide cardiOvascular oUtcomes triaL (SOUL) trial, allocation to oral semaglutide (maximal dose 14 mg) also reduced the occurrence of major adverse cardiovascular events (cardiovascular death, non-fatal MI, or non-fatal stroke) in 9650 patients with type 2 diabetes and established CVD and/or CKD, 42% of whom had CKD (including 1187 participants with an eGFR <45 mL/min/1.73 m^2).[244]

GLP-1RAs have not been definitively tested in a non-diabetic CKD population. Exploration of data from the 17 604-participant Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) trial in patients with pre-existing CVD and a BMI ≥27 kg/m^2 demonstrates cardiovascular efficacy and raises a hypothesis that semaglutide could slow kidney disease progression in individuals without diabetes.[245,246] Allocation to subcutaneous semaglutide 2.4 mg reduced the risk of the primary composite cardiovascular outcome of non-fatal MI, non-fatal stroke, or cardiovascular death by 20% compared with placebo (HR 0.80, 95% CI 0.72–0.90).[245] The pre-specified five-component kidney outcome defined as renal death, initiation of dialysis or transplantation, persistent eGFR <15 mL/min/1.73 m^2, persistent ≥50% eGFR decline from baseline, or onset of persistent macroalbuminuria was also reduced by 22% by allocation to semaglutide vs placebo (HR 0.78, 95% CI 0.63–0.96).[246] This effect was largely driven by albuminuria reduction; there were too few events to reliably assess effects on initiation of KRT or categorical eGFR outcomes. The rate of eGFR decline analysed as a continuous outcome in SELECT was, however, favourably slower in the semaglutide group vs placebo.[246] Semaglutide 2.4 mg also significantly reduced albuminuria compared with placebo in the 24-week SeMaglutide and Albuminuria Reduction Trial in Obese Individuals Without Diabetes (SMART) trial, which randomized 101 patients with non-diabetic CKD.[247]

The use of GLP-1RAs appears generally safe in CKD. Among side effects, gastrointestinal upset shortly after initiation is common. In FLOW, adverse events due to gastrointestinal disorders leading to permanent discontinuation of study treatment occurred in 79 participants in the weekly subcutaneous semaglutide group (4.5%) vs 20 in the placebo group (1.1%).[242]

Currently, semaglutide is the only GLP-1RA evaluated in a large-scale dedicated trial in patients with type 2 diabetes and CKD.[242] Dual and triple incretin-based therapies have not been specifically tested in CKD though *post hoc* analyses raise a hypothesis of renal benefit of tirzepatide.[248] It is unclear whether the cardiorenal benefits of GLP-1RAs in CKD represent a class effect. Differing potency in lowering blood glucose and body weight among GLP-1RAs has been reported, although meta-analysis of data from eight trials shows consistent effects on cardiovascular outcomes for both GLP-1RAs with structural homology to human GLP-1 (e.g. semaglutide, liraglutide, dulaglutide) and exendin-4 (e.g. exenatide, lixisenatide).[249] Based on the results from the FLOW trial and supporting evidence from a large number of trials that included patients with CKD, treatment with a GLP-1RA (semaglutide 1.0 mg subcutaneous injection weekly, which was well tolerated in FLOW) is recommended to reduce risk of CKD progression and cardiovascular events in patients with type 2 diabetes (irrespective of glycaemic control) and CKD with eGFR 25–89 mL/min/1.73 m^2 and uACR ≥10 mg/mmol (≥100 mg/g).[242] RCTs are needed to guide use of GLP-1RAs in patients with CKD without diabetes or albuminuria, and in patients with type 1 diabetes and CKD.

5.5.5. Monitoring kidney function and combined use of treatments

The aforementioned recommendations use eGFR and uACR thresholds for initiation, which are generally based on eligibility

criteria of the key RCTs (see *Recommendation Table 12* and *Figure 7*). Early initiation and long-term continuation should maximize the benefits of risk-modifying therapy. Waiting for patients' albuminuria to increase or eGFR to decrease to a treatment threshold based on trial inclusion criteria may risk missing an opportunity for early intervention in patients at increased risk of kidney failure during their lifetime. Therefore, less stringent application of eGFR and uACR thresholds may be appropriate, particularly when treatments are simple to implement, safe, and cost-effective. This also negates some of the risk of delayed treatment or under-treatment of those at risk due to the within-person variability in measures of eGFR and uACR, which can misclassify patients' CKD category on initial measurement.

The therapies discussed in *Section 5.5* are known to cause an acute dip in eGFR upon initiation, with clinicians typically tolerating <30% dips,[9] since dips might reflect the drugs correcting maladaptive hyperfiltration in CKD. Although monitoring of potassium and creatinine is routine when initiating ACEI/ARBs and MRAs, on initiation of an SGLT2 inhibitor or GLP-1RA, we do not consider it necessary to routinely monitor creatinine/eGFR more frequently than for standard CKD monitoring, unless there is another reason (such as concern about volume depletion). Additional eGFR testing after initiation has resource implications, is a burden on patients, and could lead to unnecessary treatment interruption. *Figure 8* offers simple guidance on how to approach initiation and monitoring of kidney function and electrolytes. Monitoring potassium after initiating an ACEI/ARB and MRA is recommended due to risk of hyperkalaemia. If serum potassium reaches a level considered unacceptable, optimization of other clinical factors such as dietary factors, concomitant medications, glycaemic control, and acid–base status should be considered alongside potassium binder use (see *Section 3.7.1*) and temporary treatment discontinuation. It should be noted that SGLT2 inhibitors may modestly reduce the risk of hyperkalaemia and, therefore, concomitant use might facilitate continuation of ACEI/ARBs or MRAs.[226,250] Although not supported by any strong evidence, patients may be counselled to withhold ACEI/ARBs, SGLT2 inhibitors, non-steroidal MRAs, and GLP-1RAs temporarily if not able to maintain oral intake ('sick day rules'). It is important to educate patients on the importance of restarting after re-establishing food intake to avoid losing important long-term benefits.

Available evidence from large SGLT2 inhibitor, finerenone, and semaglutide trials generally have not demonstrated any heterogeneity of treatment effect on efficacy and safety outcomes in the types of patients already treated with these medications at baseline.[251–254] The mechanisms of action of ACEI/ARBs/non-steroidal MRAs vs SGLT2 inhibitors vs GLP-1RAs are also likely to target distinct renal pathophysiological effects. This should encourage co-prescription to maximize benefits. RCTs also show co-prescription of an SGLT2 inhibitor and an MRA reduces albuminuria more than either treatment alone.[242,255,256]

The optimal order and timing of initiating proven therapies in combination is not known. The algorithm in *Figure 7* should be implemented in such a manner that benefits can be realized rapidly.[239,242] Simultaneous initiation of the SGLT2 inhibitor empagliflozin and the non-steroidal MRA finerenone is safe in patients with diabetes and albuminuria (with the expected larger acute eGFR dip than either treatment alone).[256] Where resources allow, we suggest those at high absolute risk of kidney failure or who are progressing rapidly should be prioritized for initiation and dose titration in rapid sequence in a series of clinic visits.

Recommendation Table 12 — Recommendations for specific pharmacological interventions to reduce risk of kidney failure and/or cardiovascular disease in chronic kidney disease (see Evidence Table 12)

Recommendations	Class[a]	Level[b]
Treatment with maximally tolerated ACEI or ARB is recommended in patients with CKD[c] to achieve target blood pressure, reduce risk of progression of CKD and risk of cardiovascular events.[210,211,213,215,219]	I	A
An SGLT2 inhibitor is recommended in patients with CKD who have type 2 diabetes with eGFR ≥20 mL/min/1.73 m^2 to reduce risk of kidney failure and risk of cardiovascular events, irrespective of glycaemic control.[226–229,231]	I	A
An SGLT2 inhibitor is recommended in patients with CKD without diabetes with eGFR ≥20 mL/min/1.73 m^2 and uACR ≥20 mg/mmol (≥200 mg/g) to reduce the risk of kidney failure and cardiovascular events.[226–228,231]	I	A
A non-steroidal MRA (finerenone) is recommended in patients with CKD who have type 2 diabetes with eGFR ≥25 mL/min/1.73 m^2 and uACR ≥3 mg/mmol (≥30 mg/g) to reduce the risk of kidney failure and cardiovascular events.[d,237–239]	I	A
A GLP-1RA (subcutaneous semaglutide 1.0 mg/week after dose titration) is recommended in patients with CKD who have type 2 diabetes with eGFR 25–49 mL/min/1.73 m^2 and uACR ≥10 mg/mmol (≥100 mg/g) or eGFR 50–74 mL/min/1.73 m^2 and uACR ≥30 mg/mmol (≥300 mg/g) to reduce the risk of CKD progression and cardiovascular events, irrespective of glycaemic control.[242,243,249]	I	A
An SGLT2 inhibitor should be considered in patients with CKD without diabetes with eGFR 20–44 mL/min/1.73 m^2 and uACR <20 mg/mmol to slow kidney disease progression.[226,230]	IIa	B1
Combined use of an ARB with an ACEI is not recommended in patients with CKD as the risk of AKI and severe hyperkalaemia outweighs any added cardiorenal benefits.[219–222]	III	A

ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium glucose co-transporter-2; uACR, urine albumin-to-creatinine ratio.

[a]Class of recommendation.

[b]Level of evidence.

[c]With the only potential exception of patients without albuminuria and normal/low blood pressure (who do not have HF as an indication for ACEI/ARB).

[d]The FIDELIO-DKD and FIGARO-DKD trials required serum potassium to be ≤4.8 mmol/L (at run-in and screening visits) for inclusion, and excluded patients with known significant non-diabetic kidney disease such as clinically relevant renal artery stenosis.

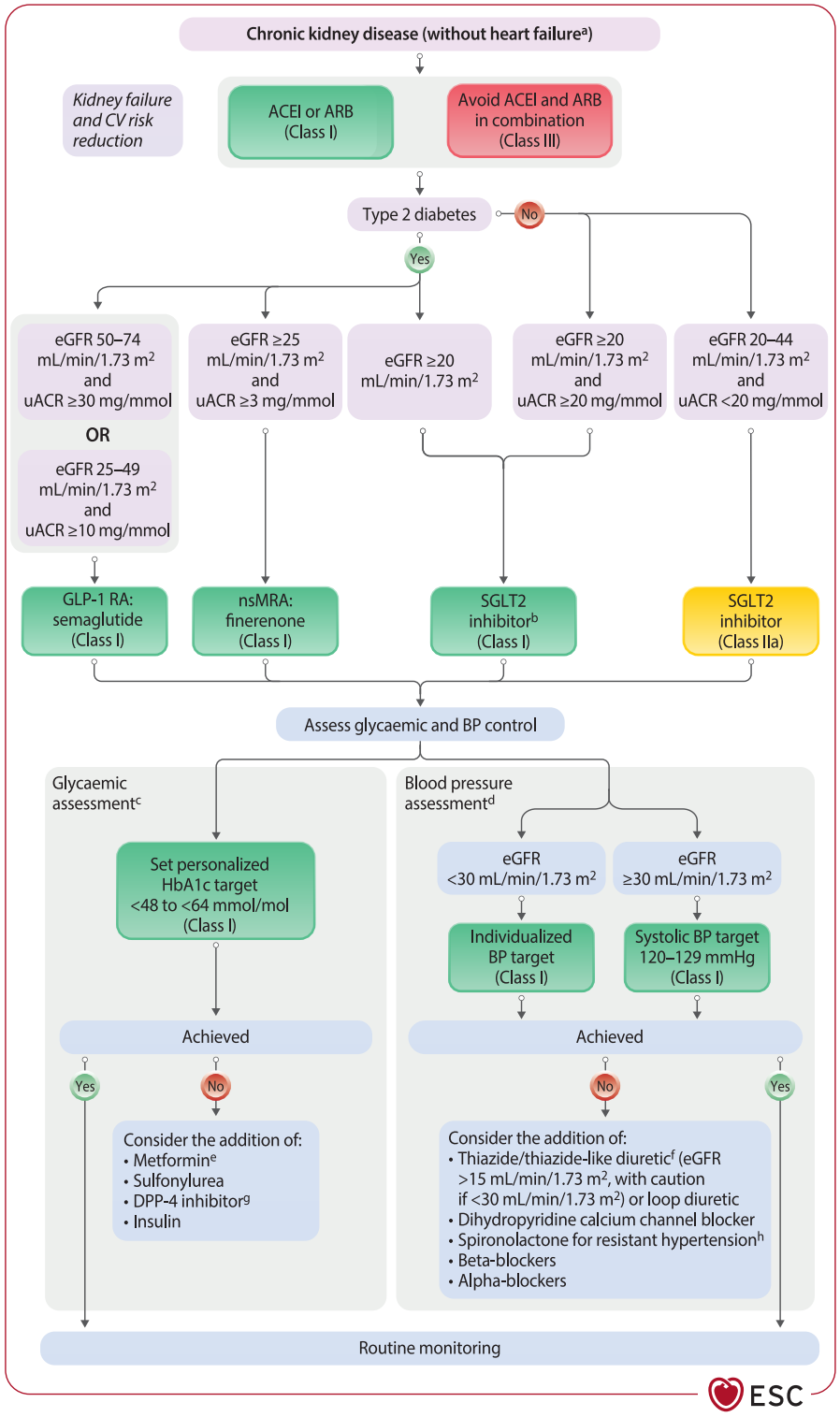

Figure 7 Algorithm for use of risk-modifying therapy and glucose lowering in patients with chronic kidney disease. ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CV, cardiovascular; DPP-4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration; GLP-1RA, glucagon-like peptide 1 receptor agonist; HbA1c, glycated haemoglobin; nsMRA, non-steroidal mineralocorticoid receptor antagonist; SGLT2, sodium glucose co-transporter 2; uACR, urine albumin-to-creatinine ratio. Approximate conversion to uACR in mg/g requires mg/mmol multiplied by 10. [a]Refer to *Section 6* for heart failure recommendations. [b]Treatment with an SGLT2 inhibitor once already established, continues in patients whose eGFR declines <20 mL/min/1.73 m^2 until KRT required. [c]For detail, refer to 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes.[30] [d]For detail, refer to the 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. [e]eGFR ≥30 mL/min/1.73 m^2. [f]Particularly use where there is residual albuminuria.[95] [g]Not in combination with GLP-1RA. [h]In eGFR ≥30 mL/min/1.73 m^2, with eGFR and blood potassium monitoring 1–4 weeks after initiation, and not in combination with finerenone

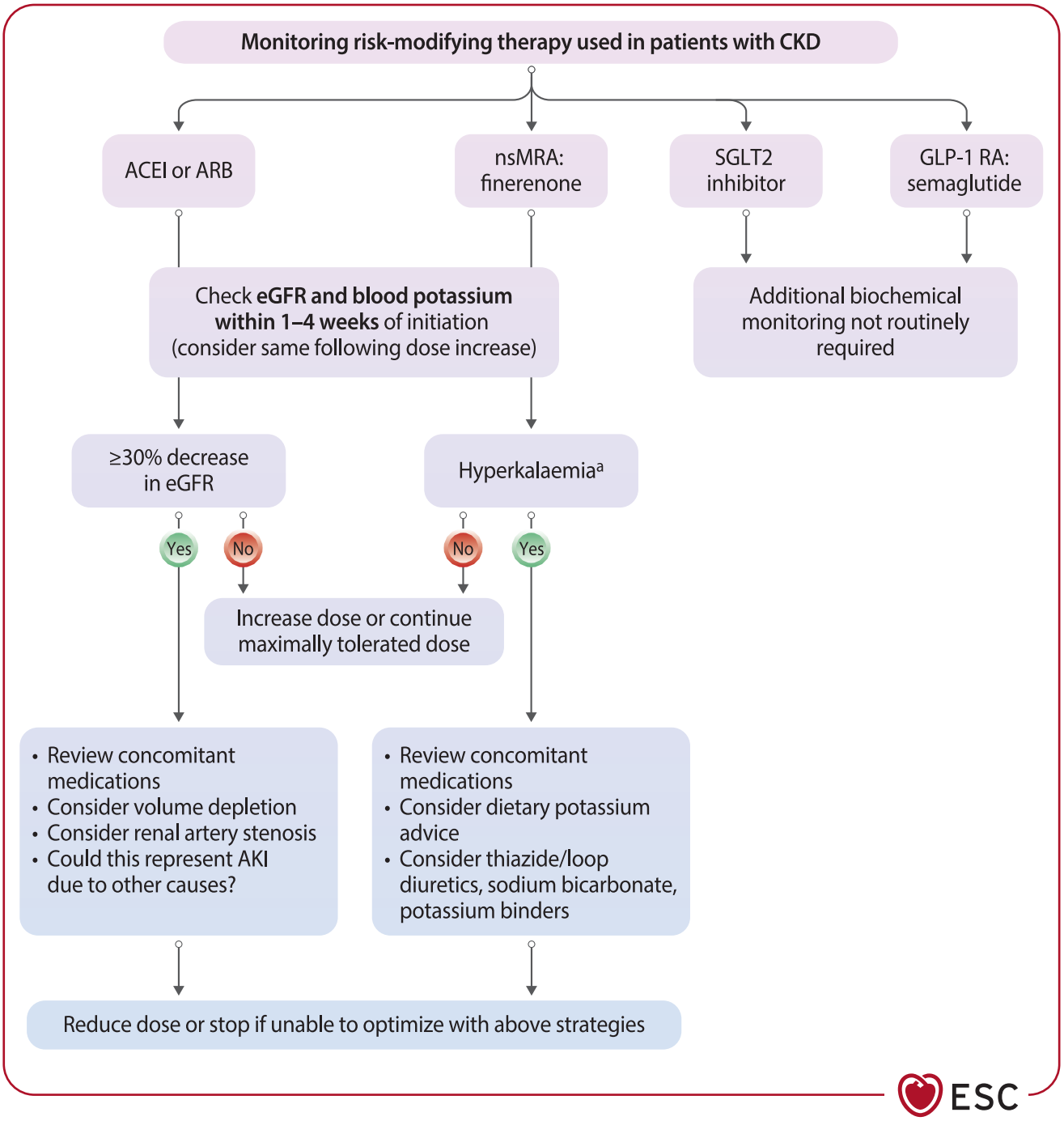

Figure 8 Simple guide to clinical and biochemical monitoring of risk-modifying therapy used in patients with chronic kidney disease. ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; nsMRA, non-steroidal mineralocorticoid receptor antagonist; SGLT2, sodium glucose co-transporter 2. [a]Stop ACEI/ARB/finerenone if potassium ≥6.0 mmol/L; in 5.5–6.0 mmol/L range, should optimize other factors and consider dose reduction, where applicable (*Section 3.7.1*). Restart stopped ACEI/ARB/finerenone when other causes of hyperkalaemia have been corrected and potassium control re-established. See *Section 6.4* for eGFR monitoring in heart failure (when dips in eGFR may be larger)

5.6. Glycaemic control in chronic kidney disease

5.6.1. Blood glucose targets

For more detailed guidance on the management of diabetes and CVD, refer to the 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes and specifically *Section 9* focusing on CKD; key points are summarized here. HbA1c should be monitored at least twice yearly in patients with diabetes and CKD, although reliability of the test diminishes in severe CKD. Personalized HbA1c targets are recommended and should be set to <48 mmol/mol (<6.5%) to <64 mmol/mol (<8.0%); with a target of <53 mmol/mol (<7.0%) to reduce microvascular complications wherever possible.[257] Intensive blood glucose lowering modestly reduces the risk of MI but does not affect risk of stroke, HF, peripheral vascular disease, or mortality outcomes.[258,259]

Haemoglobin A1c targets aim to balance minimizing microvascular complications of diabetes (i.e. nephropathy, retinopathy, and neuropathy) while avoiding hypoglycaemia, which itself increases the risk of CVD events.[260,261]

5.6.2. Pharmacotherapy

The approach to blood glucose lowering in diabetes should prioritize agents with proven benefits in reducing risk of CVD and/or kidney failure (*Figure 7*).[32] Following lifestyle modification (*Section 5.1*) and recommendations for the use of SGLT2 inhibitors and semaglutide in CKD irrespective of HbA1c (*Section 5.5*), additional agents can be added if HbA1c targets are not reached.

If semaglutide is not indicated or tolerated, other incretin-based therapies can be used in CKD for glucose lowering.[249] Clinicians should consult product literature for kidney function considerations for each medication. For patients in whom GLP-1RA therapy is not tolerated, a dipeptidyl peptidase (DPP)-4 inhibitor can be used as an alternative for glucose lowering. Linagliptin improves glycaemic indices in patients with type 2 diabetes and CKD but does not lower cardiovascular risk[262] nor risk of kidney failure,[263] and is only weight neutral.[263] DPP-4 inhibitor use in patients with HF requires caution due to suggested increased risk of HF hospitalization with saxagliptin and alogliptin (although not confirmed with sitagliptin or linagliptin).[32]

Metformin has not been conclusively shown to reduce cardiovascular risk[264] in CKD but can be used for additional blood glucose lowering when eGFR is ≥30 mL/min/1.73 m^2. Substantial dose reduction is required at eGFR <45 mL/min/1.73 m^2 (e.g. to 500 mg once or twice daily) and metformin should generally be stopped when eGFR declines <30 mL/min/1.73 m^2 due to risk of accumulation and lactic acidosis.[265,266] Sulfonylureas[262] can be used as adjunctive glucose-lowering therapy in CKD but can cause hypoglycaemia and weight gain and have no proven cardiovascular benefit. Risk of worsening HF limits the use of thiazolidinediones[267,268] and some DPP-4 inhibitors particularly in CKD since concomitant HF is common and CKD is a risk factor for HF. Insulin may be a necessary adjunct to lower blood glucose but does not confer cardiovascular benefit[269,270] and is also associated with weight gain.

Recommendation Table 13 — Recommendations for glucose lowering in patients with diabetes and chronic kidney disease (see Evidence Table 13)

Recommendations	Class[a]	Level[b]
SGLT2 inhibitors[c] and GLP-1RAs are recommended as first-line agents in patients with type 2 diabetes and CKD to lower blood glucose, due to their benefits on CKD progression and risk of cardiovascular events.[227,231,242,243,245,249,271]	I	A
Insulin is recommended in patients with type 2 diabetes and CKD if blood glucose targets are not reached with oral agents or GLP-1RA therapy, for additional blood glucose lowering.[269,270,272]	I	A
Personalized HbA1c targets within the range of <48 mmol/mol (<6.5%) to <64 mmol/mol (<8.0%) in patients with CKD who have diabetes are recommended to reduce microvascular complications, with a target of <53 mmol/mol (<7.0%) wherever possible.[257,258]	I	B1
Metformin should be considered in patients with CKD with eGFR ≥30 mL/min/1.73 m^2 and type 2 diabetes for additional blood glucose lowering.[273,274]	IIa	B1
Sulfonylurea therapy may be considered in patients with CKD and type 2 diabetes for additional blood glucose lowering.[272,274,275]	IIb	C
A DPP-4 inhibitor may be considered in patients with CKD and type 2 diabetes if GLP-1RA therapy is not tolerated or contraindicated, for additional blood glucose lowering.[262,263,274,276–278]	IIb	B1

CKD, chronic kidney disease; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HbA1c, glycated haemoglobin; SGLT2, sodium glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.
[c]Glucose-lowering effects of SGLT2 inhibitors are attenuated at decreased eGFR (particularly eGFR <30 mL/min/1.73 m^2).

6. Heart failure and chronic kidney disease

Heart failure and CKD frequently coexist due to shared risk factors (e.g. diabetes, hypertension, and ASCVD), altered renal haemodynamics in HF, and excessive salt and water retention including neurohormonal dysregulation in CKD. The two conditions have complex bidirectional pathophysiological and clinical interactions. The presence of CKD complicates the diagnosis and management of HF by limiting the use of specific management options and is associated with increased risk of adverse clinical effects. In general, management of HF should follow the 2026 ESC Guidelines for the management of heart failure, and specific recommendations in relation to CKD are discussed here.[279]

6.1. Screening and diagnosis of heart failure

Diagnosing HF in patients with CKD can be challenging due to overlapping symptoms and signs. In addition, CKD itself causes an increase and fluctuations in natriuretic peptide levels, especially in severe CKD.[280–286] Optimal natriuretic peptide thresholds to rule in or out HF by CKD stage have not been precisely defined, with more research required.[287,288] However, a prospective study that characterized 453 outpatients with severe CKD (median eGFR 27 mL/min/1.73 m^2) showed that more than 90% of participants were already in stage B or C of the HF continuum. Median N-terminal pro-B-type natriuretic peptide (NT-proBNP) was 369 pg/mL, but patients fulfilling HF criteria exhibited significantly higher concentrations. A fixed NT-proBNP threshold of ≥500 pg/mL offered balanced diagnostic performance [sensitivity 69%, specificity 80%; area under the curve (AUC) 0.74]. Conversely, low levels (<125 pg/mL) retained high sensitivity for ruling out HF.[289]

Patients with CKD are at increased risk of developing both HF with preserved or reduced ejection fraction. *Vice versa*, in patients with HF, risk of CKD is increased, with data from 15-year registry follow-up of ambulatory patients with HF estimating an annual rate of eGFR decline of 1.5–2.5 mL/min/1.73 m^2/year.[290] Additionally, albuminuria is common in HF, is associated with a higher risk of incident HF, and may inform risk stratification.[291–294]

Recommendation Table 14 — Recommendations for heart failure screening and diagnosis in patients with chronic kidney disease (see Evidence Table 14)

Recommendations	Class[a]	Level[b]
Screening for clinical suspicion of HF		
Assessment of natriuretic peptides[c] may be considered in patients with CKD as a screening tool for structural heart disease, cardiac dysfunction, or prediction of incident HF.[284–286,289]	IIb	C

CKD, chronic kidney disease; HF, heart failure; eGFR, estimated glomerular filtration rate; (NT-pro)BNP, (N-terminal pro-)B-type natriuretic peptide.
[a]Class of recommendation.
[b]Level of evidence.
[c]Serum concentrations of BNP/NT-proBNP increase at decreased eGFR and should be interpreted with caution.

6.2. Management of chronic heart failure and chronic kidney disease

A substantial proportion (about 50%) of patients with chronic HF in RCTs have an eGFR <60 mL/min/1.73 m^2. There is some under-representation of patients with severe CKD, but as a general observation, there is no good evidence that the relative effects of evidence-based HF therapies differ in patients with CKD in most HF RCTs. Despite this, foundational therapies remain under-utilized in patients with concomitant HF and CKD.

6.2.1. Chronic pharmacological treatment irrespective of left ventricular ejection fraction

The key principles of the pharmacological treatment of chronic HF in patients with CKD are shown in *Figure 9*.

6.2.1.1. Loop diuretics

Loop diuretics are the cornerstone of pharmacological treatment to alleviate symptoms attributable to volume overload and congestion in patients with HF and CKD. Response to loop diuretics is diminished at decreased eGFR, necessitating higher doses.[295] The use of other diuretics, such as thiazides or thiazide-like therapies, is associated with a higher risk of adverse events, including hypokalaemia, and is therefore not considered first-line therapy for alleviating congestion.[279,296]

6.2.1.2. Sodium glucose co-transporter 2 inhibitors

SGLT2 inhibitors, such as dapagliflozin and empagliflozin, have consistently been shown to reduce HF events and cardiovascular death in patients with HF and with CKD (eGFR >20 mL/min/1.73 m^2) irrespective of LVEF.[297–301] In the Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR-Reduced) and Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction (EMPEROR-Preserved) trials, empagliflozin reduced the risk of the composite outcome of cardiovascular death or HF hospitalization irrespective of LVEF and baseline eGFR.[301,302] In the small subgroup of patients included with eGFR 20–30 mL/min/1.73 m^2, the risk reduction with empagliflozin was maintained in both trials (all interaction $P > .10$). Similarly, in the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) and Dapagliflozin Evaluation to Improve the Lives of Patients with Preserved Ejection Fraction Heart Failure (DELIVER) RCTs, the HRs for the primary endpoint in the CKD subgroups were similar to the overall result.[300,303] These effects of SGLT2 inhibitors across the entire range of LVEF in patients with HF and CKD have been confirmed in both individual patient data and study-level meta-analyses.[297,304]

Supporting evidence on renal safety and efficacy from these trials shows that SGLT2 inhibitors, after an initial acute dip in eGFR, slow the decline in eGFR in patients with HF with and without CKD (i.e. eGFR below/above 60 mL/min/1.73 m^2).[304–306] Evidence supporting the initiation of an SGLT2 inhibitor in patients with HF and eGFR <20 mL/min/1.73 m^2 or those undergoing dialysis remains insufficient to support initiation in such patients. Nonetheless, if treatment with an SGLT2 inhibitor is already established, it may be continued in patients whose eGFR declines <20 mL/min/1.73 m^2, provided the therapy is well tolerated and KRT has not been initiated.[9]

6.2.1.3. Steroidal and non-steroidal mineralocorticoid receptor antagonists

An individual patient data meta-analysis has shown that the efficacy of MRA therapy is not consistent across LVEF, showing less effect of MRA (either steroidal or non-steroidal MRA) in patients with LVEF >40%.[307] In addition, in that group, the effect of MRA therapy was even smaller in patients with eGFR <60 mL/min/1.73 m^2 (P-value for interaction CKD vs no CKD .046).

Since non-steroidal MRA therapy has only been investigated in HF patients with LVEF >40%, steroidal and non-steroidal MRA therapy are therefore considered separately in patients with HF and CKD.

6.2.1.3.1. Steroidal mineralocorticoid receptor antagonists. Steroidal MRAs consistently reduced the risk of all-cause and cardiovascular death or HF hospitalization in patients with HFrEF (and LVEF <35%) with or without eGFR <60 mL/min/1.73 m^2, without evidence of effect modification by baseline eGFR.[308,309] Only one trial [Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT)] evaluated treatment with a steroidal MRA in patients with HFrEF and LVEF >45% and it excluded patients with eGFR <30 mL/min/1.73 m^2. The TOPCAT trial overall result was neutral, although HF hospitalizations were reduced, with similar effects seen in patients with CKD. When analysis was restricted to patients included in the Americas, spironolactone improved the primary outcome overall and in patients with CKD, without evidence of interaction. Combining results of the CKD subgroups of these three trials suggests steroidal MRA therapy improves risk of death or HF re-hospitalization in patients with HFrEF and CKD. Steroidal MRA therapy is therefore recommended in patients with HFrEF and CKD with eGFR >30 mL/min/1.73 m^2 to reduce the risk of death or HF hospitalization.[307,310]

MRAs cause an initial acute dip in eGFR but, unlike SGLT2 inhibitors, do not slow the slope of eGFR decline in patients with HF. Although there are only sparse data in patients with HFrEF and eGFR <30 mL/min/1.73 m^2, a meta-analysis of the Randomized Aldactone Evaluation Study (RALES) and Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS-HF) trials showed that the cardiovascular benefits of MRA therapy were maintained if eGFR dropped to <30 mL/min/1.73 m^2.[311] Close monitoring of potassium levels is warranted in patients with HFrEF and decreased eGFR; however, the overall benefits of MRA therapy outweigh the risks in the absence of clinically significant hyperkalaemia.[312,313]

6.2.1.3.2. Non-steroidal mineralocorticoid receptor antagonists (finerenone). In the FINEARTS-HF trial in 6001 patients with HF with LVEF ≥40%, the non-steroidal MRA finerenone reduced the risk of the primary composite outcome of cardiovascular death and worsening HF overall and in the CKD subgroup (eGFR 25–59 mL/min/1.73 m^2): HR 0.91 (95% CI 0.78–1.07), as compared with HR 0.72 (95% CI 0.59–1.07) in those with eGFR ≥60 mL/min/1.73 m^2.[314] In the individual patient data meta-analysis combining FINEARTS-HF and TOPCAT, there was a significant effect on cardiovascular death and HF hospitalizations in patients with HFpEF (and LVEF >40%), but with a smaller effect compared with HFrEF, and the effect being even smaller in patients with CKD.[301] In addition to steroidal MRA therapy in patients with LVEF <50%, non-steroidal MRA therapy (finerenone) should therefore be considered in patients with HF with LVEF ≥40% and CKD with eGFR ≥25 mL/min/1.73 m^2 to reduce the risk of cardiovascular death and HF hospitalization.

6.2.2. Pharmacological treatment across left ventricular ejection fraction ranges in patients with heart failure and chronic kidney disease

6.2.2.1. Heart failure with reduced ejection fraction

The management of patients with symptomatic HFrEF (LVEF <50%) and CKD with eGFR ≥30 mL/min/1.73 m^2, should be consistent with the approach used for those without CKD. Subgroup analyses from large RCTs have shown that the benefits of ACEI, ARB, ARNI, beta-blockers, and steroidal MRAs on cardiovascular death or hospitalization for HF were maintained among participants with an eGFR 30–60 mL/min/1.73 m^2 at baseline.[307,315–337]

6.2.2.1.1. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and angiotensin receptor/neprilysin inhibitors. Therapy with an ACEI may be considered in asymptomatic patients with left ventricular systolic dysfunction and CKD with eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of death or HF hospitalization.[317] The evidence for ACEIs (or ARBs) in patients with HFrEF and CKD with eGFR <30 mL/min/1.73 m^2 is limited. In both the Studies of Left Ventricular Dysfunction (SOLVD) and Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS) trials, patients with eGFR <30 mL/min/1.73 m^2 were eligible, as patients with creatinine up to 177 and 300 µmol/L, respectively, were enrolled, and substudies have not shown good evidence for effect modification by eGFR (or creatinine clearance) above/below 45 mL/min/1.73 m^2 and 49 mL/min/1.73 m^2, respectively.[318,338] Overall data on safety are also reassuring. Therefore, ACEIs or ARBs may be considered in patients with HFrEF with CKD and eGFR 15–29 mL/min/1.73 m^2.[315–321,339] In this context, initiation at low dose, slow uptitration, and close monitoring of kidney function and serum potassium is advisable. There are no data to support the use of these agents in patients with HFrEF with kidney failure (eGFR <15 mL/min/1.73 m^2 or dialysis). Treatment of HF with an ARNI may slow the rate of kidney function decline compared with ACEIs, making them an attractive option in patients at high risk of progressive kidney dysfunction; however, data are lacking in patients with eGFR <30 mL/min/1.73 m^2.[323] Retrospective analyses suggested that in patients treated with an ARNI with a decline in eGFR to <30 mL/min/1.73 m^2, continuation was associated with persistent benefit without additional safety concerns (and ARNIs were generally safe and well tolerated in a CKD trial recruiting down to eGFR 20 mL/min/1.73 m^2).[288,340] Continuation of therapy, under close monitoring, if eGFR falls below 30 mL/min/1.73 m^2 might therefore be appropriate.

6.2.2.1.2. Beta-blockers. Beta-blockers are one of the most effective therapies in patients with HFrEF. Unlike the RAAS inhibitor trials, many RCTs have included patients with eGFR as low as 15 mL/min/1.73 m^2 and, in one small trial, patients on dialysis.[341] Beta-blocker trial data have been analysed in an individual patient-level data meta-analysis.[335] Beta-blockers consistently lowered the risk of mortality across the range of eGFR included. There was some evidence of interaction by eGFR, suggesting that the relative effect of beta-blocker treatment may attenuate at lower eGFR, but there were low numbers of deaths among patients with the lowest eGFR. Individual trials have also

shown consistent effects of beta-blocker therapy on cardiovascular death and/or HF hospitalization.[332,333] Beta-blockers are not known to affect renal haemodynamics directly and are not associated with any appreciable acute decline in eGFR following initiation nor long term.[314] Beta-blocker therapy is therefore recommended in patients with HFrEF and CKD with eGFR ≥30 mL/min/1.73 m^2 and may be considered in patients with eGFR 15–29 mL/min/1.73 m^2 to reduce the risk of death and HF re-hospitalization.[335]

6.2.2.1.3. Additional medical treatment for heart failure with reduced ejection fraction. The above-mentioned treatment classes are the basis of treatment in patients with HFrEF and CKD. There are specific phenotypes of patients with HFrEF where there is additional evidence to support additional medical therapy (*Figure 9* and *Recommendation Table 15*).

6.2.2.1.4. Cardiac glycosides (digoxin and digitoxin). Data from the Digitalis Investigation Group (DIG) study in 6800 patients with HFrEF and CKD, performed before the introduction of beta-blockers, MRAs, or SGLT2 inhibitors, showed that digoxin reduced the risk of the composite outcome of HF hospitalization or all-cause mortality without evidence for effect modification by baseline eGFR.[342,343] Recently, the DIGitoxin to Improve ouTcomes in patients with advanced chronic Heart Failure (DIGIT-HF) randomized trial showed that digitoxin reduced the risk of the primary composite of all-cause death or first HF hospitalization vs placebo on top of optimal HFrEF therapy (HR 0.82, 95% CI 0.69–0.98), without effect modification by baseline CKD status.[344] Digoxin is renally excreted and requires close monitoring of kidney function and digoxin levels. Digitoxin undergoes enterohepatic (non-renal) elimination. Both compounds require drug monitoring, especially with digoxin and in patients with eGFR <30 mL/min/1.73 m^2.[343] Cardiac glycosides (digoxin or digitoxin) should be considered in patients with eGFR ≥20 mL/min/1.73 m^2 to reduce the risk of HF hospitalizations.[342–344]

6.2.2.1.5. Ivabradine. In the Systolic Heart Failure Treatment with the If inhibitor Ivabradine Trial (SHIFT) in patients with HFrEF in sinus rhythm with baseline heart rate >70 beats per minute (b.p.m.), ivabradine reduced the risk of cardiovascular death or HF hospitalization regardless of baseline CKD status (defined as eGFR <60 mL/min/1.73 m^2).[345] Additional medical therapy with ivabradine should be considered in patients with eGFR ≥20 mL/min/1.73 m^2 in sinus rhythm and heart rate >70 b.p.m. to reduce the risk of cardiovascular death or HF hospitalization.[346]

6.2.2.1.6. Vericiguat. Vericiguat reduced risk of the primary composite outcome of cardiovascular death or HF hospitalization by 10% (HR 0.90, 95% CI 0.82–0.98) in the Vericiguat Global Study in Subjects with Heart Failure with Reduced Ejection Fraction (VICTORIA).[347] In sub-analyses, this benefit, although modest, was consistent irrespective of baseline eGFR, but with uncertainty about any effect below an eGFR of 30 mL/min/1.73 m^2.[347,348] In the Vericiguat Global Study in Participants with Chronic Heart Failure (VICTOR), which included patients with lower risk HFrEF, vericiguat did not reduce the primary outcome of cardiovascular death or HF hospitalization.[349] The prespecified secondary outcome of cardiovascular death alone was reduced (HR 0.83, 95% CI 0.71–0.97) in patients with and without CKD at baseline, but again, there was uncertainty about the effect of vericiguat in patients with eGFR <30 mL/min/1.73 m^2. In an individual patient data meta-analysis of VICTOR and VICTORIA, vericiguat reduced the composite of cardiovascular death or HF hospitalization (HR 0.91, 95% CI 0.85–0.98), with consistent effects on both components and all-cause mortality.[350] There were consistent effects on the outcome of cardiovascular death or hospitalization for HF down to a eGFR 30 mL/min/1.73 m^2, but the HR for the eGFR 15–30 mL/min/1.73 m^2 subgroup was >1.0. Vericiguat may be considered in patients with eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of cardiovascular death and HF hospitalization,[347,349,350] but there is insufficient certainty about effects of vericiguat in patients with eGFR <30 mL/min/1.73 m^2 to make a formal recommendation.

6.2.2.1.7. Hydralazine and isosorbide dinitrate. Combined use of hydralazine-isosorbide dinitrate may be used in self-identified Black patients as first-line treatment or as an alternative to renin-angiotensin system (RAS) inhibition when not tolerated. The placebo-controlled African-American Heart Failure Trial (A-HEFT) trial was stopped early due to mortality benefit (HR 0.57, 95% CI 0.37–0.89) and provides a limited amount of information for patients with eGFR <60 mL/min/1.73 m^2 (it excluded patients with 'severe kidney disease').[351] Reported effects on a composite of risk of death or HF hospitalization were not modified by the presence of CKD.[352] Hydralazine-isosorbide dinitrate should therefore be considered in self-identified Black patients with eGFR ≥30 mL/min/1.73 m^2 and left ventricular dilatation in combination with LVEF <45%, or LVEF ≤35% to reduce the risk of death and HF hospitalization.

6.2.2.2. Treatment of heart failure with preserved ejection fraction

6.2.2.2.1. Glucagon-like peptide 1 receptor agonists (including dual agonists). In patients with HF and CKD with LVEF ≥45% and obesity, treatment with a GLP-1RA (semaglutide) or combined glucose-dependent insulinotropic polypeptide and GLP-1RA (tirzepatide) should be considered in patients with eGFR >15 mL/min/1.73 m^2 with or without diabetes, for weight loss and improved quality of life.[353–357] The Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study Comparing the Efficacy and Safety of Tirzepatide vs Placebo in Patients with Heart Failure with Preserved Ejection Fraction and Obesity (SUMMIT) of 731 patients with HFpEF raised a hypothesis that tirzepatide may reduce the risk of adverse clinical outcomes, with a 38% lower risk of the composite of cardiovascular death or worsening HF events (HR 0.62, 95% CI 0.41–0.95) over 52 weeks.[357] For semaglutide and tirzepatide, an increase in gastrointestinal adverse events (generally mild) is common irrespective of eGFR, and there have been no important renal safety issues identified.[353–357]

6.2.3. Treatment of comorbidities

6.2.3.1. Iron deficiency

Multiple trials evaluated the effect of intravenous iron supplementation in patients with HFrEF, often including patients with CKD. In the most recent meta-analysis on large published RCTs, intravenous iron supplementation consistently showed

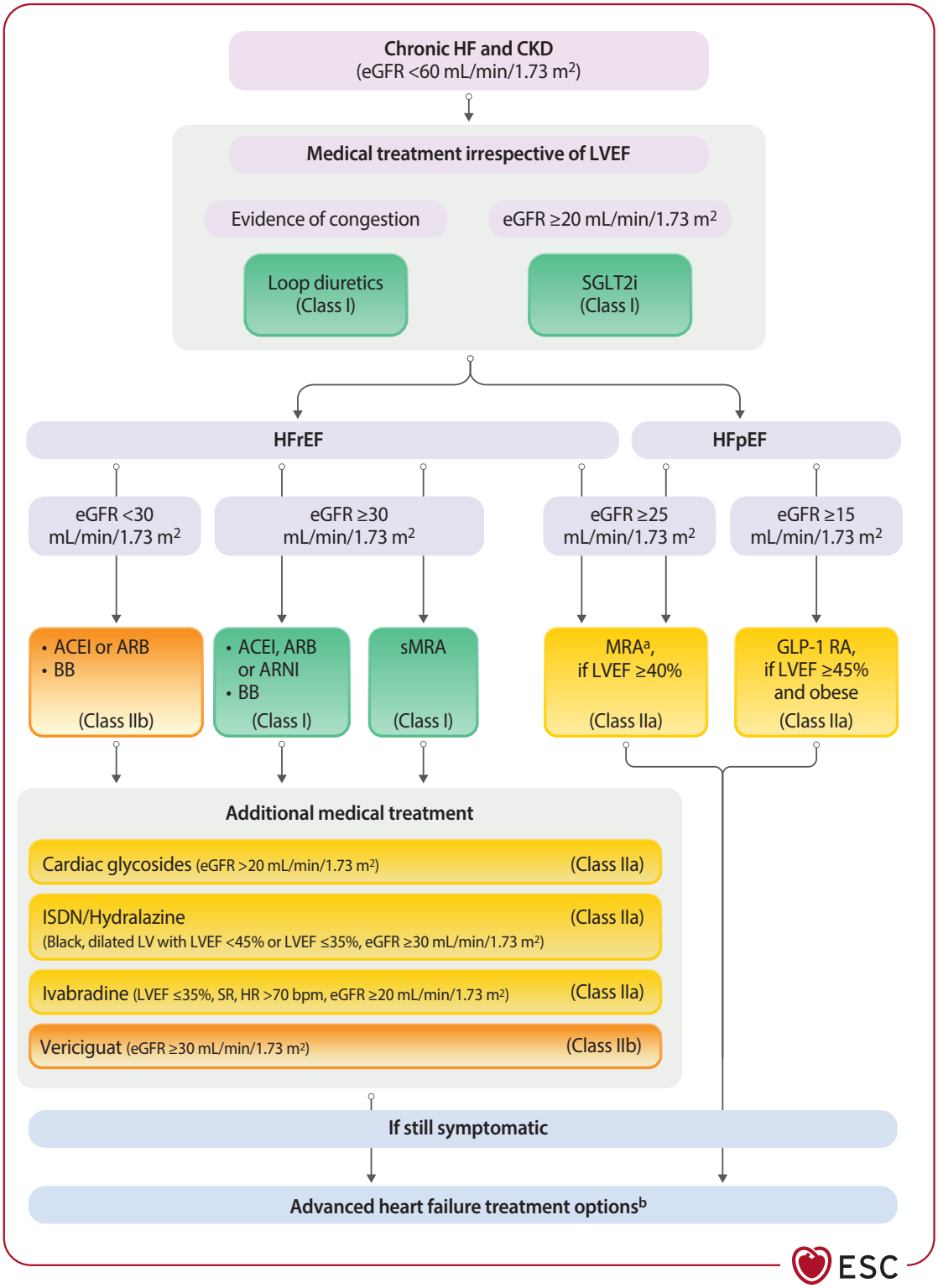

Figure 9 Pharmacological treatment of patients with heart failure and chronic kidney disease. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; BB, beta-blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ISDN, isosorbide dinitrate; LV, left ventricle; LVEF, left ventricular ejection fraction; SGLT2i, sodium glucose co-transporter 2 inhibitor; (s)MRA, (steroidal) mineralocorticoid receptor antagonist; SR, sinus rhythm. [a]Either steroidal or non-steroidal MRA. For steroidal MRA: eGFR ≥30 mL/min/1.73 m². [b]See *Section 6.5* and *Figure 13*.

beneficial effects on reducing HF re-hospitalization.[358] Available evidence shows a similar effect across different levels of kidney function.[359–366] Treatment with intravenous iron supplementation using ferric carboxymaltose or ferric derisomaltose should be considered in patients with HFrEF with iron deficiency (with or without anaemia) and CKD to reduce the risk of HF hospitalization.[358–366] An optimal definition of iron deficiency in the HF setting remains to be identified but the body of evidence increasingly favours a streamlined definition that relies solely on a TSAT value <20%.[367]

6.2.3.2. Hyperkalaemia

Treatment with oral potassium binders (patiromer or sodium zirconium cyclosilicate) may be useful in patients with HF and CKD to decrease serum potassium, reduce the risk of hyperkalaemia, and avoid down-titration or withdrawal of risk-modifying therapies such as ACEI/ARBs, ARNIs, and MRAs.[368,369] Although no randomized data exist, sodium polystyrene sulfonate can also be used to manage hyperkalaemia, especially if cost is an important consideration. The effect of oral potassium binders on clinical outcomes in HF has not been established.

6.2.4. Device therapy in heart failure and chronic kidney disease

Although patients with eGFR <30 mL/min/1.73 m^2 have been under-represented in device trials, implantable cardiac defibrillator (ICD), cardiac resynchronization therapy (CRT), and mitral valve transcatheter edge-to-edge repair (TEER) indications in HF should not differ by CKD stage.[370–374] As in populations without CKD, ICD therapy is not indicated in patients with HF and CKD who have a life expectancy <1 year.[375]

There is some evidence that the benefits of ICD therapy in HFrEF on all-cause mortality may attenuate as eGFR is <60 mL/min/1.73 m^2. An individual patient-level data meta-analysis of 2867 patients from four primary-prevention ICD trials in HFrEF reporting the overall mortality benefit (ICD vs usual care: 43.4% vs 35.8%) was made up of a subgroup-specific effect including an adjusted HR of 0.49 (95% CI 0.24–0.95) in patients with eGFR ≥60 mL/min/1.73 m^2 and 0.80 (95% CI 0.40–1.53) in patients with eGFR <60 mL/min/1.73 m^2.[376] For CRT, in a trial-level meta-analysis of three RCTs, there was no evidence of effect modification by baseline CKD status (eGFR below/above 60 mL/min/1.73 m^2).[377–380] Data on the effect of mitral valve TEER in patients with CKD are derived from the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) and Randomized Investigation of the MitraClip Device in Heart Failure: Second Trial in Patients with Clinically Significant Functional Mitral Regurgitation (RESHAPE-HF2) trials in which TEER for mitral regurgitation reduced the risk of the primary outcome, irrespective of baseline eGFR. For COAPT, in addition there was suggestive evidence of benefit in those with eGFR <30 mL/min/1.73 m^2.[373]

Recommendation Table 15 — Recommendations for treatment of chronic heart failure in patients with chronic kidney disease (see Evidence Table 15)

Recommendations	Class[a]	Level[b]
Treatment irrespective of LVEF		
Treatment with loop diuretics is recommended in patients with HF and CKD to alleviate symptoms/signs of fluid overload and improve exercise capacity.[381,382]	I	A
Treatment with an SGLT2 inhibitor is recommended in patients with HF and CKD with eGFR ≥20 mL/min/1.73 m^2 irrespective of LVEF, to reduce the risk of (repeated) HF hospitalization and cardiovascular death.[297–304]	I	A
Treatment with a steroidal MRA is recommended in patients with HF and CKD with an eGFR ≥30 mL/min/1.73 m^2 and HFrEF, to reduce the risk of HF hospitalization and death.[307,308,313,326,327]	I	A
Treatment with a MRA, either steroidal or non-steroidal, should be considered in patients with HF with LVEF ≥40% and CKD with an eGFR[c] ≥25 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and cardiovascular death.[307,311]	IIa	B1
HFrEF		
Treatment with either ACEI, ARNI, or ARB (if ACEI or ARNI not tolerated) is recommended in patients with HFrEF and CKD with an eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and death.[315,316,318,321–323,338]	I	A
Treatment with an ACEI is recommended in patients with CKD with an eGFR ≥30 mL/min/1.73 m^2 and asymptomatic left ventricular dysfunction (LVEF ≤35%) to reduce the risk of incident HF and HF-related hospitalizations.[317]	I	B1
Treatment with a beta-blocker is recommended in patients with HFrEF and CKD with an eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and death.[332,333,335,336]	I	A
Treatment with an ARNI (sacubitril/valsartan) should be considered in patients with HFrEF and CKD with an eGFR ≥30 mL/min/1.73 m^2 as an alternative to ACEI/ARB to reduce the risk of CKD progression (or slow the decline in eGFR).[322,323]	IIa	B1
Treatment with a combination of hydralazine-isosorbide dinitrate should be considered in self-identified Black patients with HFrEF and CKD with an eGFR ≥30 mL/min/1.73 m^2 and dilated left ventricle in combination with LVEF <45%, or LVEF ≤35%, when added to conventional HFrEF therapy to reduce the risk of HF hospitalization and death.[351,352]	IIa	C
Treatment with an ACEI or ARB may be considered in patients with HFrEF and CKD with an eGFR 15–29 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and cardiovascular death.[315–318,320,321,338,339]	IIb	C

Continued

Treatment with a beta-blocker may be considered in patients with HFrEF and CKD with an eGFR 15–29 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and death.[335]	IIb	C
Additional medical therapy in HFrEF		
Additional medical therapy with cardiac glycosides (digoxin or digitoxin) should be considered in patients with HFrEF and CKD with eGFR >20 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and death.[342–344,349,350]	IIa	B1
Additional medical therapy with vericiguat may be considered in patients with HFrEF and CKD with eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of HF hospitalization and cardiovascular death.[347–350]	IIb	B1
Additional medical therapy with ivabradine[d] should be considered in patients with HFrEF and CKD with eGFR ≥20 mL/min/1.73 m^2 to reduce the risk of cardiovascular and HF-related events.[345,346]	IIa	B1
HFpEF		
Treatment with a GLP-1RA (semaglutide) or glucose-dependent insulinotropic polypeptide and GLP-1RA (tirzepatide) should be considered in patients with HFpEF and CKD with an eGFR ≥15 mL/min/1.73 m^2 and LVEF ≥45% with or without diabetes who are obese, to reduce weight and improve quality of life.[353–355,357]	IIa	B1

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.
[c]Steroidal MRA: eGFR >30 mL/min/1.73 m^2.
[d]LVEF ≤35%, sinus rhythm, heart rate >70 b.p.m.

Recommendation Table 16 — Recommendations for management of comorbidities in patients with heart failure and chronic kidney disease (see Evidence Table 16)

Recommendations	Class[a]	Level[b]
Iron deficiency		
Treatment with intravenous iron supplementation should be considered in patients with HFrEF and CKD with iron deficiency[c] to reduce the risk of HF hospitalization.[358,360,361,363,366]	IIa	B1

CKD, chronic kidney disease; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; TSAT, transferrin saturation.
[a]Class of recommendation.
[b]Level of evidence.
[c]Defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%.

6.3. Management of patients with decompensated heart failure and chronic kidney disease

6.3.1. Epidemiology and intersection with chronic kidney disease

Both decreased eGFR and increased uACR are associated with increased risk for decompensated HF (DHF). Furthermore, increased albuminuria is linked to diuretic resistance.[383–385] This can lead to incomplete decongestion in patients with CKD in the setting of DHF.[386] Contemporary decompensated HF RCTs report a prevalence of CKD of 43%–81%, with some variation in part due to different eGFR cut-offs for inclusion.[382,387–391] CKD is a strong predictor of developing worsening renal function [WRF; defined as an increase in serum creatinine >26.5 µmol/L (>0.3 mg/dL)], often leading to incomplete decongestion and increased risk of early re-hospitalization and death.[392,393]

6.3.2. Diagnosis and management of decompensated heart failure in the setting of chronic kidney disease

Figure 10 gives an overview of the pathway to evaluate and manage patients with DHF and CKD. Natriuretic peptides are often used to rule out DHF. In the setting of CKD, natriuretic peptides are elevated, making ruling out more difficult.[282] There is a need for CKD-specific cut-points, which are currently lacking. Once DHF is diagnosed, the initial identification process is also directed at identifying specific causes, symptoms, and signs that need immediate attention, and the management of volume overload (*Figure 10*). Management of changes in kidney function during DHF treatment is discussed in *Section 6.4.2*.

6.3.2.1. Management of volume overload with loop diuretics

Compared with patients without CKD, patients with DHF and CKD require substantially higher doses to achieve a sufficient diuretic response, as loop diuretic excretion is decreased in patients with CKD.[394] The Diuretic Optimization Strategies Evaluation (DOSE) trial illustrated that higher doses of loop diuretics (2.5-times patient's usual doses) resulted in more dyspnoea relief, while the Pragmatic Urinary Sodium-based algoritHm in Acute Heart Failure (PUSH-AHF) trial illustrated that urinary sodium-based dose increases of loop diuretics resulted in greater natriuresis.[382,395,396] While higher doses of loop diuretics might result in a transient rise in creatinine, such a rise is not associated with adverse kidney or cardiac outcomes when the diuretic response is adequate. The PUSH-AHF trial and Efficacy of a Standardized Diuretic Protocol in Acute Heart Failure (ENACT-HF) study illustrated the feasibility of using urinary sodium and urine output to guide diuretic therapy (see algorithm in *Figure 10*).[396,397]

6.3.2.2. Management of volume overload with diuretic combination therapy

In patients with DHF and CKD, residual congestion is often present despite treatment with loop diuretics.[398]

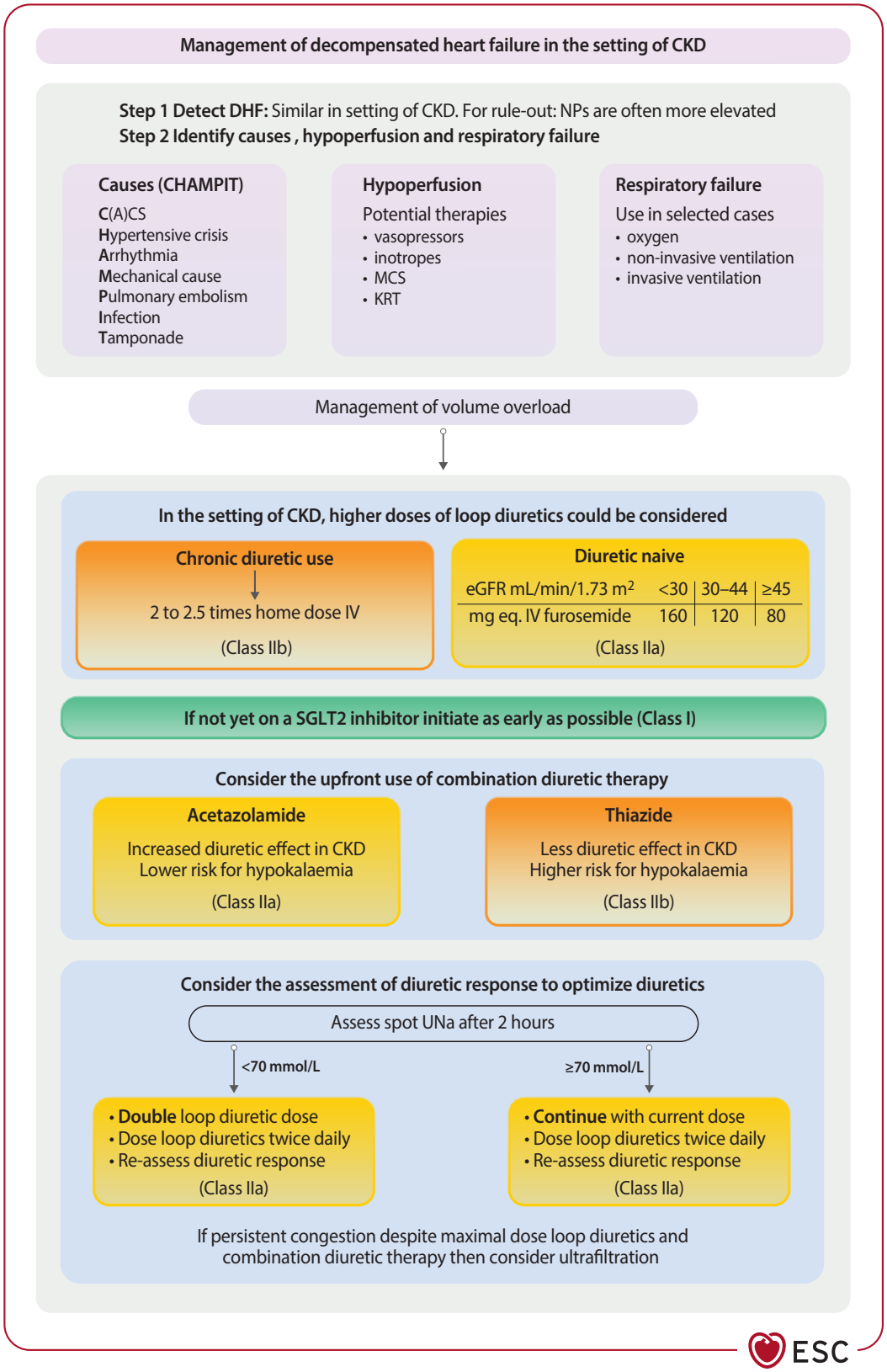

Figure 10 Management of decompensated heart failure in chronic kidney disease. ACS, acute coronary syndrome; CKD, chronic kidney disease; DHF, decompensated heart failure; eGFR, estimated glomerular filtration rate; IV, intravenous; KRT, kidney replacement therapy; MCS, mechanical circulatory support; NPs, natriuretic peptides; SGLT2, sodium glucose co-transporter 2; UNa, urinary sodium. The dose depicted relates to total daily dose

While under-dosing loop diuretics frequently causes residual congestion, true loop diuretic resistance can also occur in patients with DHF and CKD.[399] Diuretic combination therapy might overcome or prevent such loop diuretic resistance. As SGLT2 inhibitors are foundational therapies in patients with CKD or HF, most patients admitted with worsening HF will already be receiving an SGLT2 inhibitor. Early initiation of an SGLT2 inhibitor in DHF is safe and improves diuretic response.[400–403] In the Multicentre, Randomised, Double-blind, 90-day Superiority Trial to Evaluate the Effect on Clinical Benefit, Safety and Tolerability of Once Daily Oral EMPagliflozin 10 mg Compared to Placebo, Initiated in Patients Hospitalised for acUte Heart faiLure Who Have Been StabilisEd (EMPULSE), empagliflozin improved the hierarchical endpoint of death, HF admission, or a >5 point difference in change in Kansas City Cardiomyopathy Questionnaire (KCCQ) at 90 days, a finding which was consistent in patients with CKD.[387,404] Therefore, initiation should be considered as early as possible during an admission for DHF.

Administration of acetazolamide 500 mg intravenously for 3 consecutive days in the Acetazolamide in Decompensated Heart Failure with Volume Overload (ADVOR) trial resulted in a significantly larger proportion of patients achieving complete decongestion, more diuresis and natriuresis, and a shorter length of stay compared with placebo, and acetazolamide was not associated with electrolyte abnormalities.[405] In patients with a lower eGFR (<40 mL/min/1.73 m^2), acetazolamide resulted in greater natriuresis and diuresis than in patients with a higher eGFR.[388] In the Safety and Efficacy of the Combination of Loop with Thiazide-type Diuretics in Patients with Decompensated Heart Failure (CLOROTIC) trial, hydrochlorothiazide (dose adjusted to eGFR) added on top of loop diuretics, resulted in more weight loss than placebo; it was, however, associated with significantly more hypokalaemia.[406] In patients with CKD, hydrochlorothiazide was associated with a lower proportional treatment effect on weight loss compared with placebo.[389] Therefore, acetazolamide might be preferable in severe CKD.

6.3.2.3. Management of volume overload with other therapies

Vasodilators are often used to improve symptoms of congestion in patients with DHF, and are equally effective in CKD, although resistant hypertension is more common in CKD.[407] Inotropes are a treatment option in patients with CKD and DHF with signs and symptoms of hypoperfusion (cardiogenic shock). While milrinone and dobutamine showed a similar effect on a composite cardiovascular endpoint (which was mostly driven by in-hospital death from any cause) in the Dobutamine Compared with Milrinone (DOREMI) trial, the hypotensive effect of milrinone might be more pronounced in CKD.[408] If volume overload persists despite maximal diuretic therapy and haemodynamic optimization, or if severe metabolic alterations occur, haemodialysis or peritoneal dialysis, including dedicated ultrafiltration is a treatment option.[409]

Recommendation Table 17 — Management of patients with decompensated heart failure and chronic kidney disease (see Evidence Table 17)

Recommendations	Class[a]	Level[b]
Initiation of an SGLT2 inhibitor is recommended early during admission in patients with DHF and CKD with an eGFR >20 mL/min/1.73 m^2 to improve signs and symptoms of congestion and reduce the risk of HF re-hospitalization.[387,391,400–404]	I	B1
An initial intravenous diuretic dose >40 mg of furosemide-equivalent should be considered in patients with DHF with fluid overload and CKD (not on KRT) who are diuretic-naive to achieve sufficient diuretic response.[390,396]	IIa	B2
Upfront treatment with acetazolamide in addition to adequately dosed intravenous loop diuretic therapy should be considered in patients with DHF and CKD with an eGFR ≥20 mL/min/1.73 m^2 on chronic loop diuretic therapy to improve decongestion.[388,405]	IIa	B1
Assessment of diuretic response should be considered in patients with DHF and CKD (not on KRT) in the first days of hospitalization to optimize diuretic treatment and improve diuretic response.[390,396,397]	IIa	B1
Upfront treatment with thiazides in addition to adequately dosed intravenous loop diuretic therapy may be considered in patients with DHF and CKD (not on KRT) to improve decongestion.[389,406]	IIb	B1
An initial intravenous diuretic dose equivalent to 2.5-times the daily home loop diuretic dose may be considered in patients with DHF and CKD (not on KRT) on chronic loop diuretic therapy to improve dyspnoea relief, weight loss, and net fluid loss.[382]	IIb	C

CKD, chronic kidney disease; DHF, decompensated heart failure; eGFR, estimated glomerular filtration rate; HF, heart failure; KRT, kidney replacement therapy; SGLT2, sodium glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.

6.4. Monitoring kidney function in the treatment of heart failure

Several key treatments for management of decompensated or chronic HF alter eGFR over time, reflecting changes in filtration kinetics in the individual nephrons (rather than nephron damage or loss).[410] During successful decongestion in DHF, or titration of guideline-directed medicated therapy in chronic HF, the changes in eGFR when initiating RAAS inhibitors, SGLT2 inhibitors, and diuretics are not associated with a worse prognosis.[386,411]

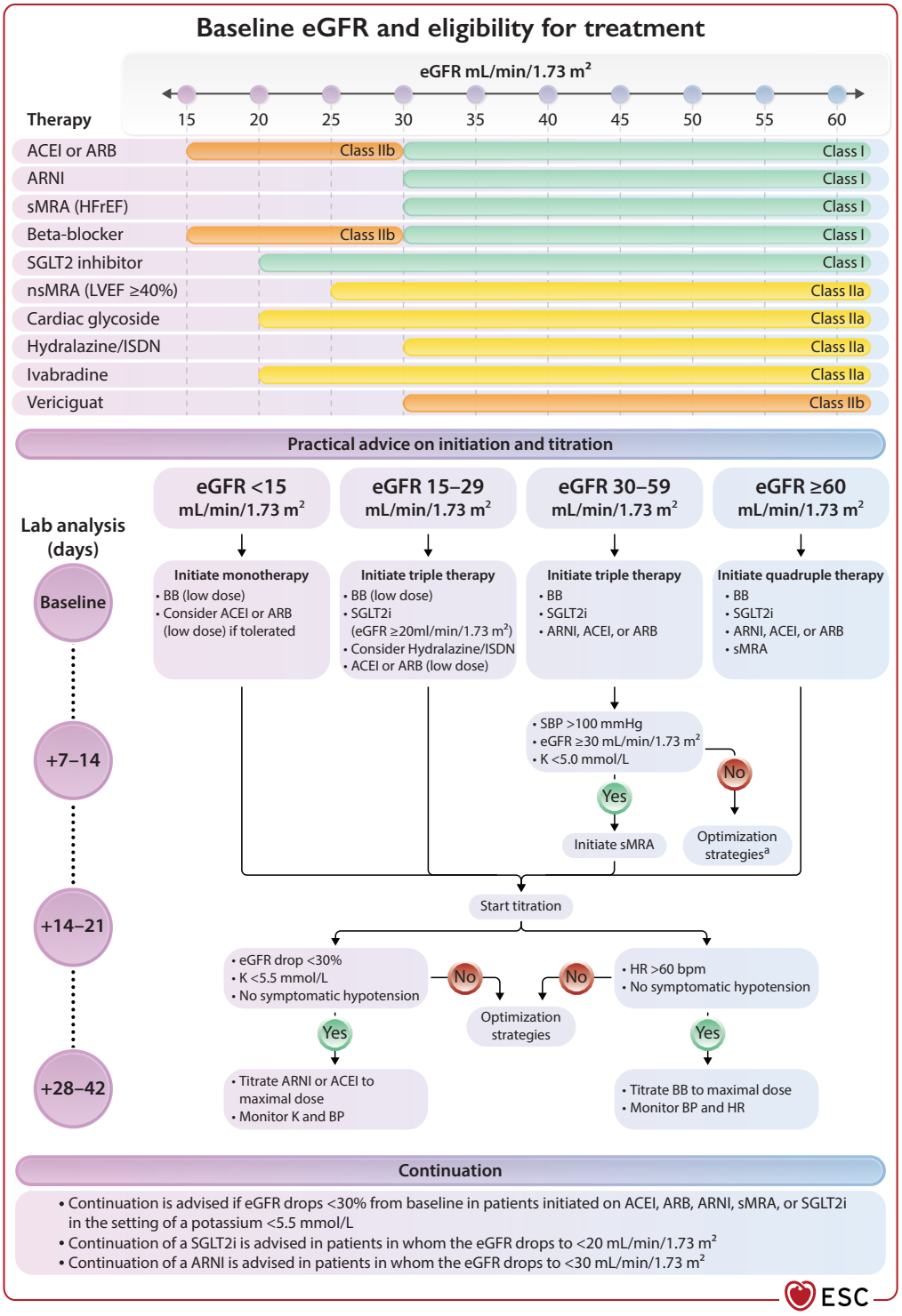

Figure 11 Monitoring kidney function in the treatment of chronic heart failure with reduced ejection fraction and chronic kidney disease. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; BB, Beta-blocker; BP, blood pressure; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; HR, heart rate; ISDN, isosorbide dinitrate; K, potassium; MRA, mineralocorticoid receptor antagonist; (ns)MRA, (non-steroidal) mineralocorticoid receptor antagonist; SBP, systolic blood pressure; SGLT2i, sodium glucose co-transporter 2 inhibitor. [a]Optimization strategies: (i) Low BP: stop other BP-lowering agents, assess volume status, possible low output state, (ii) Low eGFR: stop nephrotoxins, consider renal work-up (e.g. consider renal artery stenosis), (iii) Hyperkalaemia: if very high, perform ECG, consider lab mistake, stop potassium supplements, assess volume status, consider potassium binder, (iv) Low HR (<50 b.p.m.): perform ECG, consider stopping other HR-slowing drugs, take adequate measures if high degree artrioventricular block.

6.4.1. Monitoring kidney function in chronic heart failure

At the time of HF diagnosis, patients should undergo kidney function evaluation including serum creatinine (and eGFR), blood urea nitrogen, and electrolytes (sodium, potassium). Additionally, uACR should be measured given the prognostic relevance. *Figure 9* provides guidance on titrating therapies in patients with HF and CKD, which consists of: (i) assessing eligibility, (ii) initiating medical therapy based on kidney function, (iii) titrating, and (iv) continuation. In current practice, drugs are often initiated and titrated together. A more cautious approach could be applied in patients with moderate or severe CKD (e.g. eGFR <40 mL/min/1.73 m^2) given limited kidney reserve.[412] The Safety, Tolerability, and Efficacy of Rapid Optimization, Helped by NT-proBNP Testing, of Heart Failure Therapies (STRONG-HF) trial evaluated rapid up-titration of medical therapy and intensive follow-up. Such up-titration led to a lower risk of the composite outcome of HF admission or all-cause death.[413] *Figure 11* proposes an algorithm for titration in HFrEF patients with vs without CKD. When initiating and titrating ACEIs, ARBs, ARNIs, MRAs, and SGLT2 inhibitors, efforts should be made to continue these agents despite a dip in eGFR. Analysis from the EMPEROR programme illustrates that even after long-term use of empagliflozin, discontinuation is associated with an increased risk for cardiovascular death and HF hospitalization and worsening of functional status as measured by KCCQ.[414] Therefore, continuation of an SGLT2 inhibitor should be considered even if eGFR progresses to <20 mL/min/1.73 m^2.[414] Similar findings were observed with ARNIs, and continuation may also be considered if eGFR declines to <30 mL/min/1.73 m^2, provided generally that overall eGFR does not drop >50% from baseline.[340] Individualized decision-making is necessary considering aetiology, initial eGFR at diagnosis, clinical signs and symptoms, and potassium levels.

6.4.2. Monitoring kidney function in decompensated heart failure

Figure 12 provides an approach to creatinine changes occurring during DHF. Efforts should be made to measure diuretic response, adjust therapy where necessary, and attain complete decongestion, without prematurely terminating decongestive therapies in the face of pseudo-worsening renal function (decrease in eGFR with good diuretic response).

Recommendation Table 18 — Recommendations for management of heart failure therapy in the context of a drop in estimated glomerular filtration rate (see Evidence Table 18)

Recommendation	Class[a]	Level[b]
Chronic heart failure		
Continuation of a SGLT2 inhibitor should be considered in patients with HF and CKD in whom the eGFR progresses to <20 mL/min/1.73 m^2[c] to avoid worsening of HF.[414,415]	IIa	C
Continuation of an ARNI should be considered in patients with HF and CKD in whom the eGFR progresses to <30 mL/min/1.73 m^2[c] to avoid worsening of HF.[340]	IIa	C
Decompensated heart failure		
Continuation of decongestive therapy is recommended in congested patients with decompensated HF and CKD (not on KRT) who exhibit good diuretic response despite a rise in creatinine (up to 50%) to help achieve and maintain complete decongestion.[416]	I	C

ARNI, angiotensin receptor–neprilysin inhibitor; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; KRT, kidney replacement therapy; SGLT2, sodium glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.
[c]Overall eGFR drop needs to be <50% without hyperkalaemia >5.5 mmol/L.

6.5. Advanced heart failure and chronic kidney disease

6.5.1. Short-term mechanical circulatory support

The prevalence of AKI in the setting of cardiogenic shock is high, depending on the definition used, with the need for acute KRT reported in 6%–27% and oliguria being present in >50% of patients.[417] The Extracorporeal Life Support in Infarct-Related Cardiogenic Shock (ECLS-SHOCK) trial demonstrated no benefit in 30-day mortality with routine use of extracorporeal membrane oxygenation in patients with cardiogenic shock.[418] In the Danish–German Cardiogenic Shock (DanGerShock) trial, the use of a microaxial flow pump in the setting of non-resuscitated cardiogenic shock resulted in a lower risk of all-cause mortality. However, patients treated with a microaxial flow pump more frequently required KRT.[419] No data are available exploring the effect of baseline eGFR on treatment effect. Therefore, ideally a patient-centred multidisciplinary team-based discussion should consider the realistic goals of deploying or not deploying a short-term mechanical circulatory support (MCS) approach in patients with cardiogenic shock and severe CKD.

6.5.2. Heart transplantation and durable mechanical circulatory support

Data from the Registry Evaluation of Vital Information for VADs in Ambulatory Life (REVIVAL) indicates that 60% of patients with advanced HF have CKD.[420] A major challenge in patients with advanced HF being assessed for heart transplantation or durable MCS [left ventricular assist device (LVAD)] is determining whether a low eGFR is related to irreversible kidney damage or if it is a reversible feature secondary to the compromised haemodynamic state.[421] *Figure 13* provides a framework for dealing with pre-existing CKD in the setting of assessing eligibility for advanced HF therapies. Lower eGFR, proteinuria, structural kidney changes (e.g. small kidney size), and irreversibility of kidney function after haemodynamic optimization have been linked to poor outcomes after durable MCS.[422–425] Therefore, in patients with irreversible severe CKD, durable MCS should not be pursued as destination therapy. Similarly, in patients being evaluated for heart transplantation, international guidelines recommend assessing the need and eligibility for dual organ transplant (combined heart and kidney) in the presence of eGFR <30 mL/min/1.73 m^2.[426–428]

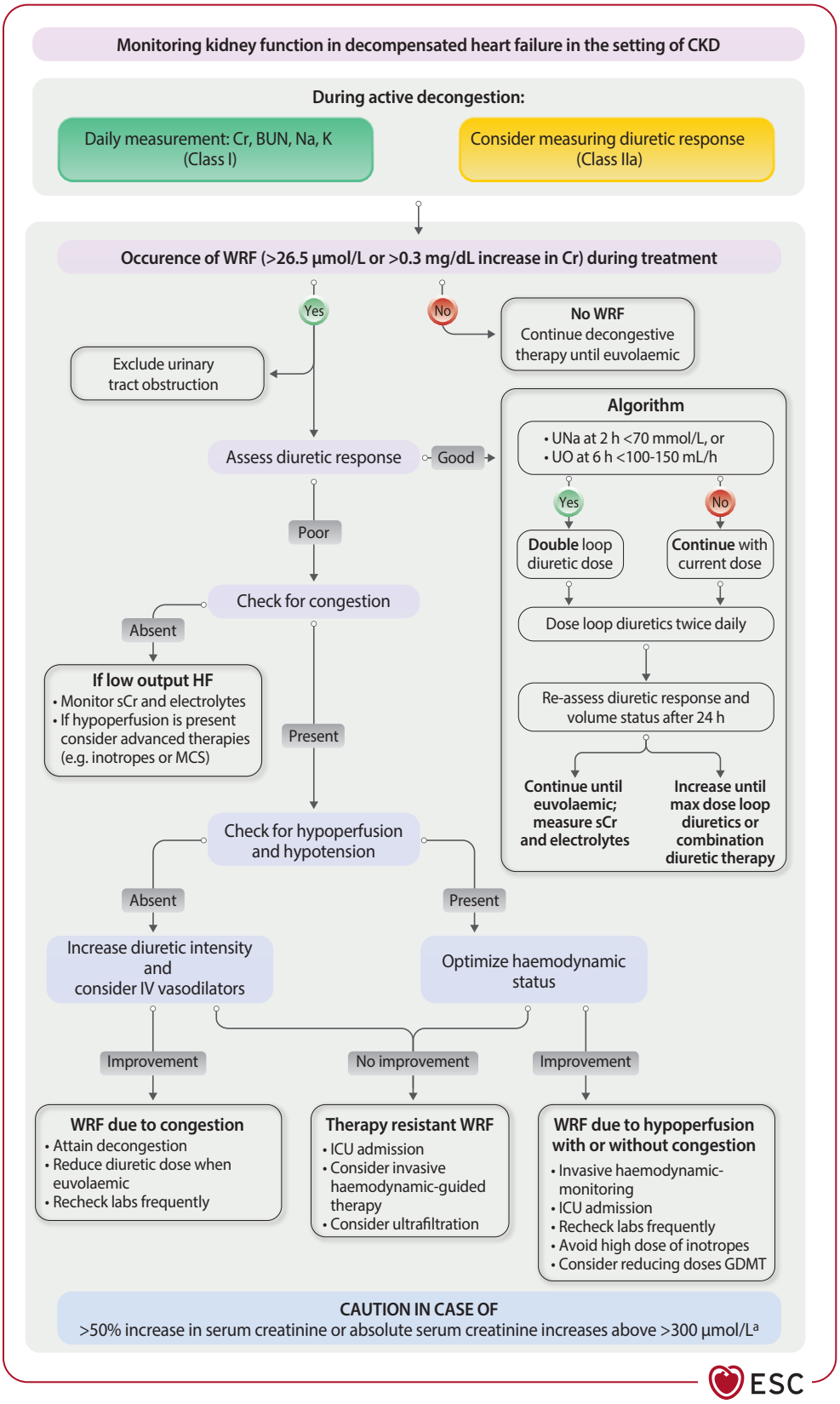

Figure 12 Monitoring kidney function in the treatment of decompensated heart failure and chronic kidney disease. BUN, blood urea nitrogen; sCr, serum creatinine; GDMT, Guideline-directed medical treatment; HF, heart failure; ICU, intensive care unit; IV, intravenous; MCS, mechanical circulatory support; UNa, urinary sodium; UO, urine output; WRF, worsening renal function. [a]300 µmol/L equals around 2.5 mg/dL (>50% increase in serum creatinine or absolute creatinine increases above >300 µmol/L)

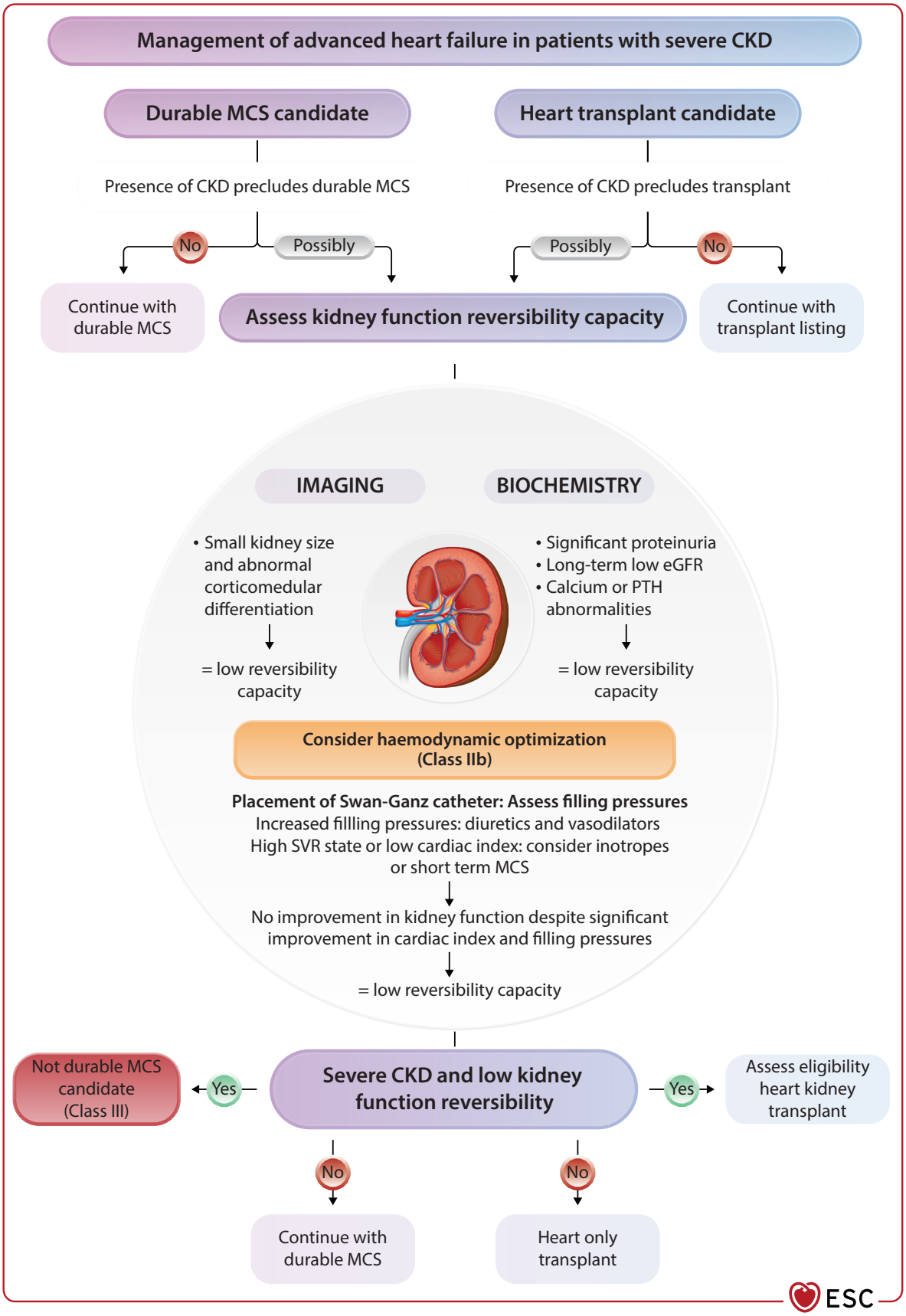

Figure 13 Advanced heart failure and chronic kidney disease assessment. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MCS, mechanical circulatory support; PTH, parathyroid hormone; SVR, systemic vascular resistance

In these patients, durable MCS may be an option to bridge the time on the transplantation waiting list. Retrospective data suggest that in patients with eGFR <30 mL/min/1.73 m^2 or requiring KRT, combined heart and kidney transplant is associated with better survival than heart transplant alone.[429–431] However, a major challenge of dual organ transplant is the rate of delayed kidney graft function of 27%–37% and a primary kidney graft failure rate of 14%–33%, which is significantly higher than for kidney transplant alone.[429–431] These challenges underscore the importance of multidisciplinary evaluation in patients with advanced HF and CKD.

Recommendation Table 19 — Management of patients with advanced heart failure and chronic kidney disease (see Evidence Table 19)

Recommendation	Class[a]	Level[b]
Evaluation by a heart–kidney transplant team should be considered in all patients with advanced HF eligible for heart transplant and a baseline eGFR <30 mL/min/1.73 m^2 to assess the need for dual organ transplant.[421]	IIa	C
A strategy of haemodynamic optimization (tailored approach of applying diuretics, inotropes, and short-term MCS based on invasive haemodynamics) may be considered in patients with CKD (not on long-term KRT) and advanced HF to assess eligibility for durable MCS or transplantation.[421]	IIb	C
Durable MCS is not recommended in patients with advanced HF with a baseline eGFR <30 mL/min/1.73 m^2 (which is unlikely to improve) who are not potential candidates for dual organ transplantation, to reduce the risk of death in this population.[432,433]	III	C

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; MCS, mechanical circulatory support; KRT, kidney replacement therapy.
[a]Class of recommendation.
[b]Level of evidence.

7. Atherosclerotic cardiovascular disease and chronic kidney disease

7.1. Chronic coronary syndrome

7.1.1. Clinical presentation and diagnosis

Chest pain characteristic of coronary disease is often absent in patients with CKD with chronic coronary syndromes (CCS).[434–437] Patients with moderate or severe CKD are more likely to present with acute MI than with stable angina as the first manifestation of CAD.[438] Approximately one in four patients with CKD report shortness of breath and cough as primary symptoms.[437] Diagnosing CAD in patients with CKD can be challenging due to the reduced sensitivity of diagnostics relative to those without CKD. Cardiac biomarkers are often observed in patients with CKD in the absence of MI, such that higher cut-offs or an acute change in biomarkers have been proposed to help distinguish MI from chronic elevations in symptomatic patients with CKD (see also *Section 7.2*).[439–441]

7.1.1.1. Non-invasive testing

The performance of non-invasive tests for detecting CAD has been best evaluated in patients with CKD during preparation for kidney transplantation. Functional testing appears to perform better as a prognostic rather than a diagnostic tool.[442] While the exercise electrocardiogram (ECG) shows poor performance [sensitivity 35%, specificity 64% compared with invasive coronary angiography (ICA)], stress echocardiography (physical or pharmacological stressor), myocardial perfusion scintigraphy [MPS, including positron emission tomography (PET)-derived measures], vasodilator stress testing (e.g. with dipyridamole or regadenoson), and coronary computed tomography angiography (CCTA) can all be used for reliably detecting or excluding abnormal myocardial perfusion or obstructive CAD.[442–446]

Stress echocardiography is associated with a higher rate of both false-positive and false-negative results in patients with CKD. Nevertheless, it demonstrates reasonable sensitivity (80%) and specificity (89%) for CAD, and may be superior to MPS (sensitivity 69%, specificity 77%).[442,447–449] Stress magnetic resonance imaging shows reasonable sensitivity (71%) and good specificity (98%), while dipyridamole radionuclide stress testing has high sensitivity (80%–86%) but lower specificity (73%–79%).[442,445,447,450] PET-derived measures like myocardial and coronary flow reserve are impaired in patients with CKD with normal regional perfusion and left ventricular function, mostly because of elevated rest flow, indicating microvascular dysfunction.[446] These measures decline as eGFR decreases. However, longitudinal assessments suggest that microvascular dysfunction in patients with CKD, independent of eGFR, is associated with an increased risk of adverse cardiovascular events, even before CAD becomes clinically apparent.[451–453]

In patients with CKD, CCTA appears to have similar sensitivity (96%) but lower specificity (66%) in comparison to data from non-CKD populations.[454] The diagnostic yield is reduced by extensive coronary calcification (blooming artefact) that is often present in patients with CKD. A key general limitation of CCTA is poor correlation between the severity of CAD and the extent of inducible ischaemia, which may be compounded in patients with CKD by coronary calcification.[455]

7.1.1.2. Invasive coronary angiography

In patients with CCS and CKD, ICA provides important prognostic information but is generally reserved for patients with persistent symptoms of CAD and/or a positive stress test in whom revascularization is considered. Observational analyses from the invasive strategy group of the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches–Chronic Kidney Disease (ISCHEMIA-CKD) trial found that, in patients with moderate or severe ischaemia, the extent of CAD on ICA was a predictor of the composite outcome of death or MI, with three-vessel disease associated with the highest risk.[456] In summary, for patients with CKD, an individualized approach to diagnostic imaging is recommended to detect CAD, assess risk, and triage patients for intervention, assessing the net absolute benefits and potential risks associated with different tests.

7.1.2. Management

Patients with CCS require medical intervention that involves secondary prevention, risk-factor modification, and decision-making regarding possible revascularization.[457] There are no dedicated RCTs assessing the role of antiplatelet therapy, beta-blockers, or other anti-anginal medications in patients with CKD and CCS, so management is based on guidelines extrapolated from general CCS patient populations.[457] There are, however, some specific areas that require consideration.

7.1.2.1. Antiplatelet therapy

Low-dose aspirin is recommended for patients with established ASCVD for secondary prevention of cardiovascular events.[457] A meta-analysis of 27 773 patients with CKD, with or without co-existing CAD, showed that treatment with antiplatelet agents, including aspirin and the $P2Y_{12}$ inhibitor clopidogrel, reduced the risk of major cardiovascular events by 15% [odds ratio (OR) 0.85, 95% CI 0.74–0.94] and dialysis access failure by 48% (OR 0.52, 95% CI 0.31–0.73), while increasing the risk of major bleeding by 33% (OR 1.33, 95% CI 1.11–1.59).[458] There was an overall net benefit: treatment of 1000 people with CKD with antiplatelet therapy for 1 year prevented 23 major cardiovascular events and caused 9 major bleeds. This may underestimate the absolute benefits in CCS, as only about one-third of patients included had CCS. Another Anti-thrombotic Treatment Trialists' Collaboration meta-analysis clearly demonstrated that, in the context of secondary prevention, the absolute benefits of antiplatelet therapy far exceed the risk of harm.[459] Antiplatelet therapy with either clopidogrel or low-dose aspirin is therefore recommended in patients with CCS and CKD to reduce the risk of major adverse cardiovascular events. Although head-to-head comparisons of clopidogrel vs aspirin for secondary prevention have not been performed specifically in patients with CKD, subgroup analysis of patients with CKD from a large systematic review and individual patient data meta-analysis indicate the superiority of clopidogrel over aspirin in reducing ischaemic events, without an increase in major bleeding.[460] Therefore, antiplatelet therapy with clopidogrel should be considered in preference to low-dose aspirin in patients with CCS and CKD with an eGFR >30 mL/min/1.73 m^2, without an indication for anticoagulation, to reduce the risk of major adverse cardiovascular events.

Patients with CKD are at increased absolute risk of bleeding with dual antiplatelet therapy (DAPT) compared with patients without CKD.[461,462] Patients with CKD who require DAPT should be treated according to the 2024 ESC Guidelines for the management of CCS.[457] These recommend minimizing the duration of DAPT following percutaneous coronary intervention (PCI) in patients at high bleeding risk, which applies to patients with CKD.[457] A recent meta-analysis of three RCTs evaluating 1 vs 3 months of DAPT after PCI with drug-eluting stents showed that 1 month of DAPT was associated with a similar risk of ischaemic events and a trend towards fewer bleeding events at 12 months after PCI, irrespective of CKD status.[463] Other studies confirm lower risk of bleeding with this strategy.[463–466] Adding the direct oral anticoagulant (DOAC) rivaroxaban at very low dose (2.5 mg b.i.d.) to antiplatelet therapy has an evidence base in patients with CKD and CCS with eGFR ≥30 mL/min/1.73 m^2. In the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial, this strategy led to a lower risk of the combined endpoint of cardiovascular death, stroke, or MI, with a particularly large effect on risk of stroke of ischaemic/uncertain aetiology.[467] Absolute benefits at eGFR <60 mL/min/1.73 m^2 were about twice the size of benefits among those with higher eGFR, and exceeded the absolute risk of major bleeding.[468]

7.1.2.2. Lipid-modifying therapy

Section 5 summarizes the data supporting a Class I recommendation for use of an intensive statin-based regimen shown to be safe in CKD in patients with eGFR <60 mL/min/1.73 m^2 not on KRT to reduce risk of major atherosclerotic events. Further risk reduction can be achieved by adding ezetimibe. Treatment with a PCSK9 inhibitor as add-on therapy should also be considered in patients with CCS and CKD (eGFR ≥20 mL/min/1.73 m^2) with LDL-C ≥70 mg/dL (≥1.8 mmol/L) or non-HDL-C ≥100 mg/dL (≥2.6 mmol/L), to reduce the risk of major adverse cardiovascular events. This statement is supported by subanalysis of the FOURIER and Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Effect of Alirocumab on the Occurrence of Cardiovascular Events in Patients Who Have Recently Experienced an Acute Coronary Syndrome (ODYSSEY OUTCOMES) trials where PCSK9 inhibitors, evolocumab and alicorumab, respectively, lowered risk, irrespective of baseline eGFR.[193,469] Inclisiran and bempedoic acid can also be used in mild-to-moderate CKD; however, there is insufficient RCT evidence to recommend use of PCSK9 inhibitors at eGFR <20 mL/min/1.73 m^2.

For patients with established ASCVD who, despite statin therapy, have a fasting triglyceride level 135–499 mg/dL (1.52–5.63 mmol/L) and LDL-C 41–100 mg/dL (1.06–2.59 mmol/L) with eGFR ≥30 mL/min/1.73 m^2, icosapent ethyl, compared with placebo, reduced major cardiovascular events.[470] Relative risk reductions were consistent across subgroups divided by eGFR at baseline, with absolute benefits largest in patients with eGFR <60 mL/min/1.73 m^2 by virtue of their higher baseline risk of CVD.[470]

7.1.2.3. Anti-anginal medication

Anti-anginal therapy should be individualized, taking into account underlying pathophysiology, resting heart rate, left ventricular function, concomitant medications, and comorbidities, including hypertension, AF, and previous MI.[457] In addition, the choice of anti-anginal medication must take eGFR into account, as the relative safety of anti-anginal drugs may not be consistent across the eGFR range.[471] Beta-blockers, CCBs, and long-acting nitrates are well established for use in CCS, but their effectiveness in patients with CKD has not been explored in dedicated RCTs. Since these drugs are considered generally safe from a kidney perspective, and patients with CKD were not excluded from the major studies of these common anti-anginal medications, it is reasonable to recommend their use even in the absence of CKD-specific trials.

A meta-analysis of eight trials demonstrated that beta-blockers reduce the risk of death in patients with CKD and HF (mainly due to CAD) similar to the effect in patients without CKD.[472] Depending on drug kinetics, dose adjustment may be required for some beta-blockers (e.g. atenolol, nadolol) but not others (e.g. bisoprolol, metoprolol, carvedilol), and low-dialysability beta-blockers (i.e. bisoprolol or propranolol) may be preferred to avoid under-treatment.[473]

Non-dihydropyridine CCBs are commonly used to treat angina in patients without left ventricular dysfunction or when angina is due to coronary spasm.[457] Dihydropyridine CCBs are often prescribed in addition to beta-blockers for patients who remain symptomatic despite beta-blockers.[457] CCBs are not usually used as first-line anti-hypertensive therapy in patients with CKD as, although they are effective at lowering blood pressure (and treating stable angina), they have less effect on albuminuria (and may increase it), raising uncertainty about renal effects.[474,475]

Long-acting nitrates are hepatically metabolized; therefore, may be safely used in patients with CKD, including those on haemodialysis. For other anti-anginal medications (ranolazine, ivabradine, nicorandil, and trimetazidine), subgroup analyses suggest that they may also be useful in patients with CKD. Ranolazine is an effective anti-anginal agent, but careful dose titration is recommended in patients with mild-to-moderate CKD (eGFR 30–60 mL/min/1.73 m^2) and should be avoided when eGFR is <30 mL/min/1.73 m^2.[476] Ivabradine may improve angina symptoms and exercise capacity, although data in patients with severe CKD are limited. Trimetazidine, when added to metoprolol, improves exercise tolerance in patients with CCS, although data in patients with CKD are lacking.[477]

7.1.2.4. Revascularization

The current randomized evidence supports the recommendation that in patients with CCS and CKD, an initial conservative strategy with optimal medical therapy is recommended to reduce the risk of death or non-fatal MI (with PCI reserved for patients whose clinical status deteriorates despite medical therapy).[478,479] A *post hoc* analysis of patients in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed that there was no difference in treatment effects between patients with and without CKD, albeit including only 16 patients with eGFR <30 mL/min/1.73 m^2.[480] The ISCHEMIA-CKD trial found that among 777 patients with CKD categories G4–5 (53% of whom were on dialysis) and moderate-to-severe ischaemia, there was no difference in the primary composite outcome of death or MI between the invasive vs medical therapy groups.[481] Revascularization also did not improve angina symptoms compared with a conservative strategy.[482] ISCHEMIA-CKD also demonstrated that an invasive strategy was associated with an increased risk of short-term harm, with a greater risk of stroke (HR 3.76, 95% CI 1.52–9.32) and the composite outcome of death or initiation of dialysis (HR 1.48, 95% CI 1.04–2.11).[481]

When considering revascularization options in patients with CKD, it is essential to consider the complexity of CAD and co-morbidities, anticipated technical limitations, likely long-term outcomes with PCI vs coronary artery bypass graft (CABG), the risks of contrast-induced AKI (CI-AKI), and life expectancy. Short- and long-term procedural risks of both PCI and CABG are greater among patients with CKD compared with those with normal kidney function. An individual patient level meta-analysis of randomized trials compared PCI with CABG in 3993 patients, of whom 526 had CKD G3–5.[483] This showed that, compared with PCI, CABG substantially reduced the risk of MI by 51% and repeat revascularization by 86% in patients with CKD, without impacting survival.[483] Possible superiority of CABG over PCI in patients with CKD and complex or multivessel CAD is also supported by other meta-analyses.[484,485] In patients with CKD, revascularization with PCI generally carries a lower procedural risk than CABG, while CABG offers better long-term outcomes, with fewer re-interventions.[486] Compared with patients with normal kidney function, CABG in patients with CKD carries a higher risk of peri-operative death and complications including stroke, re-operation, infection, prolonged hospitalization, and a new requirement for dialysis.[487] Individualized decision-making is therefore recommended to choose between PCI, CABG, or optimal medical therapy following multidisciplinary team decision-making, taking into account anatomical suitability, risks, technical limitations and benefits, and patient preferences. Due to more calcified CAD in patients with CKD, PCI is often more technically challenging, frequently requiring extensive lesion preparation and post-dilatation, and carries greater procedural risks, with higher rates of re-stenosis and stent thrombosis.[488–490] In these patients with complex CAD (multi-vessel and/or left main disease), CABG may be preferred over PCI. For PCI, a radial approach should be considered over a transfemoral approach, since it is associated with lower risks of AKI, bleeding, transfusion, and in-hospital mortality.[491,492] Care should be taken to avoid radial artery trauma, including use of alternative access, in patients with a contralateral fistula or at high risk of future kidney failure (to preserve arteries for future haemodialysis vascular access).

Recommendation Table 20 — Recommendations for management of chronic coronary syndromes in chronic kidney disease (see Evidence Table 20)

Recommendation	Class[a]	Level[b]
An individualized approach to diagnostic imaging is recommended in symptomatic patients with CKD, to detect obstructive CAD, improve risk stratification, and triage patients for intervention, balancing the relative benefits and potential risks associated with different diagnostic modalities.	I	C
Antiplatelet therapy with low-dose aspirin or clopidogrel is recommended in patients with CCS and CKD, without an indication for anticoagulation, to reduce the risk of major adverse cardiovascular events.[458,459]	I	C
Antiplatelet therapy with clopidogrel should be considered in preference to low-dose aspirin in patients with CCS and CKD with eGFR >30 mL/min/1.73 m^2, without an indication for anticoagulation, to reduce the risk of major adverse cardiovascular events.[460]	IIa	B1
A statin-based regimen with or without ezetimibe is recommended in patients with CCS and CKD not on dialysis, to reduce the risk of major atherosclerotic events.[184]	I	A

Continued

Treatment with a beta-blocker, calcium channel blocker, long-acting nitrate, or a combination of these, is recommended in patients with CCS and CKD for the relief of angina or equivalent symptoms.	I	C
An initial conservative strategy with optimal medical therapy is recommended in patients with CKD and CCS to reduce the risk of death or non-fatal MI.[480,481]	I	B1
Individualized decision-making regarding revascularization (PCI or CABG vs optimal medical therapy) and type of revascularization (PCI vs CABG) is recommended in patients with CCS and CKD, following multidisciplinary team decision-making, consideration of anatomical suitability, short- and long-term risks, technical limitations and benefits of each intervention, and patient preferences, to optimize clinical outcomes.	I	C
Treatment with a PCSK9 inhibitor as add-on therapy should be considered in patients with CCS and CKD (eGFR ≥20 mL/min/1.73 m^2) with LDL-C ≥70 mg/dL (≥1.8 mmol/L) or non-HDL-C ≥100 mg/dL (≥2.6 mmol/L) despite moderate- or high-intensity statin-based regimen with or without ezetimibe, to reduce the risk of major adverse cardiovascular events.[193,469]	IIa	B1
Ranolazine should be considered for patients with CCS and CKD with eGFR >30 mL/min/1.73 m^2, who remain symptomatic despite treatment with beta-blockers/calcium channel blockers/long-acting nitrates (especially if patients have a slow heart rate and low systolic blood pressure) for relief of angina or equivalent symptoms.	IIa	C
Abbreviated DAPT duration (1–3 months) should be considered for patients with CKD and CCS undergoing elective PCI, without an indication for anticoagulation, to reduce the risk of bleeding.[463–466]	IIa	B2
A radial approach should be considered over a femoral approach, when feasible, in patients with CKD (including those on KRT) undergoing PCI for CCS, to reduce the risk of bleeding and in-hospital mortality.[492]	IIa	C
Treatment with icosapent ethyl as add-on therapy to a statin may be considered in patients with CCS and CKD (eGFR ≥30 mL/min/1.73 m^2) with a fasting triglyceride level >1.5 mmol/L (>135 mg/dL) and LDL-C >1.04 mmol/L (>40 mg/dL) to reduce the risk of major adverse cardiovascular events.[470,493]	IIb	B1
Treatment with a statin-based regimen with or without ezetimibe may be considered in patients with CCS and CKD on dialysis, to reduce the risk of recurrent atherosclerotic events.	IIb	C
CABG may be considered in preference to PCI in patients with CKD and complex CAD (multi-vessel and/or left main disease), considering anatomical suitability, short- and long-term risks, technical limitations and benefits of each intervention, and patient preference, to reduce the long-term risks of MI and repeat revascularization.[483,485]	IIb	B2
Ivabradine may be considered in patients with CCS and CKD with eGFR ≥30 mL/min/1.73 m^2, to reduce angina frequency and improve exercise capacity in the setting of reduced left ventricular systolic function (LVEF <40%), especially if patients have a resting heart rate >70 b.p.m.	IIb	C
Trimetazidine may be considered in patients with CCS and CKD with eGFR >30 mL/min/1.73 m^2, in combination with beta-blockers and/or calcium channel blockers, in patients who remain symptomatic, for the relief of angina or equivalent symptoms.	IIb	C
Nicorandil may be considered in patients with CCS and CKD with any eGFR, including those on KRT, in combination with beta-blockers and/or calcium channel blockers, for the relief of angina or equivalent symptoms in patients who remain symptomatic.	IIb	C

CABG, coronary artery bypass graft; CAD, coronary artery disease; CCS, chronic coronary syndrome; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, primary coronary intervention; PCSK9, proprotein convertase subtilisin/kexin type 9.
[a]Class of recommendation.
[b]Level of evidence.

7.2. Acute coronary syndrome

The risk of acute coronary syndrome (ACS) increases substantially with increasing severity of CKD, and the prognosis associated with ACS is worse in patients with CKD.[494] *Vice versa*, many patients who present with ACS have some degree of CKD, with moderate-to-severe CKD present in >30% of patients with ACS.[495]

7.2.1. Clinical presentation and diagnosis

Patients with CKD and ACS may present in an atypical manner.[437] The severity of CKD influences clinical presentation, with the likelihood of having an MI without typical angina increasing as GFR decreases.[496] Data from the United States demonstrate that in patients with a serum creatinine >220 µmol/L, including those on dialysis, presenting with an MI, only ~40% presented with chest pain, with a large proportion exhibiting only non-specific changes on the initial ECG.[497] Other symptoms, such as dyspnoea, orthopnoea, or fatigue are also less specific, as many of these symptoms are also related to the volume status of the patient with CKD, especially those with kidney failure.[498] Left ventricular hypertrophy with strain pattern is also common in CKD, which may affect interpretation of diagnostic ST-segment abnormalities on ECG.[498] This may contribute to delayed or missed ACS diagnosis in patients with CAD and CKD.[497,499]

7.2.1.1. Biomarker assessment in patients with chronic kidney disease and suspected acute coronary syndrome

High-sensitivity cardiac troponin (hs-cTn) testing is now the gold standard to rule in/rule out MI, as a rise and/or fall in hs-cTn points towards a diagnosis of MI. Typically, algorithms rely on a baseline and follow-up troponin measurement.[500] Algorithms should be refined based on local assay and clinical practice.

In CKD, it is important to follow the pathways for diagnosing MI as set out by the ESC Guidelines on management of ACS and definition of MI in the Universal Definition of Myocardial Infarction.[500,501] Cardiac troponin concentrations are frequently elevated but stable in CKD. This partly reflects reduced clearance due to decreased GFR, but also possibly chronic myocardial disease or injury. Therefore, serial cardiac troponin testing is particularly important to differentiate acute from chronic cardiac troponin elevations when patients with CKD present with suspected ACS. The specificity and positive predictive value of the 99th percentile and high-risk thresholds are lower among patients with CKD.[440,502–505] However, no study has robustly and prospectively evaluated a dedicated adjusted troponin rule in/rule out pathway in patients with CKD. Therefore, there is no consensus on the use of adjusted thresholds in patients with CKD, which also would need to be assay specific. Clinicians need to realize that many patients with CKD who present with suspected ACS will have elevated troponin levels, that relying solely on this single measurement will lead to many false-positive ACS diagnoses, and that serial troponin testing in patients with CKD is important (particularly in severe CKD).

7.2.2. Management

Conventional, guideline-directed treatment to manage patients with ACS in the general population should also be employed in patients with CKD.[500]

7.2.2.1. Acute phase of acute coronary syndrome

Management of patients with CKD who present with ACS should be initiated according to the 2023 ESC Guidelines on the management of ACS for the general population. Guidance is focused on alleviating symptoms of ACS and evaluating risk to determine re-perfusion strategy and timing for invasive management (early and immediate) to improve long-term outcomes (*Figure 14*).[500]

7.2.2.2. ST-segment elevation myocardial infarction

For patients with CKD presenting with a working diagnosis of ST-segment elevation MI (STEMI), the goal should be to triage for an immediate re-perfusion strategy as soon as possible. It is not recommended to delay invasive re-perfusion therapy in patients with CKD, as the benefits associated with this immediate strategy far outweigh the AKI risk associated with the procedure. If KRT might be needed, contact services that can support provision of temporary KRT early, and continue to prioritize timely implementation of pharmacological and procedural interventions that are indicated to treat ACS. If a primary PCI strategy is chosen, contrast-sparing protocols and techniques are recommended in patients with eGFR <30 mL/min/1.73 m^2 to reduce the risk of CI-AKI. In addition, intravenous hydration in patients with ACS undergoing primary PCI with an eGFR <30 mL/min/1.73 m^2 may be considered (*Section 11*).

7.2.2.3. Non-ST segment elevation acute coronary syndrome

For patients with CKD presenting with a working diagnosis of NSTE-ACS, risk stratification is indicated according to current guidelines.[500] Patients with very high-risk features should be considered for an immediate invasive strategy, irrespective of CKD (see *Figure 8* in the 2023 ESC Guidelines on the management of ACS).[500] Although patients with CKD and NSTE-ACS should be considered at high risk independent of other factors, it is important to further risk stratify these patients to decide on the timing of an invasive strategy. Similar to the general population, patients with CKD who present with NSTE-ACS and have high-risk features [dynamic ST-segment or T-wave changes, transient ST-segment elevation, or Global Registry of Acute Coronary Events (GRACE) score >140] should be considered for an early invasive strategy (<24 h). For patients with ACS and CKD without other high-risk features, individual decision-making regarding the timing of angiography, and revascularization if needed, is reasonable.

7.2.2.4. Pharmacotherapy for acute coronary syndrome

Pharmacotherapy for ACS follows recommendations for the general population, as there is a paucity of data in patients with CKD. In the early phase of STEMI and primary PCI, anticoagulation therapy with unfractionated heparin is still the first choice, but bivalirudin is an alternative as, at least in one study, the risk of bleeding was lower with bivalirudin compared with unfractionated heparin, including in the subgroup of patients with eGFR 30–60 mL/min/1.73 m^2.[506] Data on enoxaparin vs unfractionated heparin in patients with CKD are lacking. In NSTE-ACS, initial anticoagulation therapy should follow the recommendations in the general population, as there are only sparse data on NSTE-ACS patients with CKD. The data published from larger trials showed similar results in CKD and non-CKD subgroups.[507–509] Of note, dose reduction may be required in patients with CKD (*Table 6* of the 2023 ESC Guidelines on the management of ACS).[500]

For antiplatelet therapy, the increased risk of bleeding and recurrent ischaemic events in patients with ACS and CKD is important for the choice, intensity, and duration of antiplatelet therapy, especially for maintenance therapy. In the Study of Platelet Inhibition and Patient Outcomes (PLATO) and Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction (TRITON-TIMI) 38 trials, ticagrelor and prasugrel were superior to clopidogrel in reducing major cardiovascular events, independent of baseline CKD status, while also leading to a slightly increased bleeding risk.[510,511] In the Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS) trial, no difference between prasugrel and clopidogrel for these outcomes was observed, irrespective of CKD status.[512] Analysis of patients with CKD enrolled in the Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment (ISAR-REACT) 5 trial showed no significant difference in bleeding between patients randomized to ticagrelor or

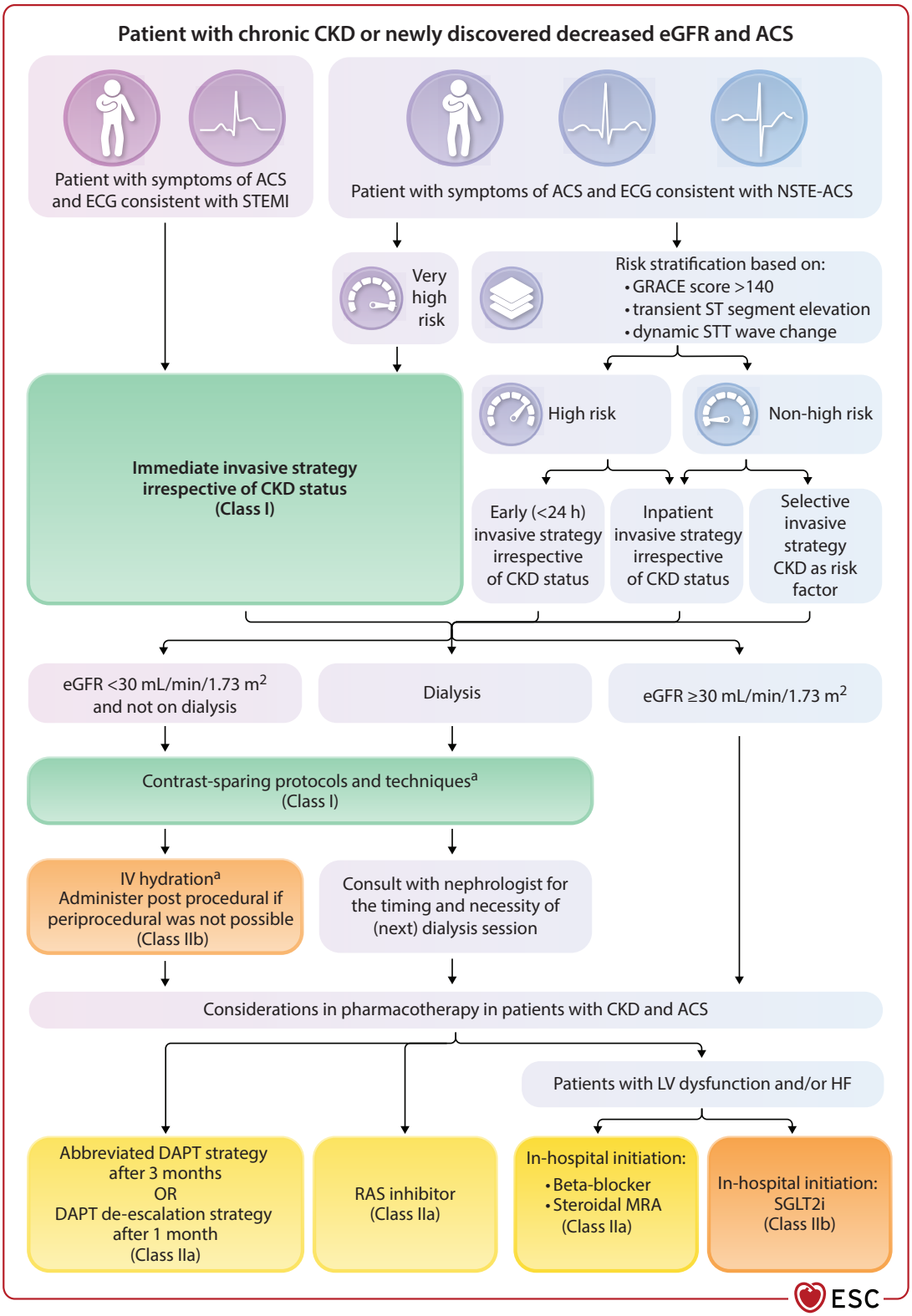

Figure 14 Algorithm for management of acute coronary syndrome in chronic kidney disease. ACS, acute coronary syndrome; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; IV, intravenous; LV, left ventricular; MRA, mineralocorticoid receptor antagonist; NSTE-ACS, non-ST elevation acute coronary syndrome; RAS, renin-angiotensin system; SGLT2i, sodium glucose co-transporter 2 inhibitor; STEMI, ST-elevation myocardial infarction. [a]*Section 11* (note that IV hydration is not required for dialysis patients)

prasugrel across all categories of decreased eGFR, although very few patients had eGFR <30 mL/min/1.73 m^2.[513] As patients with CKD have increased risk of bleeding with DAPT after ACS, they may be suitable candidates for either a strategy employing shorter duration of DAPT or de-escalation of DAPT (switching from prasugrel/ticagrelor to clopidogrel).[514,515] Trials of DAPT abbreviation that provide a subgroup analysis by baseline CKD status have shown that the benefit of reduced DAPT duration or intensity appears to extend to patients with CKD.[466,516,517] The best evidence is for DAPT abbreviation after 3 months followed by ticagrelor monotherapy, which reduces bleeding risk without increasing ischaemic events, including in patients with CKD.[514,515,518] There have been no dedicated RCTs in patients with CKD to assess the optimal antiplatelet monotherapy after DAPT. An individual patient data meta-analysis specifically assessing ticagrelor monotherapy after a short duration of DAPT showed similar rates of ischaemic events and lower bleeding risk both in patients with and without CKD, and independent of clinical presentation (ACS or CCS).[515] Therefore, single antiplatelet therapy with either aspirin or a $P2Y_{12}$ receptor inhibitor after 3 months should be considered in patients with CKD and ACS to reduce the risk of major bleeding. In an individual patient data meta-analysis of four non-inferiority trials, de-escalation was safe, led to slightly lower risk of ischaemic events, and lowered bleeding risk compared with conventional DAPT, irrespective of baseline CKD status.[519–522] Therefore, de-escalation of DAPT after 1–3 months should also be considered in patients with CKD and ACS to reduce the risk of bleeding. Individual assessment to gauge the risks of bleeding and ischaemic events should also guide decision-making when deciding on the duration of (combined) antiplatelet therapy in patients with concomitant indication for anticoagulation therapy with CKD.

Longer-term maintenance treatment after ACS follows the recommendations for CCS pharmacotherapy in *Section 7.1*. Patients with ACS and CKD differ from the general population as they are a very high-risk patient group, and as such, efforts should be made to start early and maximize therapies that provide long-term benefit in reducing cardiovascular events. These include high-intensity lipid lowering and ACEI therapy. In the ACEI Myocardial Infarction Collaborative Group individual patient data meta-analysis including ~100 000 patients with acute MI, ACEI therapy reduced risk of death by 7% (95% CI 2–11%; $P < .004$). Considering the inclusion and exclusion criteria and reported mean baseline kidney function (mean creatinine 97 µmol/L), a large proportion of these patients will have had decreased GFR, and this is also supported by real-world evidence and registry data.[523–525]

Furthermore, in patients with either left ventricular dysfunction (LVEF <50%) or HF complicating ACS, there is consistent evidence to support starting beta-blocker and steroidal MRA therapy early; although in the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) trial, the *P*-value (unadjusted for multiplicity) for effect modification of serum creatinine on the treatment effect of eplerenone on all-cause mortality was marginally significant.[326,336,526] Effects of steroidal MRAs on serum potassium levels need monitoring. Considering the totality of the evidence, including the evidence provided in HF (*Section 6*), in-hospital initiation of these therapies in patients with ACS and CKD and left ventricular dysfunction or HF should be considered to reduce the risk of important cardiovascular events.

Two trials have evaluated the effect of SGLT2 inhibitor treatment early after MI complicated by left ventricular dysfunction or HF. In the Dapagliflozin in Patients with MI (DAPA-MI) and the Study to Evaluate the Effect of Empagliflozin on Hospitalization for Heart Failure and Mortality in Patients with Acute Myocardial Infarction (EMPACT-MI) trials, neither dapagliflozin nor empagliflozin, respectively, reduced the combined endpoint of cardiovascular/all-cause death or HF re-admissions compared with placebo.[527,528] In the EMPACT-MI trial, there was reduced risk of HF re-admission independent of baseline CKD and diabetes status.[529,530] There are other benefits of SGLT2 inhibition in patients with CKD (see *Sections 5.5* and *6*) and, considering the safety and efficacy of SGLT2 inhibitor therapy in acute and chronic HF and CKD, SGLT2 inhibitor therapy may be considered in patients with ACS complicated by HF (or left ventricular dysfunction) and with CKD to reduce the risk of HF re-admission.

Recommendation Table 21 — Recommendations for acute coronary syndrome in chronic kidney disease (see Evidence Table 21)

Recommendation	Class[a]	Level[b]
Avoiding delays in immediate or early invasive strategies is recommended in patients with CKD with STEMI or NSTE-ACS with high or very-high risk to ensure timely treatment.	I	C
Early in-hospital treatment with an ACEI should be considered in patients with ACS and CKD with eGFR >20 mL/min/1.73 m^2 to reduce the risk of all-cause mortality.[523]	IIa	C
In-hospital initiation of beta-blocker and steroidal MRA treatment should be considered in patients with ACS and CKD[c] complicated by left ventricular dysfunction or HF to reduce the risk of cardiovascular events.[326,336]	IIa	B1
Abbreviated DAPT duration (3 months[d]) or DAPT de-escalation[e] after 1–3 months should be considered in patients with ACS and CKD without an indication for anticoagulation to reduce the risk of major bleeding.[464,514,515,519–522,531–533]	IIa	B1
In-hospital initiation of an SGLT2 inhibitor in patients with ACS and CKD with an eGFR >20 mL/min/1.73 m^2 complicated by left ventricular dysfunction or HF may be considered to reduce the risk of HF hospitalization.[527,528]	IIb	C

ACEI, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HF, heart failure; hs-cTn, high-sensitivity cardiac troponin; MRA, mineralocorticoid receptor antagonist; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; SGLT2, sodium glucose co-transporter 2; STEMI, ST-segment elevation myocardial infarction.
[a]Class of recommendation.
[b]Level of evidence.
[c]CKD with eGFR >20 or 30 mL/min/1.73 m^2 for beta-blocker and steroidal MRA therapy, respectively.
[d]With either aspirin or a $P2Y_{12}$ receptor inhibitor.
[e]Switching from prasugrel/ticagrelor to clopidogrel.

7.3. Peripheral arterial and aortic disease

Management of peripheral and aortic disease in CKD generally should follow standard approaches recommended by the 2024 ESC Guidelines for the management of peripheral arterial and aortic diseases,[534] with a few additional considerations. There is an increased risk of PAD in patients with CKD compared with the general population.[535,536] Ankle–brachial index (ABI) is used both at rest or after exercise for PAD diagnosis and surveillance. An ABI ≤0.90 confirms a diagnosis of PAD. Values >1.40 raise the possibility of 'non-compressible arteries' and are associated with arterial stiffness, which is common in patients with diabetes, CKD, and in older adults. In this situation, assessing resting toe–brachial index is recommended.[534,537] ABI is also a predictor of other CVD. Among patients with CKD, compared with patients without PAD, those with PAD have a two- to three-fold increased risk of cardiovascular morbidity and mortality, including MI, stroke, and mortality related to CAD. Therefore, a diagnosis of PAD in patients with CKD should trigger screening for other CVD in addition to intensive management of risk factors.[538]

The incidence of aortic aneurysms in patients with CKD is also higher compared with general populations.[539,540] CKD is not a classical indication for abdominal aortic aneurysm (AAA) screening, which can be performed without risk of CI-AKI by ultrasonography or non-enhanced abdominal computed tomography (CT). In Korean adults with CKD G4–5, the incidence of AAA is about 1.2 per 1000 patient-years, providing a possible argument for AAA screening in patients with eGFR <30 mL/min/1.73 m^2.[541] Data derived from European regions on AAA incidence by CKD stage are needed before recommending AAA screening according to eGFR. The risk of adverse outcomes 1 year after intervention (e.g. major amputation or death) in patients with PAD and CKD is high compared with patients with PAD without CKD. This is true for endovascular and open-surgical intervention, and for both chronic limb-threatening ischaemia (CLTI) and claudication. Re-stenosis requiring re-intervention is more common in patients with CKD after endovascular procedures, following both femoropopliteal and infra-inguinal interventions.[542–544] Similarly, CKD independently predicts poorer long-term prognosis after surgical or endovascular aneurysm repair for aortic aneurysms, with a clear trend to lower 1-year survival with worsening CKD stage.[545] To ensure patients with CKD and CLTI can benefit from revascularization, to reduce risk of post-operative complications, and to ensure other CVD is identified and managed appropriately, a multidisciplinary approach should be considered in patients with CKD and complicated CLTI.[546]

Recommendation Table 22 — Recommendations for diagnosis and management of peripheral artery disease in chronic kidney disease (see Evidence Table 22)

Recommendations	Class[a]	Level[b]
The addition of toe pressures and/or toe–brachial indices when testing for PAD is recommended in patients with CKD to diagnose the underlying disease and direct management.[547,548]	I	C
An individualized multidisciplinary treatment approach should be considered in patients with CKD and complicated chronic limb-threatening ischaemia to ensure CKD-related considerations are included in decision-making and to ensure patients with complicated comorbidity can benefit from revascularization, where indicated.	IIa	C
Screening for CVD in other vascular territories should be considered in patients with CKD undergoing aortic surgery or PAD revascularization to inform peri-procedural risk stratification and a holistic approach to management of CVD.	IIa	C

CKD, chronic kidney disease; CVD, cardiovascular disease; PAD, peripheral artery disease.
[a]Class of recommendation.
[b]Level of evidence.

7.4. Cerebrovascular disease

7.4.1. Stroke and transient ischaemic attack

The risk of stroke increases progressively and additively with decreasing GFR and increasing albuminuria.[549,550] This section focuses primarily on secondary prevention strategies in individuals with a history of atherothrombotic stroke or transient ischaemic attack (TIA). Much of the evidence for the prevention and treatment of stroke in CKD (*Recommendation Table 23*) is limited to *post hoc* analysis of RCTs or observational data.[551] Nevertheless, the task force suggest management of cerebrovascular disease in CKD generally follows standard approaches, with a few additional considerations (*Figure 15*).

In CKD, the net benefit of antiplatelet and antithrombotic therapies needs to be carefully counterbalanced with the higher bleeding risk in this population.[552] Also see *Section 9.1.2* for prevention of cardioembolic stroke in AF.

In CKD, there are no RCT data to alter the general population approach of DAPT for 1–3 months post-stroke/TIA and then long-term antiplatelet monotherapy. Key evidence is from extrapolation,[553] and *post hoc* analyses from two RCTs: Hypertension Optimal Treatment (HOT), testing aspirin 75 mg vs placebo in primary prevention, and Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE), testing clopidogrel at an initial dose of 300 mg, followed by 75 mg daily for 90 days, plus aspirin 75 mg daily for the first 21 days vs placebo plus aspirin 75 mg for 90 days post-TIA or minor stroke.[203,554,555]

Note that in patients with mild-to-moderate CKD (eGFR ≥30 mL/min/1.73 m^2) and CCS or PAD, the addition of rivaroxaban 2.5 mg b.i.d. (i.e. very low dose) to low-dose aspirin (e.g. 75–100 mg once daily) may be considered in patients, as it reduced the risk of stroke in the COMPASS trial.[468,552]

Statin-based therapy is associated with a ~20% reduction in ischaemic stroke risk per 1.0 mmol/L lowering of LDL-C, and thus, is recommended in patients with CKD (see *Section 5.3.2*).[175,177,181,182,184] In line with the 2024 ESC Guidelines for the management of elevated blood pressure and hypertension, treating to a target systolic blood pressure of 120–129 mmHg,

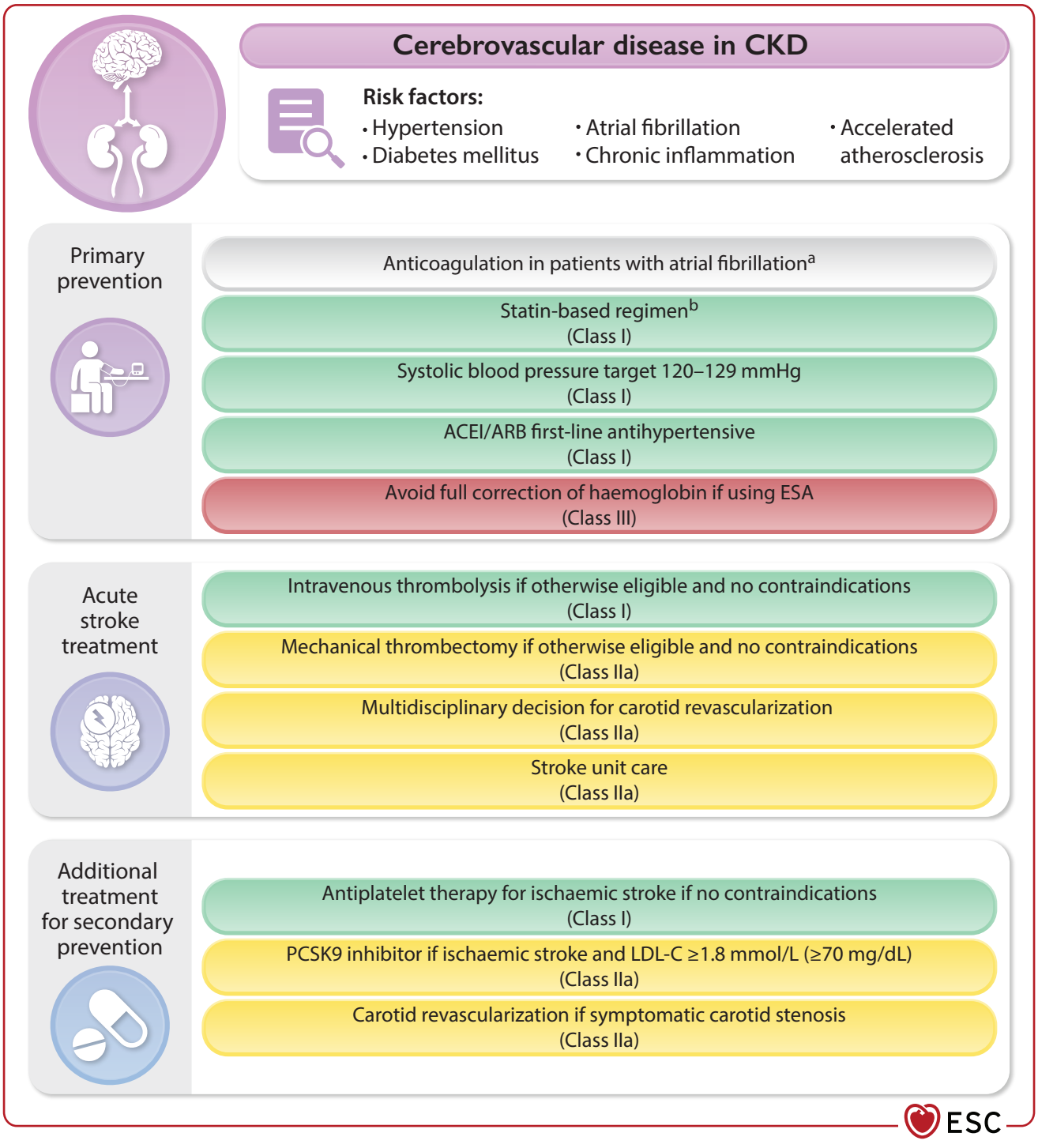

Figure 15 Prevention and management of stroke in chronic kidney disease. ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BP, blood pressure; CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agents; IV, intravenous; LDL-C, low-density lipoprotein–cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9. [a]See *Section* 9.1.2. [b]See *Section* 5.3.2

preferentially with an ACEI or ARB, is advised to reduce the risk of recurrent stroke.[97] In a *post hoc* analysis of the China Stroke Primary Prevention Trial, there was a nearly 50% reduced first stroke risk (HR 0.51, 95% CI 0.26–0.99) with a time-averaged systolic blood pressure <135 mmHg (compared with systolic blood pressure 135 to ≤140 mmHg).[556] In the Perindopril Protection Against Recurrent Stroke Study (PROGRESS), compared with placebo, perindopril reduced the risk of stroke by 35% (95% CI 17%–50%) in participants with CKD and a history of cerebrovascular disease.[557]

While carotid disease is highly prevalent in patients with CKD and associated with more unstable plaque morphology, there is a lack of well-powered RCT evidence on how best to treat patients with symptomatic high-grade stenosis.[558] Although there is a higher rate of peri-procedural complications associated with carotid endarterectomy, there was an 82% (95% CI 55%–93%) reduction in stroke risk for patients with CKD (not on KRT) in a *post hoc* analysis of the North American Symptomatic Carotid Endarterectomy Trial (NASCET).[559] Symptomatic patients on KRT who receive carotid interventions appear to have high risk profiles and poor long-term survival, leading to uncertainty regarding the net benefit of such treatment in this group.[560–562] More recent data from the Vascular Quality Initiative suggest that most patients may survive long enough to benefit from the potential stroke risk reduction provided by revascularization procedures.[563] Multidisciplinary team decision-making and judicious patient selection are key in this context. There are no RCT data to inform the decision regarding the choice of carotid endarterectomy vs carotid artery stenting in CKD.[560]

In the hyperacute setting, where indicated for acute ischaemic stroke, eligible patients with CKD (including those on KRT) should receive intravenous thrombolysis in the absence of contraindication.[564] Although there may be a higher risk of symptomatic intracerebral haemorrhage and mortality compared with the general population, the benefits in terms of favourable functional outcomes appear not to be abrogated in this group.[565–568] Similarly, mechanical thrombectomy is associated with a greater complication risk in patients with CKD compared with the general population, and CKD-specific RCT data have not been reported from trials to date.[569–571] As for antiplatelet and thrombolytic therapies, it is unlikely that the large benefits observed at a population level would be completely nullified at low eGFR and, therefore, otherwise-eligible patients with CKD and large-vessel occlusive stroke should be considered for intervention. Thrombolysis and mechanical thrombectomy can be a combined treatment approach.[572] After their initial treatment, where feasible, patients with CKD should be admitted to an acute stroke unit for further monitoring and rehabilitation. Patients on dialysis should have their dialysis delivery arranged to ensure they can benefit from rehabilitation, as outcomes after stroke are poor and there is evidence that acute stroke units are under-utilized in this population.[573]

7.4.2. Cognitive impairment

Cognitive disorders are also highly prevalent in patients with CKD, particularly in those with a history of CVD.[574,575] Subclinical or symptomatic cerebrovascular disease may contribute significantly to this burden as the cognitive phenotype is typically consistent with vascular cognitive impairment, and structural imaging often reveals features of cerebral small-vessel disease.[576,577] There are currently few evidence-based interventions for the prevention or treatment of cognitive impairment in CKD.[578–583]

Recommendation Table 23 — Recommendations for atherothrombotic stroke prevention and treatment in patients with cerebrovascular disease or other ASCVD, and chronic kidney disease (see Evidence Table 23)

Recommendations	Class[a]	Level[b]
Antiplatelet agents		
Antiplatelet therapy[c] is recommended in patients with CKD (including those on KRT) with a history of ischaemic stroke to reduce the risk of recurrent stroke.[203,553,554,584]	I	B2
The addition of anticoagulation with very low-dose rivaroxaban (2.5 mg b.i.d.) to low-dose aspirin (75–100 mg o.d.) may be considered in patients with CKD with an eGFR ≥30 mL/min/1.73 m^2, established ASCVD, and low risk of bleeding to reduce the risk of stroke.[468]	IIb	B1
Lipid-lowering therapy		
LDL-C lowering with statin-based therapy or a statin/ezetimibe combination regimen is recommended in patients with CKD not on dialysis and a history of ischaemic stroke to reduce the risk of recurrent stroke.[177,184,194]	I	A
Treatment with a PCSK9 inhibitor as add-on therapy may be considered in patients with a history of ischaemic stroke and CKD with an eGFR ≥20 mL/min/1.73 m^2 and LDL-C ≥70 mg/dL (≥1.8 mmol/L) or non-HDL-C ≥100 mg/dL (≥2.6 mmol/L) despite moderate- or high-intensity statin regimen, to reduce the risk of recurrent stroke.[193,469]	IIb	C
Anti-hypertensive therapy		
A systolic blood pressure target of 120–129 mmHg is recommended in patients with CKD (who are not on KRT) and a history of stroke to reduce the risk of recurrent stroke.[127,133,134,161,556,585]	I	C
The maximum tolerated dose of an ACEI or ARB is recommended as the first-line blood pressure lowering agent in patients with CKD (including those on KRT) and a history of cerebrovascular disease for the secondary prevention of stroke.[211,556,557,586]	I	B1
Carotid revascularization procedures		
Carotid endarterectomy should be considered in patients with CKD who have symptomatic high-grade carotid stenosis to reduce the risk of stroke.[559,560,587]	IIa	B2
Multidisciplinary team decision-making regarding carotid revascularization procedures should be considered in patients on KRT who have symptomatic carotid stenosis, given the higher peri-operative risk and lower long-term survival.	IIa	C

Continued

Routine carotid revascularization is not recommended over optimal medical treatment in patients with CKD (including those on KRT) and asymptomatic carotid stenosis to reduce stroke risk.[561]	III	B2
Erythropoiesis-stimulating agents		
The use of erythropoiesis-stimulating agents to achieve full correction of anaemia is not recommended in patients with CKD and anaemia (including those on KRT) to avoid increased risk of stroke.[71,588,589]	III	A
Hyperacute stroke therapies and interventions		
Treatment with intravenous thrombolysis is recommended in eligible patients with acute ischaemic stroke and CKD (including those on KRT) to reduce the risk of disability.[565–568,590]	I	B2
Treatment with mechanical thrombectomy should be considered in eligible patients with large-vessel occlusive stroke and CKD (including those on KRT) to reduce the risk of disability.[569–571,591]	IIa	C
Acute stroke unit admission after initial treatment should be considered in patients with acute ischaemic stroke and CKD (including those on KRT) for further monitoring and rehabilitation post-stroke.[573,592]	IIa	C

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; b.i.d., twice daily; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy; PCSK9, proprotein convertase subtilisin/kexin type 9.
[a]Class of recommendation.
[b]Level of evidence.
[c]DAPT (aspirin + clopidogrel) for 21–30 days then single antiplatelet (aspirin or other) thereafter. Alternative approaches should be considered in patients on oral anticoagulants.

8. Thromboembolic disease and chronic kidney disease

8.1. Risk of venous thromboembolism

Patients with CKD are at an increased risk of developing VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE).[593] In patients with nephrotic syndrome, risk of VTE is particularly high and requires expert nephrological consultation. The risk increases as CKD advances; even mildly decreased GFR is associated with higher risk of VTE compared with the general population. In individuals with kidney failure on maintenance KRT, the risk of VTE is more than double that of the general population.[594] Patients with CKD are also at increased risk of VTE complications, including bleeding.[595]

The increased risk of VTE in patients with CKD can be attributed to several factors.[596] Management of such risk typically entails assessing individual risk factors, considering prophylactic measures in high-risk scenarios such as orthopaedic surgery and nephrotic syndrome,[34] and using anticoagulant therapy while balancing the risk of bleeding according to the specific clinical setting.

8.2. Management of venous thromboembolism

Anticoagulant treatment is recommended to treat VTE and prevent recurrence and should be the standard of care in all patients, including those with severe CKD.[597] It is typically characterized by an intensive initial phase followed by a maintenance phase. The duration of anticoagulant therapy is based on an assessment of the presence (either reversible or persistent) or the absence (unprovoked) of risk factors for VTE in all patients.[598] The selection of the specific anticoagulant drug needs to consider patient preference, other concomitant medications, pharmacokinetic properties, and the relative efficacy and safety of DOACs compared with conventional low molecular-weight heparin (LMWH) and vitamin K antagonist (VKA) therapy. Factor Xa inhibitors with appropriate dose adjustment can be prescribed for the treatment of VTE in all patients with CKD, including those with eGFR <30 mL/min/1.73 m^2, unless contraindicated by other conditions (*Figure 16*).[599] RCTs have shown that DOACs are non-inferior to VKAs in reducing the risk of recurrent VTE in patients with mild-to-moderate CKD.[600–604] From a safety perspective, in the open-label EINSTEIN programme (consisting of the Acute DVT Study, the Acute PE Study, and the Continued Treatment Study), which compared a fixed-dose of rivaroxaban with an enoxaparin/VKA regimen, risk of major bleeding was 46% lower (HR 0.54, 95% CI 0.37–0.79) in the DOAC group, with a suggestion of larger benefits at decreased GFR (interaction P = .03).[603] There remains limited RCT data with DOAC therapy in patients with eGFR <30 mL/min/1.73 m^2. It has not been confirmed that a better safety profile of DOACs compared with VKAs extends to patients with severe CKD or those on KRT.[605] There are theoretical concerns about accelerated vascular calcification and calciphylaxis associated with VKA use in patients with kidney failure, which encourages preferential use of DOACs.[606]

Although early RCTs with DOAC therapy excluded[600–603] or enrolled very few[604] patients with eGFR <30 mL/min/1.73 m^2, anticoagulation treatment with DOACs may be considered in patients with CKD and eGFR 15–29 mL/min/1.73 m^2 or on KRT if the decision is made to anticoagulate to treat VTE and prevent recurrence. This is based on pharmacokinetic data, which supports dose adjustment at low eGFR[607,608] and reassuring RCT safety data from use of DOACs compared with VKAs in moderate CKD.[601,602,604,605,609,610] Two small RCTs in patients with AF on haemodialysis—including the Renal Hemodialysis Patients Allocated Apixaban Versus Warfarin in Atrial Fibrillation (RENAL-AF) and Compare Apixaban and Vitamin K Antagonists in Patients With Atrial Fibrillation and End-Stage Kidney Disease (AXADIA-AFNET 8) trials—demonstrated similar bleeding risks between apixaban and VKA,

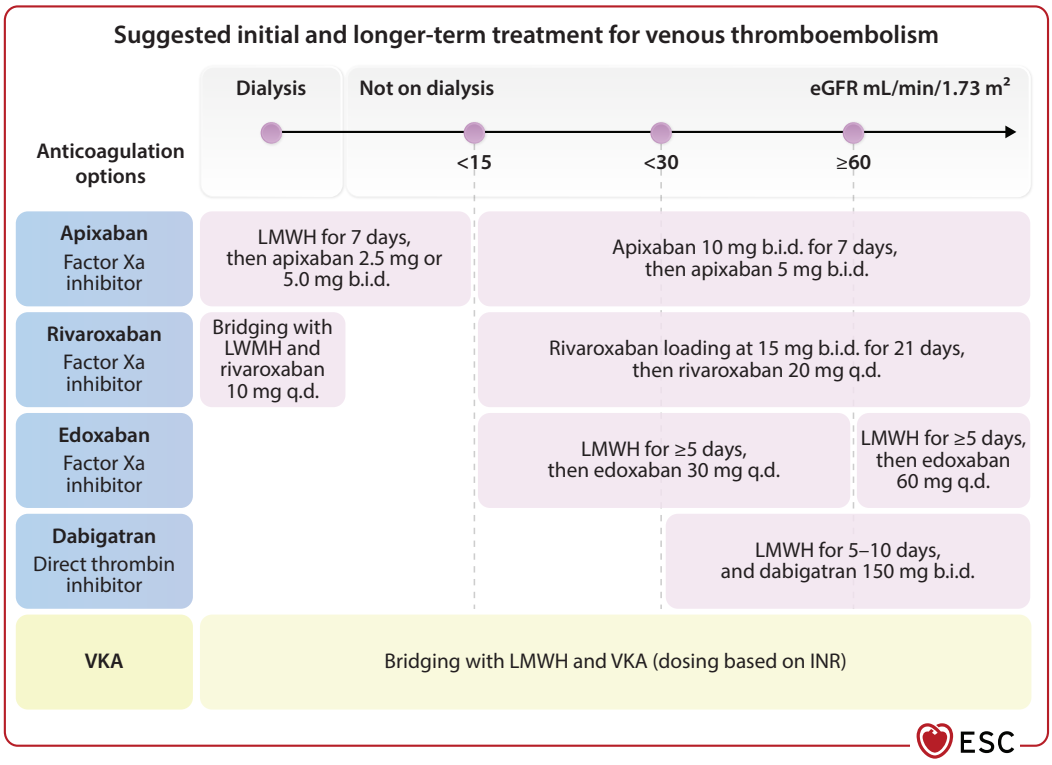

Figure 16 Suggested initial and longer-term treatment for venous thromboembolism. b.i.d., twice daily; BSA, body surface area; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; INR, international normalized ratio; KRT, kidney replacement therapy; LMWH, low molecular weight heparin; q.d., once a day; VKA, vitamin K antagonist. Treatment options shown to be considered when the decision has been made to anticoagulate. Doses at eGFR <30, and particularly <15 mL/min/1.73 m^2, are suggested due to limited information. Always consult product summaries and local prescribing advice/experts in severe CKD and kidney failure. Apixaban 5 mg b.i.d. may also be used in patients with eGFR <15 who are on dialysis to treat venous thromboembolism when weight >60 kg and age ≤80 years. eGFR is indexed to 1.73 m^2 of BSA, which results in important limitations when used for drug dosing in patients with high or low BSA (see *Section 3.4*). A simple approach is to de-index routine eGFR value from estimated BSA (e.g. when estimated BSA is 2.31 m^2 then multiplying eGFR by a factor of 2.31/1.73). For LMWH dose reduction and anti-Xa–guided titration is necessary when eGFR <30 mL/min/1.73 m^2; if anti-Xa monitoring is not available or bleeding risk is high, unfractionated heparin is an option

although the overall bleeding risk was high with both agents.[611,612]

For patients with eGFR <15 mL/min/1.73 m^2 not on dialysis, there is limited evidence to guide anticoagulant choice. Data supporting factor Xa inhibitors over VKAs or LMWH rely on available experience—primarily with apixaban in severe CKD and dialysis cohorts.[603,605,610] Other factor Xa inhibitors have been less well studied in these patients. Therefore, if the decision is made to start anticoagulation in these patients, considering available observational evidence, using either a VKA or low-dose apixaban (after initial LMWH) may be considered in patients with eGFR <15 mL/min/1.73 m^2 not on dialysis. See also *Section 9.1.2* and *Figure 17*.

Recommendation Table 24 — Recommendations for the treatment of venous thromboembolism in patients with chronic kidney disease (see Evidence Table 24)

Recommendations	Class[a]	Level[b]
Anticoagulant treatment with DOACs (oral factor Xa or direct thrombin inhibitors) is recommended over treatment with LMWH and a VKA in patients with CKD with an eGFR ≥30 mL/min/1.73 m^2 for the treatment of VTE and prevention of recurrent VTE.[600–604,613]	I	B2
Anticoagulant treatment with oral factor Xa inhibitors may be considered instead of conventional treatment with LMWH and a VKA in patients with CKD and an eGFR 15–29 mL/min/1.73 m^2 if the decision is made to anticoagulate for the treatment of VTE and prevention of recurrent VTE.[603,604,607,608]	IIb	C

Continued

Anticoagulant treatment with either a VKA or low-dose apixaban (2.5 mg b.i.d.) may be considered in patients with CKD and an eGFR <15 mL/min/1.73 m^2 who are not receiving dialysis if the decision is made to anticoagulate for the treatment of VTE and prevention of recurrent VTE.	IIb	C
Anticoagulant treatment with oral factor Xa inhibitors may be considered instead of conventional treatment with LMWH and a VKA in patients with CKD on dialysis if the decision is made to anticoagulate for the treatment of VTE and prevention of recurrent VTE. [603,604,607,608]	IIb	C

CKD, chronic kidney disease; DOAC, direct oral anticoagulants; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy; LMWH, low molecular-weight heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism.
[a]Class of recommendation.
[b]Level of evidence.

9. Arrhythmias, sudden death, and chronic kidney disease

9.1. Atrial fibrillation

9.1.1. Screening and risk assessment

There is an increased risk of incident AF in patients with CKD. Compared with people with normal kidney function, risk of AF increases progressively from about 50% higher risk at eGFR 30–59 mL/min/1.73 m^2 to 2.4-times higher when eGFR is <30 mL/min/1.73 m^2.[614] In a systematic review of 25 studies, the prevalence of AF in patients on KRT was 11.6%, with a range of 4.5%–27%.[615] Therefore, opportunistic screening (e.g. during clinic attendance) by pulse taking and/or ECG may be considered in all patients with decreased GFR to enable earlier diagnosis and potential treatment.

Patients with CKD and AF are also at higher risk of stroke compared with patients with AF without CKD.[616] This risk increases by five-fold in those with CKD who also have albuminuria (A3).[617] Patients with CKD and AF should therefore be considered at high risk of ischaemic stroke for the purposes of thromboprophylaxis decision-making. Established risk prediction tools to quantify stroke risk in individuals with AF in the general population include $CHADS_2$, CHA_2DS_2-VASc, and more recently, CHA_2DS_2-VA. These scores have poor discrimination and predictive performance (c-statistics ranging from 0.49 to 0.68) in patients with severely decreased eGFR or kidney failure (eGFR <30 mL/min/1.73 m^2) and particularly in patients on KRT.[618–624] This is in part likely due to the exclusion of those with eGFR <30 mL/min/1.73 m^2 from the derivation of most of these scores.[623] Scores that have incorporated more nuanced measures of kidney function, such as eGFR or proteinuria also do not accurately predict risk of ischaemic stroke in severe CKD.[619,622]

Similarly, traditional bleeding risk-assessment tools and scores to evaluate patients at high bleeding risk, such as HAS-BLED, ATRIA, HEMORR2HAGES, and ORBIT, perform poorly in patients with severely decreased eGFR or kidney failure.[625,626] Therefore, it is not recommended to use existing stroke and bleeding risk-assessment tools in patients with eGFR <30 mL/min/1.73 m^2, even if they include kidney parameters. Such patients should always be considered at high risk of stroke, systemic thromboembolism, and major bleeding. Although new CKD-specific prediction tools are required to better counterbalance the benefits and risks of anticoagulation in this group, many studies describe a general trend to under-treat these patients, which should be taken into account in clinical decision-making.[622,627]

Recommendation Table 25 — Recommendations for atrial fibrillation screening and risk prediction in chronic kidney disease (see Evidence Table 25)

Recommendations	Class[a]	Level[b]
Opportunistic screening for AF by pulse taking or ECG may be considered in patients with CKD (including those on KRT) for earlier detection of AF.[614,615,624]	IIb	C
Existing ischaemic stroke risk scores are not recommended for use in patients with AF and CKD with an eGFR <30 mL/min/1.73 m^2 even if they include kidney parameters due to poor predictive performance.[619–625,628]	III	B
Existing bleeding risk scores are not recommended for use in patients with AF and CKD with an eGFR <30 mL/min/1.73 m^2 even if they include kidney parameters due to poor predictive performance.[625,626]	III	C

AF, atrial fibrillation; CKD, chronic kidney disease; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy.
[a]Class of recommendation.
[b]Level of evidence.

9.1.2. Anticoagulation

It is encouraged to implement the general recommendations to avoid stroke and thromboembolism, and minimize bleeding risk associated with anticoagulation from the 2024 ESC Guidelines for the management of AF,[629] particularly for patients with AF, CKD, and eGFR ≥30 mL/min/1.73 m^2. The 2024 Guidelines for the management of AF recommend oral anticoagulation in patients with AF and a CHA_2DS_2-VA score of ≥2. Anticoagulation should also be considered for a CHA_2DS_2-VA score of 1. As hypertension is so prevalent, the default position will usually be to offer anticoagulation to patients with decreased eGFR. There is consistent evidence from pooled RCT data that DOACs are superior to VKAs for preventing stroke, systemic thromboembolism, and major bleeding events in patients with CKD and eGFR ≥30 mL/min/1.73 m^2.[630,631] In a recent pairwise network meta-analysis of 170 059 participants with CKD, DOACs (both factor Xa and direct thrombin inhibitors) reduced risk of thromboembolic and bleeding events by 14% (95% CI 5%–22%) and 19% (95% CI 1%–34%) compared with VKAs, respectively.[630] A DOAC is therefore recommended in

preference to a VKA in patients with CKD and AF and eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of stroke, systemic thromboembolism, and bleeding.

For patients with eGFR 15–29 mL/min/1.73 m^2 there is less evidence to support such a strong recommendation, as only a limited number of patients within this eGFR range has been included in RCTs. Importantly, only trials with factor Xa inhibitors have been conducted with eGFR <30 mL/min/1.73 m^2. Therefore, if the decision has been made to anticoagulate after balancing individualized risk of thromboembolic events and bleeding, factor Xa inhibitors should be considered in preference to VKAs in patients with CKD and AF (eGFR 15–29 mL/min/1.73 m^2) to reduce the risk of stroke, systemic thromboembolism, and bleeding.[630,632,633]

No RCT evidence exists for the subgroup with eGFR <15 mL/min/1.73 m^2 not on dialysis. Individualized clinical decision-making must dictate whether to anticoagulate in this patient population. If the decision is made to anticoagulate, reassuring observational data suggest apixaban at a reduced dose (2.5 mg b.i.d.) or a VKA are possible treatment options.[634] Risk–benefit assessment regarding risk of thromboembolic stroke and bleeding in these patients should be highly individualized.

Decision-making regarding anticoagulation therapy in patients with AF on KRT is similarly challenging. Observational studies have reported associations between VKA use and stroke that suggest attenuated or no prophylactic effects on ischaemic stroke, and even suggest that the use of VKAs is associated with increased risk of stroke in these patients.[635,636] Substantial residual confounding may explain these observational associations, in part due to the comorbidity of patients on dialysis. There are, however, theoretical effects of VKAs on vascular calcification that might prompt cautious use of VKAs.[637,638] Successful pilot trials will hopefully lead to definitively powered RCTs, as samples sizes of existing trials have been insufficient to assess effects on stroke and major bleeding events.[611,612,639,640]

In the absence of large outcome trials, individualized clinical decision-making about anticoagulation should be considered in patients with AF and eGFR <15 mL/min/1.73 m^2 on KRT to balance the benefits and risks.[611,639,641] Where anticoagulation is offered, experience suggests factor Xa inhibitors appear to have a reasonable safety profile and may therefore be considered preferentially over VKAs (e.g. low-dose apixaban 5 mg b.i.d. unless target weight ≤60 kg or age ≥80 years, when 2.5 mg b.i.d. should be used).

Left atrial appendage occlusion (LAAO) devices are used to lower the thromboembolic risk in those with absolute or relative contraindications to long-term oral anticoagulation, but patients with CKD have often been under-represented or excluded from clinical trials.[642,643] Observational data suggest peri-procedural risks (e.g. in-hospital mortality, AKI, pericardial effusion/tamponade, and major bleeding events) are higher in patients with CKD.[644–648] The Left Atrial Appendage closure in patients with non-valvular AF and end-stage chronic KIDNEY disease (LAA-KIDNEY) trial (NCT05204212) is a multicentre RCT currently under way, designed to compare the efficacy of LAAO vs best medical care specifically in patients with non-valvular AF and kidney failure. Contrast-free closure is also being explored as a potentially safer option for those with severe CKD.[649]

Recommendation Table 26 — Recommendations for anticoagulation for prevention of systemic embolism and stroke in patients with atrial fibrillation and chronic kidney disease (see Evidence Table 26)

Recommendations	Class[a]	Level[b]
Anticoagulation treatment with a DOAC is recommended in preference to a VKA in patients with AF and CKD with an eGFR ≥30 mL/min/1.73 m^2 to reduce the risk of stroke, systemic thromboembolism, and bleeding.[630,631]	I	A
Anticoagulation treatment with an oral factor Xa inhibitor should be considered in preference to a VKA in patients with AF and CKD with an eGFR 15–29 mL/min/1.73 m^2 to reduce the risk of stroke, systemic thromboembolism, and bleeding.[630,631]	IIa	B1
Individualized clinical decision-making regarding anticoagulation should be considered for patients with AF and an eGFR <15 mL/min/1.73 m^2, including those on KRT, to balance the benefits and risks in this population.[611,612,630,631,635,636,639,650,651]	IIa	C
Anticoagulation with a VKA or apixaban at a reduced dose (2.5 mg b.i.d.) may be considered for patients with AF and an eGFR <15 mL/min/1.73 m^2 who are not receiving dialysis if the decision is made to anticoagulate to reduce the risk of stroke and systemic thromboembolism.[630,631,635,651]	IIb	C
Anticoagulation with low-dose oral factor Xa inhibitors[c] may be considered preferentially over VKAs in patients with AF and an eGFR <15 mL/min/1.73 m^2 who are on dialysis if the decision is made to anticoagulate to reduce the risk of stroke, systemic thromboembolism, and bleeding.[611,612,639,650]	IIb	C

AF, atrial fibrillation; b.i.d., twice daily; CKD, chronic kidney disease; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.
[c]Particularly low-dose apixaban 5 mg b.i.d. unless target weight ≤60 kg or age ≥80 years, when use 2.5 mg b.i.d.

9.1.3. Pharmacotherapy and other interventions to control rate or rhythm

Patients with CKD and AF can be managed with rate or rhythm control, in line with the 2024 ESC Guidelines for the management of AF, although some special considerations apply.[629]

When deciding on rate or rhythm control in patients with CKD, consideration should be given to: (i) potential side effects/toxicity of anti-arrhythmic drugs (AADs) in the CKD population, particularly those on dialysis; (ii) pro-arrhythmic effects

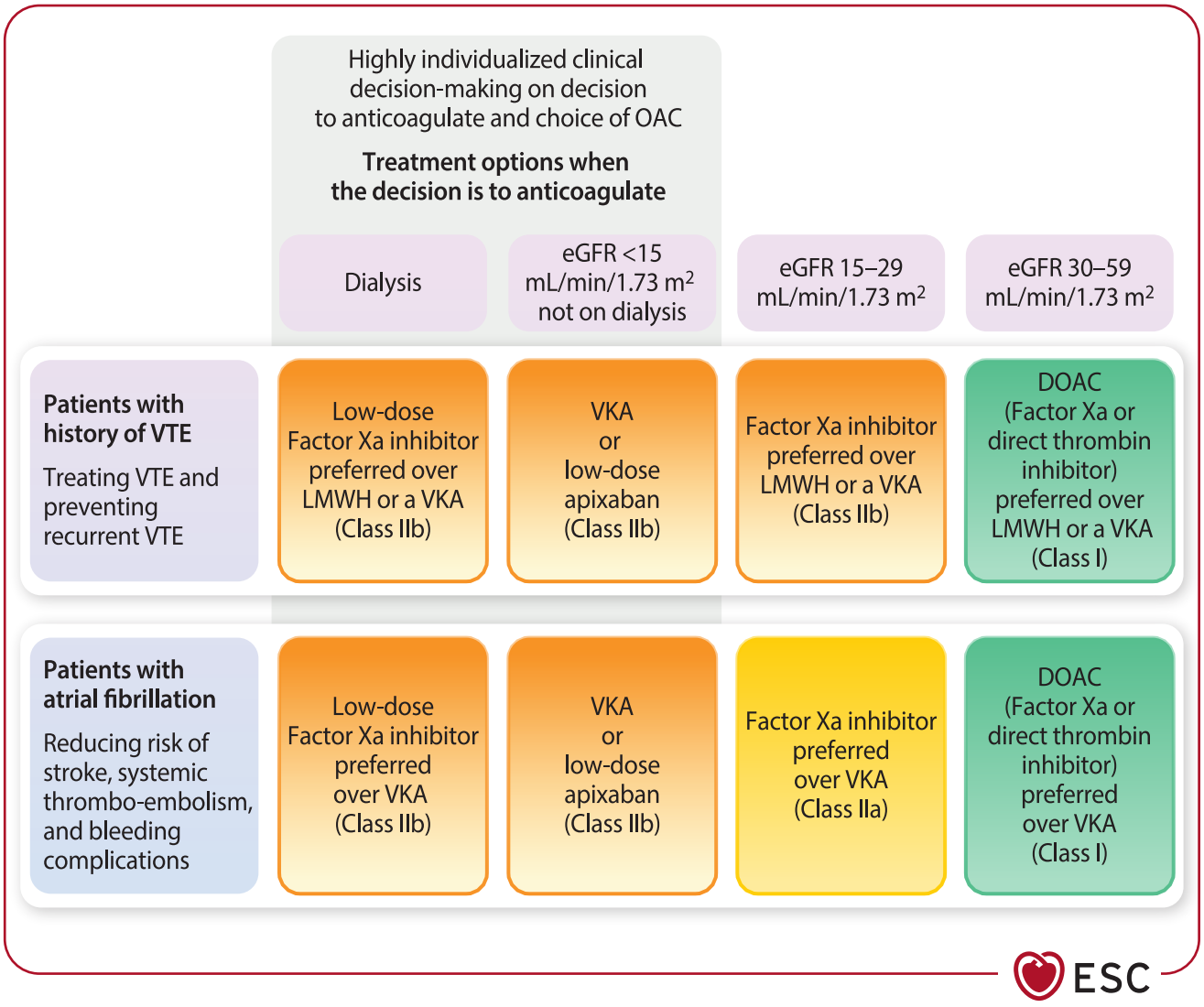

Figure 17 Recommendations on the use of anticoagulation therapy for patients with venous thromboembolism or atrial fibrillation in the context of chronic kidney disease. DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; LMWH, low molecular weight heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism. Each box shows recommended anticoagulation treatment in preference over conventional treatment such as VKA, LMWH, or not providing anticoagulation at all. The indication to start anticoagulation therapy is an individualized decision based on patient characteristics, including but not limited to kidney and liver function and patient preferences. See *Figure 16* for suggested strategies and dosing for treatment of VTE

(such as QT prolongation) that may be pronounced because of electrolyte imbalances in CKD; (iii) how well tolerated the AF or paroxysms of AF may be haemodynamically, particularly in those on dialysis; (iv) possible alterations in symptomatology; (v) the high prevalence of coronary and structural heart disease; and (vi) the potentially increased propensity to develop tachycardia-mediated cardiomyopathy. It is important to evaluate these factors in patients with AF and CKD where possible when deciding on individualized management, especially electrolyte disturbances, QT prolongation, and underlying structural heart disease.

Trials comparing rate vs rhythm control have generally included very few patients with CKD, and almost no patients on dialysis.[652–654] Early rhythm control was associated with a lower risk of adverse cardiovascular outcomes among patients with early AF with other cardiovascular conditions in the Early Treatment of Atrial Fibrillation for Stroke Prevention Trial (EAST-AFNET4), but only 12% of patients had an eGFR <60 mL/min/1.73 m^2.[654] There was no apparent effect modification based on baseline CKD status (although no formal *P*-value for interaction was provided). In the Atrial Fibrillation and Congestive Heart Failure (AF-CHF) study of patients with

HF, there was no difference between a rate- or rhythm-control strategy in reducing cardiovascular death, and the lack of difference was found irrespective of baseline serum creatinine.[652] Non-randomized data from the Global Use of Strategies To Open occluded coronary arteries (GUSTO III) trial in patients with new-onset AF post-MI are consistent with these findings, showing that a rhythm- or rate-control strategy was not associated with reduced short- or long-term mortality, regardless of kidney disease status.[655] Patients with kidney failure with haemodynamic instability due to AF during dialysis sessions may benefit from rhythm control, but this has not been evaluated in clinical trials. There is no evidence to indicate whether moderate or intensive rate control impacts outcomes in patients with CKD beyond providing symptomatic relief.

Beta-blockers, CCBs, and digoxin are the main medications used for rate control in the general population of patients with AF. Lipophilic beta-blockers (metoprolol, carvedilol, propranolol, bisoprolol, and nebivolol) may provide more reliable rate control than water-soluble beta-blockers (atenolol, nadolol, and sotalol), although this has not been definitively established.[656] Digoxin is about 75% renally excreted and requires substantial dose reduction and monitoring of digoxin levels, particularly at eGFR <30 mL/min/1.73 m^2.

Pharmacologically, rhythm control is generally achieved with class I and class III anti-arrhythmic medications and some of these agents are at least partially renally cleared. Considering their pro-arrhythmic properties in specific circumstances (such as accumulation, electrolyte disorders), dose adjustments may be considered for specific medications. Sotalol required dose adjustment in CKD and may impart pro-arrhythmic effects. For flecainide, dose reduction is also required when GFR is <35 mL/min/1.73 m^2. The lipophilic drug propafenone may have low pro-arrhythmic potential and may be a better choice in CKD.[657] Amiodarone is not renally excreted, not dialysable, and no dose adjustment is required in CKD.

Dronedarone treatment increases serum creatinine by ~9 µmol/L (~0.1 mg/dL) following treatment initiation, reaching a plateau after 7 days. This effect is reversible on discontinuation. In the Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg bid for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter (ATHENA), dronedarone reduced the risk of death or hospitalization for CVD in patients with AF/atrial flutter.[658] Ibutilide should be used cautiously in patients with CKD because of its pro-arrhythmic potential in hypokalaemia and hypomagnesaemia, while dofetilide requires dose adjustment in patients with decreased GFR.

9.1.4. Cardioversion and catheter ablation

The success rate of direct current cardioversion appears similar regardless of kidney function.[659] Patients with mild-to-moderate CKD in whom sinus rhythm is maintained may experience an improvement in kidney function.[660,661] Direct current cardioversion alone is generally insufficient to maintain sinus rhythm, and long-term AADs or pulmonary vein isolation may be necessary for rhythm control,[661] as the risk of recurrence of AF increases as eGFR decreases.

Patients with CKD experience higher rates of AF recurrence following catheter ablation compared with the general population.[662] The risk of AF recurrence gradually increases with decreasing eGFR.[663,664] Following AF ablation, at 5-year follow-up, about 20% of haemodialysis patients remained AF free compared with around 60% of patients without CKD.[665–667] When multiple ablation procedures were performed to maintain sinus rhythm, 80%–85% of patients with CKD (on dialysis or not) were free of atrial arrhythmias at 5 years.[667] Maintaining sinus rhythm following AF ablation is associated with improved kidney function.[668,669] In a study of 392 patients with CKD and eGFR ≥30 mL/min/1.73 m^2, eGFR significantly increased after successful ablation in those with CKD stages G2–3.[670] Late recurrence of atrial arrhythmia is an independent risk factor for CKD progression.[671]

Some smaller studies have indicated that patients with CKD have a higher rate of procedure-related complications when undergoing AF ablation, although data from a large US registry indicated similar rates of complications in patients with and without CKD (although patients with CKD were more likely to be re-admitted for HF).[672,673] Ablation in general requires peri-procedural anticoagulation, which should be adapted for CKD stage. Considering the current evidence on ablation in patients with CKD, catheter ablation should be considered in patients on KRT with AF who experience haemodynamic instability during dialysis to improve dialysis tolerability. Catheter ablation may also be considered as a rhythm-control strategy in patients with AF (particularly paroxysmal AF) and CKD, to reduce symptoms and avoid long-term adverse outcomes with AADs.

Recommendation Table 27 — Recommendations for rate or rhythm control in patients with atrial fibrillation and chronic kidney disease (see Evidence Table 27)

Recommendations	Class[a]	Level[b]
The choice of AAD is recommended to take into account the high prevalence of coronary and structural heart disease, and pro-arrhythmic effects (such as QT prolongation) that may be pronounced because of electrolyte imbalances in patients with AF and CKD to minimize pro-arrhythmic AAD-related events.	I	C
Rhythm control should be considered as an alternative to rate control in patients with AF and CKD to reduce symptoms.[652,674]	IIa	C
Catheter ablation should be considered in patients on KRT with AF associated with haemodynamic instability during dialysis, to maintain sinus rhythm and improve the tolerability of dialysis.	IIa	C
Catheter ablation may be considered in patients with AF, particularly paroxysmal AF, and CKD, as a rhythm-control strategy to reduce symptoms and avoid long-term adverse outcomes with AADs.[665,667]	IIb	C

AAD, anti-arrhythmic drug; AF, atrial fibrillation; CKD, chronic kidney disease; KRT, kidney replacement therapy.
[a]Class of recommendation.
[b]Level of evidence.

9.2. Ventricular arrhythmia and sudden cardiac death

9.2.1. Impact of chronic kidney disease on sudden cardiac death

Sudden cardiac death is an important cause of death among patients with CKD, with risk increasing with the severity of CKD.[498,675] In patients with kidney failure, the risk of SCD appears particularly high. In United States Renal Data System (USRDS) registry data, SCD accounts for >40% of deaths among patients on dialysis.[30,676] Specific factors such as electrolyte disturbances, volume shifts, and KRT probably play a role in this increased SCD risk. Despite such high risk and poor outcomes, there is a lack of adequately powered RCTs in patients with CKD to assess the impact of prevention or treatment of ventricular arrhythmias on outcomes.

9.2.2. Pharmacological therapies

SGLT2 inhibitors are indicated to reduce risk of kidney disease progression and cardiovascular death in CKD, and meta-analysis of 11 large trials has identified that reductions in SCD appear to be an important component of the effect on cardiovascular mortality in these large clinical outcome trials (with similar effects in the CKD trials vs other trials; see *Section 5.5*). Anti-arrhythmic agents should be used in accordance with their pharmacological profile and their specific label, as dose adjustment for GFR may be required for many AADs when eGFR is decreased (see *Section 9.1.3* for considerations in AF rate and rhythm control).[629]

9.2.3. Device therapy

Patients with CKD should be treated in accordance with the 2022 ESC Guidelines on ventricular arrhythmias and prevention of SCD,[677] and 2021 ESC Guidelines on cardiac pacing.[678] ICDs can be considered in patients on dialysis with an indication for ICD implantation and with more than 1 year predicted life expectancy. Although patients with severe CKD have a high risk of SCD, it is not recommended to implant an ICD for primary prevention of SCD in patients on haemodialysis following results of the prospective randomized Implantable Cardioverter-Defibrillator in Dialysis Patients (ICD2) trial. The trial evaluated the efficacy and safety of ICD implantation to prevent SCD in 200 patients on dialysis with a LVEF ≥35%. ICD implantation did not impact SCD rate at 5 years nor overall mortality.[679]

9.2.3.1. Device infections

Compared with patients without CKD, patients with CKD experience increased rates of cardiac implantable electronic device (CIED) infection, with higher risk of sepsis and healthcare utilization after such infection.[680–688] Infection risk is increased when more complex CIED systems are implanted, procedure times are prolonged,[680–687] or when central haemodialysis catheters are present.[689] In the Worldwide Randomized Antibiotic Envelope Infection Prevention Trial (WRAP-IT), 6983 patients were randomized to an absorbable antibiotic envelope or control and there was a significant reduction of the risk of CIED infections, without evidence of effect modification by baseline kidney function.[681] The risk score BLISTER was derived from multivariate analysis of factors associated with CIED infection.[685] This includes eGFR <30 mL/min/1.73 m^2 at the time of procedure as an important factor in the score. In decision-analytic modelling, using an antimicrobial envelope in patients with a BLISTER score ≥6 was the optimal approach for cost-effective reduction of CIED infections. Therefore, applying an antibiotic envelope in patients on KRT may be considered to prevent CIED infections.[690–692] Additionally, due to high risk of infection in kidney failure, implantation of a subcutaneous defibrillator may be considered as an alternative to transvenous ICDs in patients with CKD on haemodialysis if there is no need for either bradycardia pacing, resynchronization, or anti-tachycardia pacing (ATP), to reduce the risk of SCD and CIED-related infection.[686,687] In addition, a subcutaneous defibrillator may be preferred in patients with limited vascular access. The 2021 ESC Guidelines on cardiac pacing recommend leadless pacemakers as an alternative to transvenous pacing in patients on haemodialysis to reduce infection risk.[678]

Recommendation Table 28 — Recommendations for device management considerations when treating patients with chronic kidney disease (see Evidence Table 28)

Recommendations	Class[a]	Level[b]
Application of an antibiotic envelope may be considered in addition to peri-operative antibiotic prophylaxis in patients on haemodialysis or after kidney transplantation who undergo CIED implantation to reduce the risk of CIED-related infection.[681,685,693,694]	IIb	C
Where an ICD is indicated, implantation of a subcutaneous defibrillator may be considered as an alternative to transvenous ICD if there is no need for either bradycardia pacing, cardiac resynchronization, or ATP in patients with CKD on haemodialysis to reduce the risk of SCD and CIED-related infections.[691,692,695]	IIb	C
Routine ICD implantation is not recommended in patients with CKD on haemodialysis with a LVEF ≥35% for primary prevention of SCD.[679]	III	C

ATP, anti-tachycardia pacing; CIED, cardiac implantable electronic device; CKD, chronic kidney disease; ICD, implantable cardiac defibrillator; LVEF, left ventricular ejection fraction; SCD, sudden cardiac death.
[a]Class of recommendation.
[b]Level of evidence.

10. Valvular heart disease and chronic kidney disease

Patients with CKD have a 1.2–1.8-fold higher adjusted risk of developing valvular heart disease compared with the general population.[696–698] Multiple valves are often affected in CKD, with aortic valve and mitral valve calcification being most common. Valve disease progression rates are also faster for aortic stenosis in patients with CKD, with aortic valve area declining at an annual rate of 0.1–0.2 cm^2 per year in patients with eGFR <15 mL/min/1.73 m^2 compared with 0.05–0.1 cm^2 per year in the general population.[699–701] Lower eGFR is also associated with poorer outcomes in patients with valve disease. The

5-year survival estimates among patients with CKD with at least mild aortic stenosis or mitral regurgitation was 40%–50% compared with 50%–70% in adults without CKD.[697,702]

The non-specific symptoms of valvular heart disease are similar to symptoms of kidney failure (including fatigue, dyspnoea, and fluid overload). Therefore, cardiac auscultation is important during physical examination of patients with CKD to identify abnormalities in heart sounds prompting further investigation. Echocardiographic assessment by transthoracic echocardiography (TTE) is then recommended in patients with suspected valvular heart disease and CKD, irrespective of symptoms. Once identified, patients with eGFR ≥45 mL/min/1.73 m^2 should follow management strategies for valvular heart disease as set out for the general population.[703] Frequent clinical and TTE re-evaluation (e.g. every 6–9 months) should be considered in patients with moderate-to-severe aortic stenosis and eGFR <45 mL/min/1.73 m^2 to identify optimal timing for intervention, as these patients often present with unreliable symptoms and can progress quickly.[699,701] Clinical and TTE evaluation should also be considered after initiating haemodialysis in patients with known moderate-to-severe valvular heart disease to identify optimal timing for intervention due to haemodynamic changes during dialysis that may impact both the severity of the valvular heart disease and its symptoms.

Medical treatment options for valvular heart disease are limited due to a paucity of trials demonstrating effective therapies. In theory, secondary hyperparathyroidism in patients on dialysis may accelerate vascular calcification, but cinacalcet has not been shown to reduce the risk of death or major cardiovascular events in these patients on dialysis.[704]

In RCTs in general populations with valvular heart disease, no pharmacological therapies have shown meaningful effect on progression of calcific aortic stenosis or risk of clinical outcomes. These include statin/ezetimibe in combination, denosumab, and alendronic acid.[705–707] There are no CKD-specific trials, and patients with CKD were under-represented in these trials.

A multidisciplinary team discussion (involving nephrology) is often needed for decision-making regarding type of intervention (if any) and type of prosthesis in severe valvular heart disease in patients with moderate or severe CKD.[708] The choice of intervention in patients with CKD and aortic stenosis can be particularly complex, as CKD is associated with both early and late cardiovascular complications.[709–711] Pre-operative estimation of peri- and post-operative mortality using a risk score that incorporates eGFR, such as the EuroSCORE and the STS score, may be informative.[712,713] Although long-term kidney function is usually not negatively impacted by valvular procedures or could even improve as a result, there is an increased risk of peri-procedural AKI (see *Section 11*).[714] Consideration of increased bleeding risk in CKD relating to lifelong use of anticoagulants if a mechanical valve is implanted needs to be balanced against increased risk of structural valve deterioration with bioprosthetic valves (for which thromboembolic complication risk is lower). Finally, patients on haemodialysis should be made aware of the increased risk of endocarditis after prosthetic valve intervention.[715]

No RCTs have compared valvular procedural intervention vs medical management in patients with CKD. In RCTs comparing transcatheter aortic valve intervention vs surgical replacement, similar outcomes within the first 3–5 years have been observed between the two approaches in patients with eGFR 15–60 mL/min/1.73 m^2.[716–718] Transcatheter aortic valve intervention may therefore be preferentially considered over surgical replacement in patients aged ≥70 years with CKD as the procedure is less invasive, has a lower rate of complication, and has similar outcomes over 5 years (confirmatory RCTs are required). Bioprosthetic valve durability is a concern for younger patients with severe CKD because of increased structural valve deterioration, but no RCT data are available to guide decisions regarding type of valve intervention.[716] As indicated by the dedicated ESC Guidelines on valvular heart disease, all decisions on valvular interventions need to be made within specialist valvular heart teams.[708]

Recommendation Table 29 — Recommendations for diagnosis and management of valvular heart disease in chronic kidney disease (see Evidence Table 29)

Recommendations	Class[a]	Level[b]
Comprehensive TTE is recommended in patients with suspected valve disease and CKD irrespective of symptoms to evaluate the presence and severity of valvular heart disease and assess cardiovascular risk.	I	C
More frequent clinical and TTE re-evaluation (every 6–9 months) should be considered in patients with moderate to severe aortic stenosis and CKD with an eGFR <45 mL/min/1.73 m^2 to identify optimal timing for intervention due to unreliable symptoms and fast progression rate.[699–701]	IIa	C
Clinical and TTE evaluation should be considered after initiating dialysis in patients with known moderate to severe valvular heart disease to identify optimal timing of intervention due to haemodynamic changes during dialysis.	IIa	C
Transcatheter aortic valve intervention instead of surgical replacement should be considered in patients with severe aortic stenosis[c] with CKD aged ≥70 years due to the less invasive procedure, lower risk of complications, and similar outcomes over 3–5 years.[716–718]	IIa	C

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Tricuspid aortic valve stenosis if the anatomy is suitable.

11. Acute kidney injury and prevention of important peri-procedural changes in kidney function

KDIGO defines AKI as an increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred

within the prior 7 days; or a urine volume <0.5 mL/kg/h for 6 h. In patients with increased serum creatinine, relying on lower thresholds for changes in serum creatinine (such as ≥26.5 µmol/L or 0.3 mg/dL) to define AKI is not advisable due to the exponential relationship between eGFR and serum creatinine.[719] The relationship between AKI and CKD is bidirectional. AKI can accelerate the progression of CKD, leading to further loss of GFR and increased risk of kidney failure. Conversely, CKD itself contributes to a heightened susceptibility to AKI, as the kidneys' reduced ability to recover from injury can exacerbate both the severity and duration of acute episodes. Furthermore, AKI episodes in patients with CKD are associated with increased mortality and morbidity, including a higher risk of cardiovascular events.[720]

Peri-procedural changes in GFR are common and can follow administration of iodinated contrast agents. Potential causes of AKI include haemodynamic instability, atheroma dislodgement with cholesterol emboli, and the use of contrast agents causing CI-AKI. The most frequently used definition of CI-AKI is an increase in serum creatinine ≥26.5 µmol/L (≥0.3 mg/dL) within 48 h post-procedure. It should be noted that permanent harm directly from CI-AKI (i.e. death, dialysis, or sustained important reduction in eGFR after 6 months) is relatively rare.[721] For example, pooled data from 37 RCTs including 12 166 patients undergoing invasive angiography found a pooled incidence of AKI around the time of the procedure of 9.5% (95% CI 8%–12%), but the need for KRT (usually temporary) was only 1.1%.[722] Low risk of harm is also evident during cardiac evaluation of potential kidney transplant recipients.[723] This low risk of KRT means that any risk of serious harm from CI-AKI is likely to be outweighed by the benefits of diagnostic imaging and therapeutic interventions when procedures are indicated. Harm of withholding or delaying procedures or therapies should be avoided, especially when early or urgent interventions are required. Furthermore, CI-AKI often occurs in the context of other causes of AKI. Even though about 1 in 10 patients with an eGFR >45 mL/min/1.73 m^2 may have measurable temporary changes in kidney function around the time of invasive angiography, once patients with other potential causes of AKI are excluded, the proportion of CI-AKI approaches 0%.[724] CI-AKI incidence is about 2% for patients with eGFR 30–44 mL/min/1.73 m^2 and 0%–17% for patients with eGFR <30 mL/min/1.73 m^2.[724] This large range of estimated risk has been attributed to differences in study size and limited numbers of patients with severe CKD studied. These caveats notwithstanding, patients with eGFR <30 mL/min/1.73 m^2 should be considered for an integrated individual assessment of CI-AKI risk based on current kidney function, specific patient risk factors, and the nature of the planned procedure (*Figure 18*).[725,726]

Baseline kidney function is the most important risk factor for CI-AKI, but other patient- and procedure-related factors are pertinent.[726–728] These include advanced age, HF, anaemia, and diabetes.[726,727] The total administered volume as well as the choice of contrast media additionally impacts the risk of CI-AKI, although, adding this to risk-prediction models for contrast-associated AKI only slightly improved the discrimination of the risk score.[726] Low-osmolar, or iso-osmolar contrast agents are preferred, particularly for patients with eGFR <30 mL/min/1.73 m^2, to reduce the risk of CI-AKI, in addition to limiting the amount of contrast media used. [729–741]

A common approach to reduce the risk of CI-AKI is use of intravenous hydration with isotonic saline. The exact mechanism through which intravascular volume expansion protects the kidney from injury by iodinated contrast administration is unknown. Several trials have shown that oral hydration is non-inferior to intravenous hydration in patients with eGFR >30 mL/min/1.73 m^2.[721,742–744] Importantly, dehydration prior to contrast administration should be avoided, regardless of eGFR. Unless there is intravascular fluid overload, prophylactic hydration may be considered in patients with eGFR <30 mL/min/1.73 m^2 undergoing elective or urgent procedures requiring iodinated contrast to decrease the risk of CI-AKI.[722,745–748] The optimum protocol regarding the type of hydration, timing (pre- and/or post-contrast), duration of administration, volume, and rate of administration remains uncertain.[749–751] Intravenous sodium bicarbonate is an alternative to intravenous saline, with neither demonstrating superiority in a head-to-head comparison.[745–748,752–754] Short infusions are less burdensome for patients and healthcare systems.[744,747] Administration of 250 mL of 1.4% sodium bicarbonate during the hour before contrast administration might therefore be a pragmatic and practical approach. If this is not feasible before contrast administration, such as in an emergency setting, this can instead be done post-contrast. Several pharmaceutical interventions, such as statins and *N*-acetylcysteine, have been tested in trials, but are not consistently effective at reducing the risk of clinical outcomes that represent harm from CI-AKI.[745,755,756]

It is often advised to stop metformin before or at the time of contrast administration. This is not due to nephrotoxicity, but due to the theoretical risk of accumulation if significant CI-AKI develops. Use of metformin should not delay the use of contrast, as it could be withheld after the procedure if risk of CI-AKI is high. Although there is no randomized evidence to support other approaches to prevent CI-AKI, temporary discontinuation of RAAS inhibitors, and cessation of nephrotoxic medication (e.g. non-steroidal anti-inflammatory drugs) can be considered in patients with moderate or severe CKD. Where time allows, their discontinuation before the procedure should be considered, but use of potentially nephrotoxic medication on the day of a procedure should generally not be an absolute reason to postpone procedures/interventions. In patients at very high risk of post-procedural dialysis, it is advisable to undertake these procedures in centres where KRT is available. Prophylactic haemodialysis is not recommended in patients with CKD to prevent CI-AKI as this has been associated with harm.[757–760]

When using gadolinium contrast for magnetic resonance imaging scans, only older group one gadolinium-based contrast agents have been associated with an increased risk of the debilitating skin and connective tissue condition nephrogenic systemic fibrosis in patients with CKD categories G4–5.[761,762] This is rarely observed with the group two or three gadolinium-based contrast agents (<0.07%), and these should therefore be used preferentially.[763] Side effects of gadolinium-based contrast agents, such as diarrhoea and headache, are more pronounced in patients with CKD categories G4–5.[764,765] Intravenous aminophylline significantly reduces the incidence of these side effects in patients with eGFR <30 mL/min/1.73 m^2 and, therefore, may be considered when using group two or three gadolinium-based contrast.[766]

Post-operative AKI is common, with the prevalence dependent on the definition used (with or without inclusion of oliguria),

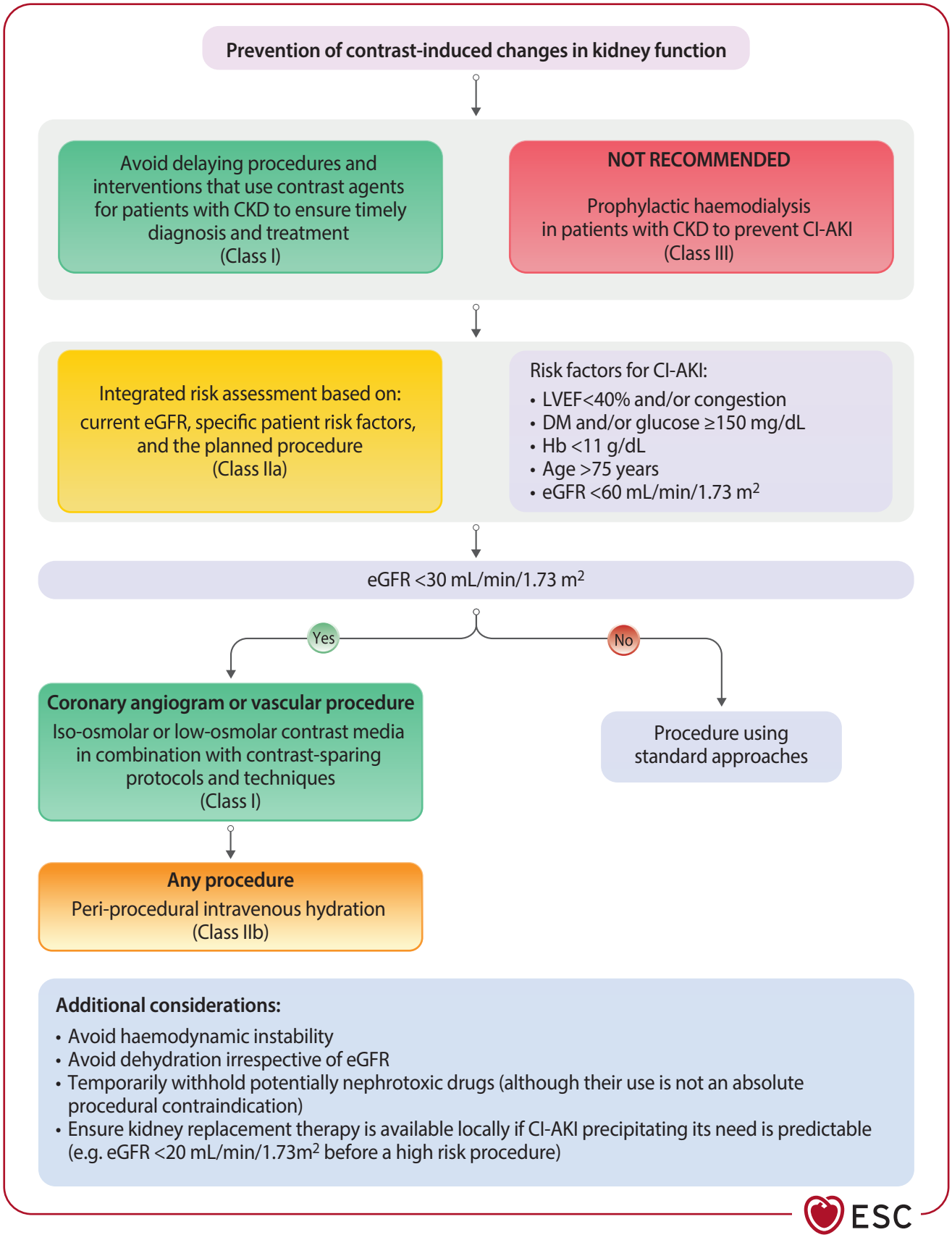

Figure 18 Algorithm to support safe use of contrast in chronic kidney disease. CI-AKI, contrast-induced acute kidney injury; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; LVEF, left ventricular ejection fraction.

enrolled population, and type of surgery. AKI risk is especially high following cardiac surgery (estimated at 3%–42%), and this has been associated with an increased risk of adverse in-hospital and long-term outcomes.[767,768] A pre-operative integrated assessment of risk including patient- and procedure-related factors can help identify patients at risk. Several pharmacological and non-pharmacological prophylactic interventions have been tested in RCTs including dopamine and diuretics, but none have convincingly and consistently reduced the incidence of serious harm associated with post-operative AKI.[769–771]

Recommendation Table 30 — Recommendations to support safe use of contrast in chronic kidney disease (see Evidence Table 30)

Recommendations	Class[a]	Level[b]
Avoiding delays in procedures and interventions that use contrast agents is recommended for patients with CKD to ensure timely diagnosis and treatment.	I	C
Use of iso-osmolar or low-osmolar iodinated contrast media in combination with contrast-sparing protocols and techniques is recommended in patients with an eGFR <30 mL/min/1.73 m^2 not on dialysis undergoing coronary angiography or vascular procedures to reduce the risk of CI-AKI.[731,732,734–736]	I	A
Use of group two or three gadolinium-based contrast agents is recommended in patients with an eGFR <30 mL/min/1.73 m^2 for MRI scans requiring such contrast due to the low risk of toxicity (nephrogenic systemic fibrosis).[762,763]	I	B2
An integrated assessment of risk based on current eGFR, specific patient risk factors, as well as the planned procedure should be considered to identify patients with CKD at high risk of harm associated with CI-AKI.[726,727,772]	IIa	C
Peri-procedural intravenous hydration may be considered in patients with an eGFR <30 mL/min/1.73 m^2 not on dialysis, undergoing any procedure requiring administration of iodinated contrast to reduce the risk of CI-AKI.[722,745,750,773]	IIb	C
Prophylactic haemodialysis is not recommended in patients with CKD to prevent CI-AKI, as this has been associated with harm.[757–760]	III	B2

CI-AKI, contrast-induced acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MRI, magnetic resonance imaging.
[a]Class of recommendation.
[b]Level of evidence.

12. Cardiovascular disease and maintenance dialysis

12.1. Cardiovascular effects of dialysis

Patients receiving maintenance dialysis experience ~5–10-fold higher risk for mortality from CVD compared with age- and sex-matched general populations (similar for both haemodialysis and peritoneal dialysis, higher in younger patients).[774] In addition to traditional cardiovascular risk factors, which are common in patients with kidney failure (i.e. hypertension, dyslipidaemia, and diabetes), the excess cardiovascular risk in patients receiving maintenance dialysis may be explained by several maladaptive structural and functional changes within the heart and vascular tree.[775] Vascular calcification is observed in ~85% of patients on dialysis within the vascular intima (related to atherosclerosis) and in the vascular media (resulting in increased arterial stiffness).[776] Combined volume and pressure overload contribute to increased risk of left ventricular hypertrophy and dilatation.[777] As many as three-quarters of new dialysis patients have such structural changes,[778] which are themselves associated with increased risk of HF. Myocardial fibrosis develops because of subclinical ischaemia and haemodynamic disturbances. Anaemia, Chronic Kidney Disease-Mineral and Bone Disorder, gut dysbiosis and accumulation of toxic metabolites, and the haemodynamic effects of arteriovenous fistulae are suggested to further accelerate CVD (see *Figure 19*).[779,780]

In patients undergoing haemodialysis thrice-weekly (the most common regimen for in-centre treatment), the long interdialytic interval is associated with substantially heightened risks of cardiovascular events including MI, stroke, decompensated HF, and sudden death.[781] Arrhythmias, including tachyarrhythmias and AF, are common, can be related to the dialysis cycle, but are often not routinely detected on baseline or ambulatory ECGs.[782] Implantable loop recorder studies in patients receiving maintenance haemodialysis have suggested that SCD is most associated with bradyarrhythmias.[783] This perhaps provides an explanation for the lack of efficacy of an ICD in preventing SCD in a dialysis RCT (*Section 9.2*).

12.2. Management of cardiovascular disease in patients on dialysis

12.2.1. Pharmacotherapy

There are only a few proven therapies and many negative dialysis trials.[784–786] This is perhaps due to the highly multifactorial nature of CVD in patients on dialysis, which means each intervention may only have small relative effects. Multiple approaches are therefore used by nephrologists to minimize CVD risk on dialysis, despite limited evidence (*Figure 19*).

There is evidence from a large trial that intravenous iron improves cardiovascular outcomes among patients on dialysis. Proactive regular high-dose intravenous iron—irrespective of haemoglobin level, and unless the serum ferritin concentration is >700 μg/L or TSAT is ≥40%—is recommended in patients on maintenance haemodialysis to reduce risk of cardiovascular events, including HF. The Proactive IV Iron Therapy in Haemodialysis Patients (PIVOTAL) trial[787] tested the efficacy of high-dose iron sucrose, administered intravenously in a proactive fashion (400 mg monthly, unless the ferritin concentration was >700 μg/L or TSAT ≥40%), or low-dose iron sucrose, administered intravenously in a reactive fashion (0–400 mg monthly, with a ferritin concentration <200 μg/L or TSAT <20% being a trigger for iron administration). The high-dose iron strategy appeared safe during the median 2.1 years of follow-up, and there was a 15% reduction in the primary

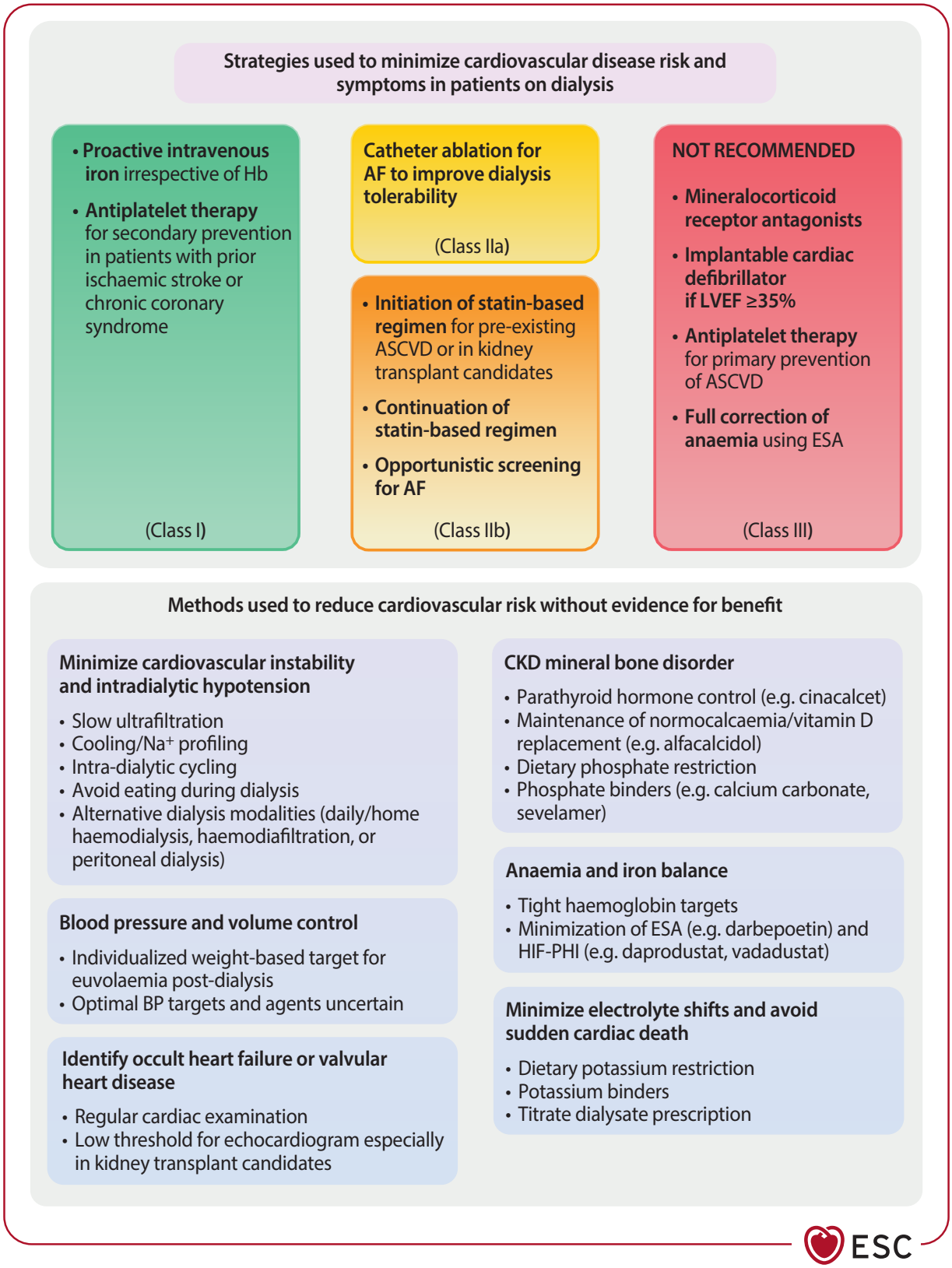

Figure 19 Cardiovascular disease and symptoms in patients on dialysis. AF, atrial fibrillation; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; DAPT, dual antiplatelet therapy; ESA, erythropoiesis-stimulating agents; Hb, haemoglobin; HIF-PHI, hypoxia-inducible factor prolyl hydroxylase inhibitors; LVEF, left ventricular ejection fraction

composite outcome of non-fatal MI, non-fatal stroke, hospitalization for HF, or all-cause death (HR 0.85, 95% CI 0.73–1.00), and fewer occurrences of first and recurrent HF.[788] Patients treated with proactive intravenous iron received lower doses of ESAs. High-dose ESAs to maintain higher target haemoglobin levels have adverse cardiovascular safety profiles; some of the cardiovascular risk reduction afforded by proactive intravenous iron treatment could result simply from ESA dose-sparing.[787]

Section 3.7.2 explained that nephrologists treat renal anaemia to tight haemoglobin targets to safely reduce the need for blood transfusions and improve symptoms and quality of life. In general, a target haemoglobin <11.5 g/dL is employed. See *Section 7.4.1* for the recommendation that full correction of anaemia is avoided due to increased risk of stroke.[71,588] This same strategy is also used in patients on dialysis after mortality concerns led to the early closure of the Normal Hematocrit Trial in 1233 patients on haemodialysis.[789] Hypoxia-inducible factor prolyl hydroxylase inhibitors (e.g. daprodustat, vadadustat) are an alternative to ESAs but have not been shown to be superior in safety studies in patients on dialysis[790] (nor among patients with CKD not on dialysis).[791]

The relative benefits of statin-based treatment attenuate in severe CKD and are uncertain in patients on dialysis (*Section 5.3*).[184] Antiplatelet therapy may be effective at reducing risk of vascular events in patients on dialysis,[792] with a large confirmatory trial ongoing (NCT04381143). Any aspirin use needs to be balanced against the risk of bleeding, which requires clinical judgment due to the lack of RCT data and validated bleeding risk scores in this population (see *Section 9.1.2*).

Although excess aldosterone is implicated as a modifiable risk factor for HF and is increased in CKD,[240,307,793,794] MRA therapy did not improve cardiovascular outcomes in the Aldosterone Blockade for Health Improvement Evaluation in End-stage Renal Disease (ACHIEVE) and other high-quality trials in dialysis populations.[795,796]

Although common practice, dietary and pharmacological interventions that modify parathyroid hormone and phosphate control have generally not been tested in adequately powered RCTs, and so their effectiveness at modifying cardiovascular risk in CKD is uncertain.[9,797,798]

Blood pressure varies considerably in patients on dialysis, particularly on days when haemodialysis is performed. There is uncertainty about optimum time to measure blood pressure and targets.[777] Cardiovascular instability on dialysis negatively impacts adequacy of haemodialysis and patient experience. Occult HF or valvular heart disease should be considered. To address cardiovascular instability, nephrologists review patients' 'dry weight' regularly, may cool or sodium profile dialysate, slow ultrafiltration, discourage eating on dialysis, or switch to haemodiafiltration or peritoneal dialysis.[799] Observational studies have suggested lower risk of CVD associated with peritoneal dialysis vs haemodialysis.[800–802] In two small trials, frequent haemodialysis (e.g. four–six times/week vs three) had promising effects on reducing left ventricular mass and blood pressure control as surrogate markers for cardiovascular morbidity.[803–805] There is no adequately powered cardiovascular outcome RCT to confirm benefit on clinical outcomes.

Recommendation Table 31 — Recommendations for prevention of cardiovascular disease in patients on dialysis (see Evidence Table 31)

Recommendations	Class[a]	Level[b]
Proactive regular high-dose intravenous iron (e.g. iron sucrose) is recommended in patients on maintenance haemodialysis, unless the serum ferritin concentration is >700 μg/L or transferrin saturation is ≥40%, to reduce risk of cardiovascular events, including heart failure.[787,788]	I	B1
Routine use of MRAs is not recommended in patients on dialysis because of the risk of serious hyperkalaemia without evidence of clear benefit on cardiovascular death or hospitalizations for heart failure.[795,796,806]	III	A

MRA, mineralocorticoid receptor antagonist.
[a]Class of recommendation.
[b]Level of evidence.

13. Cardiovascular disease and kidney transplantation

Kidney transplantation is often the preferred KRT modality in kidney failure, as it is cost effective and associated with lower cardiovascular risk, longer survival, and better quality of life compared with dialysis modalities.[807]

CVD remains a leading cause of morbidity and mortality in both kidney transplant candidates and recipients, especially in the peri-transplant period.[808] This section provides a framework to address cardiovascular issues in kidney transplant candidates and recipients. Other societies' guidelines provide recommendations for management of immunosuppressive therapy, prevention of graft rejection, and management of non-cardiovascular complications (e.g. opportunistic infection or cancers).[809]

13.1. Prior to kidney transplantation

13.1.1. Pre-transplant cardiovascular assessment

According to the 2022 ESC Guidelines on cardiovascular management for patients undergoing non-cardiac surgery, kidney transplantation is considered an intermediate-risk procedure, with a 1%–5% risk of 30-day major adverse cardiovascular events.[810] As such, all kidney transplant candidates are recommended to undergo a comprehensive pre-operative cardiovascular assessment, including history, physical examination, ECG, and laboratory tests. Risk assessment in kidney transplant candidates is complicated, as symptoms of cardiovascular disorders may be atypical due to polyneuropathy, fluid overload, or low functional capacity. TTE is recommended as a risk-free and low-cost investigation to diagnose structural and functional heart disease including valve disease and reduced LVEF, but results may need to be interpreted cautiously in the context of fluid overload.

The necessity for and benefits vs risks of more advanced screening for CAD in kidney transplant candidates remains

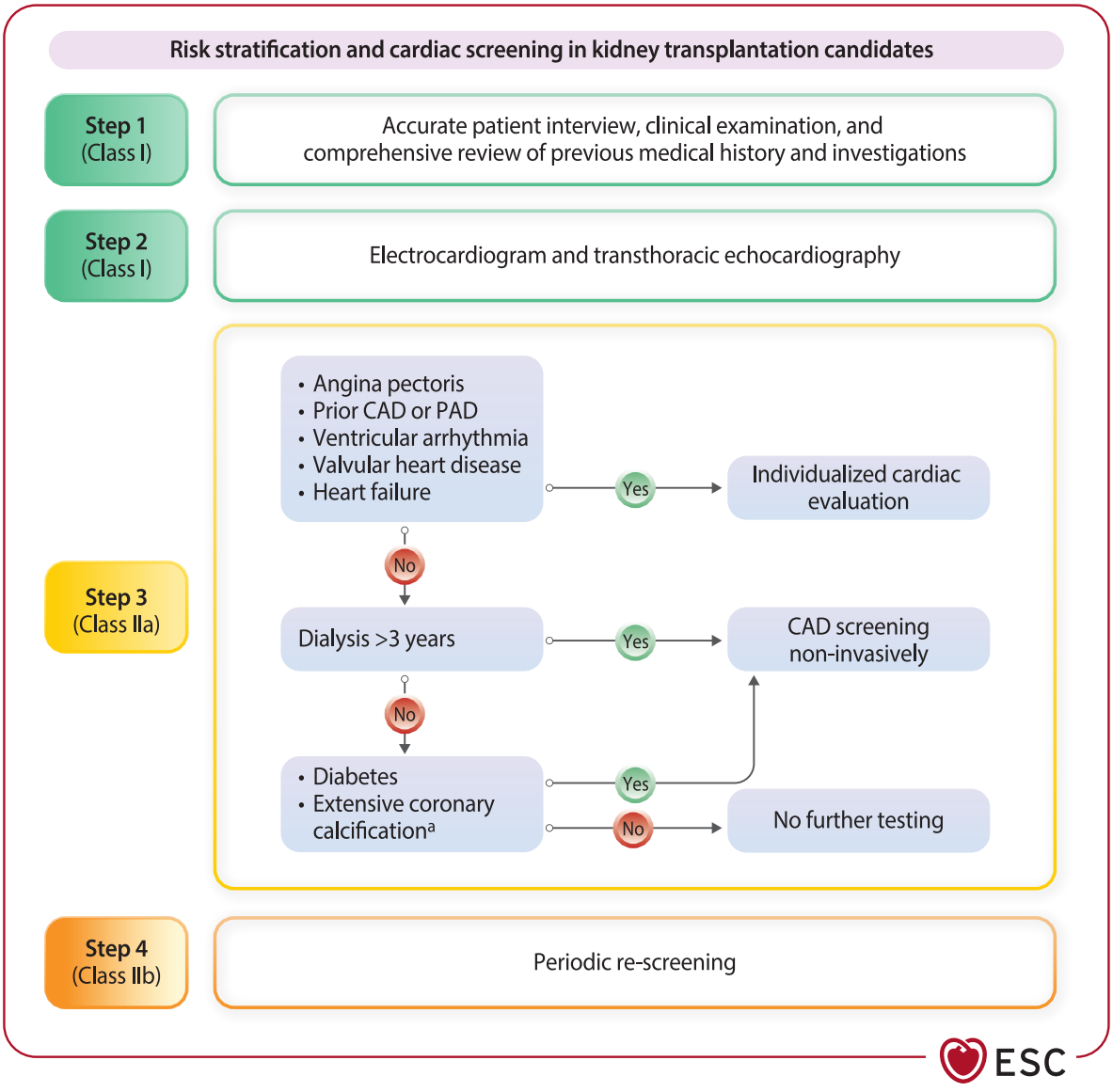

Figure 20 Risk stratification and cardiac screening in kidney transplant candidates. CAD, coronary artery disease; CT, computed tomography; PAD, peripheral artery disease. [a]Extensive coronary calcification present at previous chest CT scans.

uncertain despite the high prevalence of asymptomatic CAD. The potential harms include both delayed access to transplantation and procedural complications during revascularization. Any screening algorithm needs to be implemented promptly to avoid delaying transplantation. Cost effectiveness of screening is also uncertain.[811] Previous guidelines have limited certain investigations to those patients with sufficiently high cardiovascular risk who are considered likely to benefit.[809,812,813] However, no consensus has been established regarding precisely how to identify those at sufficiently high risk that intensive screening with/without intervention is warranted.[814] *Figure 20* provides a simple risk-based algorithm for screening. Risk stratification could be further improved using assessments of coronary artery calcification. Such data are increasingly available from previous chest CT scans (although such tests are not part of standard pre-transplant assessment). Coronary artery calcium score both discriminates obstructive CAD and carries prognostic value for both major adverse cardiovascular events and mortality in kidney transplant candidates.[815–819]

In kidney transplant candidates with high CVD risk, choices regarding advanced diagnostic testing of obstructive CAD depend on the presence of established CAD and comorbidities, and the local availability and expertise for different diagnostic techniques. Previous meta-analyses have shown moderate-to-high diagnostic accuracy and equivalent prediction of cardiovascular mortality for myocardial perfusion imaging tests compared with ICA.[448,820] ICA is therefore not recommended as a first-line diagnostic test in asymptomatic kidney transplant candidates with or without established ASCVD.

CCTA is useful to assess kidney transplant candidates as it uses a single contrast bolus for evaluating CAD, and can be extended to assess for pelvic vascular disease. CCTA may improve risk stratification by diagnosing both non-obstructive and obstructive CAD, together with analysing plaque characteristics and CT-derived fractional flow reserve.[455,821] CCTA's high sensitivity for obstructive CAD has been validated in patients with severe CKD, but specificity is reduced in such populations due to high burden of coronary calcium and high and/or irregular heart rate.[454] In a head-to-head diagnostic accuracy comparison study including kidney transplant candidates, sensitivity was higher and specificity lower for CCTA compared with myocardial perfusion imaging using single-photon emission CT (SPECT).[822] Of the other alternatives to CT, available evidence suggests that dobutamine stress echocardiography may offer higher diagnostic accuracy than MPS.[816,820]

The benefit of screening for CAD in kidney transplant candidates (e.g. lower peri-operative complications and reduced risk of loss of graft function if revascularization is required post-transplant) has not been tested in adequately powered RCTs in a contemporary setting. Reported retrospective non-randomized studies have found no association between screening and different outcomes, but are susceptible to selection bias and residual confounding limiting any interpretation.[823–825] The ISCHEMIA-CKD trial ($n = 777$) did not find evidence that an initial invasive strategy, compared with an initial conservative strategy, reduced the risk of death or non-fatal MI in patients with CKD and moderate or severe ischaemia on stress testing.[481] The trial enrolled 194 patients (25%) listed for transplant and, among patients assigned to an invasive vs conservative strategy, the adjusted HRs for the primary outcome were 0.91 (95% CI 0.54–1.54) and 1.03 (95% CI 0.78–1.37) for those listed and not listed, respectively (interaction $P = .68$).[826] Similar to the ISCHEMIA-CKD trial, other large studies have shown no benefit of coronary artery revascularization before elective major vascular surgery. In patients with CCS, revascularization only has a minor impact on risk of major adverse cardiovascular events.[827–829] These data are underpowered but suggest that an important proportion of screened kidney transplant candidates will have little or no change in their management after screening. New confirmatory large long-term RCTs comparing different screening strategies are needed.[481,825,827,829,830]

Optimal surveillance of ASCVD after listing for transplantation is another area of uncertainty. Kidney transplant candidates on waiting lists often undergo additional cardiac evaluations after years waiting for transplantation.[831] A cost-utility analysis suggested that surveillance cardiac testing may lead to lower overall patient survival due to complications from revascularization and delayed transplantation access.[832] The ongoing Canadian Australasian Randomized Trial of Screening Kidney Transplant Candidates for CAD (CARSK) trial has been specifically designed to compare a strategy of ongoing vs no surveillance with a non-invasive CAD screening test in kidney transplantation candidates ($n = 3306$) on waiting lists following initial screening.[833] Nevertheless, it is advisable to re-evaluate for cardiac disease if relevant new symptoms develop.

Recommendation Table 32 — Recommendations for cardiac evaluation of kidney transplant candidates (see Evidence Table 32)

Recommendations	Class[a]	Level[b]
Patient interview, clinical examination, and comprehensive review of previous medical history are recommended in all kidney transplant candidates with the aim of stratifying cardiac risk.	I	C
Resting electrocardiogram and transthoracic echocardiography are recommended in kidney transplant candidates with the aim of identifying valvular disease, and to assess ventricular structure and function.	I	C
Individualized decision-making (including multidisciplinary discussion) regarding revascularization is recommended in asymptomatic kidney transplant candidates with established obstructive CAD to minimize risk associated with transplantation.[825]	I	B2
Individualized cardiac evaluation and potential multidisciplinary team discussion should be considered in kidney transplant candidates with angina, established atherosclerotic disease, ventricular arrhythmia, valvular heart disease or HF to identify the optimal pre-, peri-, and post-operative management.	IIa	C
Myocardial perfusion imaging test or anatomic testing with coronary CT angiography should be considered in high-risk asymptomatic kidney transplant candidates with the aim of risk stratifying, diagnosing obstructive CAD, and guiding treatment of modifiable risk factors and revascularization.[448,816,817,820,822,823]	IIa	B
Using coronary artery calcification findings from previous chest CT scans, if available, should be considered in kidney transplant candidates with the aim of enhancing risk stratification and guiding treatment of modifiable risk factors for CAD.[815,817]	IIa	C
Periodic re-screening of CAD may be considered in kidney transplant candidates on the waiting list with either symptoms, earlier abnormalities or new unexpected (cardiac) findings to reduce risks of complications from revascularization and delayed access to transplantation.	IIb	C
Pre-operative CAD screening using diagnostic testing is not recommended in kidney transplant candidates with low probability of obstructive CAD due to risk of potential harms of screening including delaying listing suitable candidates.	III	C

CAD, coronary artery disease; CT, computed tomography; HF, heart failure.
[a]Class of recommendation.
[b]Level of evidence.

13.2. Kidney transplant recipients

13.2.1. Cardiovascular disease risk management

When initiating new treatment, consultation with the patient's transplant team is advisable to ensure that there are no important considerations for the graft, and particularly relevant drug interactions.

High blood pressure affects ~90% of kidney transplant recipients and increases CVD risk.[834,835] Diagnosis should follow recommendations in *Section 5.2*. This guideline recommends titrating treatment to a systolic blood pressure target of 120–129 mmHg. This is justified on the basis of extrapolating results from RCTs in other populations (including in the context of primary and secondary prevention),[836] and because lower blood pressure (systolic blood pressure <140 mmHg) is associated with lower risk of cardiovascular mortality, and longer patient and graft survival in observational studies of kidney transplant recipients.[837,838] There is uncertainty about more intensive blood pressure lowering due to concerns about potential adverse graft outcomes.[839,840]

Some immunosuppressive drugs can impact blood pressure, lipids, and glucose homeostasis, with therapeutic levels monitored to avoid exposure to high levels as well as to ensure optimum immunosuppression.[841,842] Statin-based regimens should be widely implemented. Data from the United States have reported that post-transplant diabetes mellitus (also known as new-onset diabetes after transplantation) developed in about one-quarter of patients.[843] Post-transplant diabetes mellitus is associated with an approximately three-times increased risk of non-fatal acute MI.[844,845] Too few kidney transplant recipients have been studied in trials of more intensive vs less intensive glycaemic targets, or with specific glucose-lowering agents to provide direct evidence of benefits on clinical outcomes.[846] An individualized approach combining lifestyle modifications, oral hypoglycaemic agents, with or without insulin is advised, with a preferential use of medications that are safe and effective in CKD, do not require dose adjustment by level of GFR, and may impart CVD or kidney benefits.[847]

Observational data provide evidence to encourage intentional weight loss among obese or overweight patients with CKD before and after transplantation to reduce risk of surgical complications, and improve short- and long-term graft outcomes.[107,848,849] Bariatric surgery improves weight in individuals with morbid obesity, but there should be awareness of increased risk of oxalate nephropathy.[850] Physical inactivity before transplantation is a predictor of mortality and poor cardiovascular outcomes post-transplantation, particularly in older frail individuals.[851,852] We advise individualized advice on increasing physical activity in kidney transplant recipients.[853,854]

13.2.2. Pharmacotherapy

A recently updated Cochrane meta-analysis suggested CCBs may reduce the risk of all-cause death [relative risk (RR) 0.83, 95% CI 0.72–0.95] and graft loss (RR 0.84, 95% CI 0.75–0.95).[855] This result is driven by open-label data from a single centre and would therefore benefit from replication. Nevertheless, CCBs are generally well tolerated, do not increase the risk of hyperkalaemia, and should be considered among first-line approaches for controlling blood pressure in kidney transplant populations.[856,857] *Section 5.3.2* details statin-based regimens that are suitable for use in transplant recipients.

SGLT2 inhibitors[227] and GLP-1RAs[242] reduce the risk of important clinical cardiorenal outcomes in large trials in populations with diabetic kidney disease. Dedicated trial data in kidney transplant recipients are limited. In a placebo-controlled trial with 44 patients with post-transplant diabetes, empagliflozin had a small effect on HbA1c but was generally safe and well tolerated.[858] Other data are limited to retrospective non-randomized analyses.[859,860] Extrapolating data from non-kidney transplant recipients with diabetes, both SGLT2 inhibitors and GLP-1RAs may be considered in kidney transplant recipients with type 2 diabetes to treat hyperglycaemia and modify cardiovascular risk, but RCTs should ideally be conducted to assess effects on cardiovascular outcomes and graft outcomes, and to assess safety.

Low-dose aspirin is often prescribed in the post-operative period in kidney transplant recipients to reduce risk of graft thrombosis. RCT evidence of long-term benefits to reduce cardiovascular risk is needed. Data comparing safety of DOACs with VKAs in kidney transplant recipients (e.g. in the context of AF) are generally limited to non-randomized single-centre series.[861,862]

Recommendation Table 33 — Recommendations for management of cardiovascular disease risk in kidney transplant recipients (see Evidence Table 33)

Recommendations	Class[a]	Level[b]
A systolic blood pressure target of 120–129 mmHg is recommended in kidney transplant recipients to improve cardiovascular outcomes.[132,838,863]	I	C
Calcium channel blockers should be considered in kidney transplant recipients to lower blood pressure to an individual's target and reduce risk of graft loss.[855–857]	IIa	B2
SGLT2 inhibitors may be considered in kidney transplant recipients with either pre- or post-transplant diabetes to reduce cardiovascular risk.[858–860]	IIb	C
GLP-1RAs may be considered in kidney transplant recipients with either pre- or post-transplant diabetes to reduce cardiovascular risk.[864]	IIb	C

SGLT2, sodium glucose co-transporter 2; GLP-1RA, glucagon-like peptide-1 receptor agonist.
See *Section 5.3.2* for statin-based regimen recommendations.
[a]Class of recommendation.
[b]Level of evidence.

14. Person-centred care

14.1. Sex and age considerations

The recommendations in *Sections 3–13* should be applied to all persons. National and local audits should review use of guideline-recommended treatments to ensure they are applied equitably. There are some important sex differences in the

prevalence of CKD, the relevance of eGFR to risk of CVDs, and the quantity of trial data generated in women compared with men. The crude prevalence of CKD categories G3–4 is somewhat higher in women than in men. This higher prevalence among women is evident in high-, middle-, and low-income countries, with US data suggesting women represent 56%–59% of all individuals with CKD. This pattern reverses at CKD category G5, with the age-standardized prevalence of kidney failure estimated to be about 1.5-times higher in men than in women.[3,865]

From a cardiovascular perspective, the incidence of non-ASCVD (i.e. HF, AF, and other arrhythmias) rises steeply as eGFR decreases, and the pattern is mirrored in men and women at all levels of eGFR.[866] Observations from half a million patients on dialysis have found that, compared with men and after adjustment for relevant confounders, women on dialysis have a 16% higher risk of HF and 31% higher risk of stroke, a similar risk of ACS, while having an 11% lower risk of cardiovascular death and 4% lower risk of death from any cause.[866,867]

In general, the participation of women in RCTs is lower than their representation in the underlying CKD population globally, with a participation-to-prevalence ratio estimated to be about 0.75.[868,869] Similarly, trials have often excluded patients of older age. Data from age-specific subgroup analyses of the newer therapies (e.g. SGLT2 inhibitors and GLP-1RAs) have shown consistent beneficial effects of these therapies across age subgroups and those with frailty, multimorbidity, and polypharmacy.[870] An approach to achieve more diversity in trials is to use population-level invitation methods which provide wider opportunity to participate than selection of individual patients by clinicians.[869]

14.2. Psychological considerations

Severe CKD and particularly kidney failure can result in a range of unpleasant chronic symptoms, including anorexia with nausea, fatigue, pruritus, and oedema. Clustering of symptoms is common, and treatment can be challenging.[871] Symptomatic CVD can also have psychological consequences.[872,873] Depression and anxiety are highly prevalent in patients with CVD and CKD.[874,875] Furthermore, the coexistence of both conditions likely has even greater psychological burden since multimorbidity is strongly associated with anxiety and depression.[876] Being aware of the high risk of these psychological impacts is important, and clinicians must be alert to signs such as social isolation, decreased self-care, and sleep disturbance. Early detection, integrated support, and personalized interventions can improve patient outcomes and quality of life.[877] Education of patients and their family/caregivers on these psychological impacts should be offered to those affected by CVD and CKD to improve understanding and coping strategies.[878] Health services should implement effective psychosocial interventions and may integrate mental health services within CKD or CVD care teams, particularly in centres caring for large numbers of patients with kidney failure.[877,879,880] The task force supports general approaches outlined in the 2025 ESC Clinical Consensus Statement on mental health and CVD[881] for adoption in patients with CKD.

14.3. Communication and cross- and multidisciplinary care

From a patient perspective, communication about CKD is key. Mild-to-moderate CKD is generally asymptomatic; therefore, communication and education is particularly necessary to communicate individuals' increased risks of CVD and kidney failure, facilitate treatment adherence, and ensure patients are sufficiently informed to engage in shared decision-making processes. Effective communication is particularly important when explaining modification of asymptomatic risk factors like blood pressure, blood glucose, and dyslipidaemia.[882,883] In severe CKD there are also additional considerations around patient–clinician communication. These include competing priorities of patients and their clinicians such as patient preferences to focus on the present vs clinician focus on planning for the future. Patients also cite power differences within the patient–clinician therapeutic relationship, of which clinicians should be better aware.[884]

From a health service perspective and given the high risk associated with CVD among patients with CKD, it is important that services expedite access to appropriate care and management of patients with CVD and CKD. The objective should be to deliver CVD management in a timely manner for all patients, particularly when management becomes more complex in the context of CKD. Active and efficient cross-speciality communication is often necessary. Multidisciplinary teams should ensure delivery of guideline-recommended care and personalize other treatment strategies considering the higher prevalence of treatment complications and comorbidities in patients with CVD and CKD (*Figure 21*). Teams managing patients with CVD should consider involving relevant nephrology team members to provide advice on CKD considerations, particularly when eGFR is <30 mL/min/1.73 m^2 and for patients on KRT. Active engagement of patients and family/caregivers in the multidisciplinary care process will also help ensure patients' priorities are met, improve their experience, and promote patient-centred care.[882,883] More RCT data are required to confirm how integrated, multi-specialty, patient-centred care models improve clinical outcomes, to support appropriate implementation.[885]

14.4. Palliative and advanced care

Palliative care planning is critically important for a symptom-controlled and dignified death among those approaching the end stages of CVD or CKD. Patients with kidney failure may decide to opt for conservative care from the outset, or withdraw from KRT for various reasons, including severe symptoms or disability from CVD. Patient-centred approaches help ensure that care aligns with an individual's goals, whether that involves maximizing comfort, managing specific symptoms, or supporting emotional, cultural, religious, and spiritual well-being.[886–888]

Recommendation Table 34 — Recommendation for multidisciplinary care in chronic kidney disease (see Evidence Table 34)

Recommendations	Class[a]	Level[b]
Involvement of relevant nephrology team members in CVD multidisciplinary care teams should be considered to support patients with CKD with an eGFR <30 mL/min/1.73 m^2 or on KRT to ensure CKD-related considerations are included in shared decision-making processes.	IIa	C

CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy.
[a]Class of recommendation.
[b]Level of evidence.

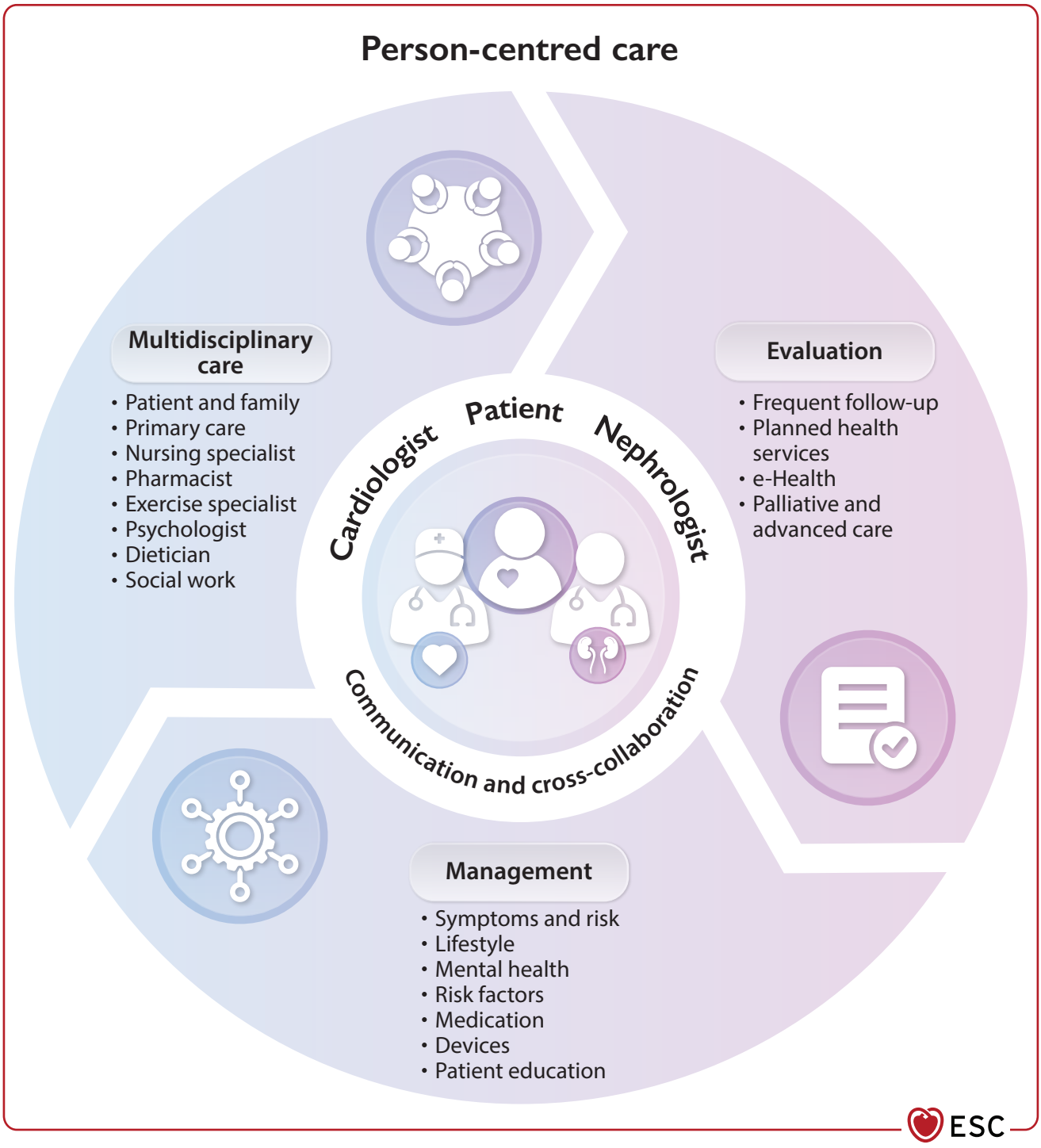

Figure 21 Person-centred care in cardiovascular disease and chronic kidney disease

15. Practical guidance

These new ESC Guideline recommendations for the management of CVD in the context of CKD are evidence based and practical. They aim to ensure patients with CKD, who are at high risk of adverse consequences of CVD, receive timely, safe, and effective care. This ESC Guideline summarizes for healthcare systems the additional factors and modifications required in the management of CVD in patients with CKD. To emphasize the importance of identifying and treating coexisting CVD and CKD, we have developed the **STAMP on CKD** acronym—Screen, Triage, and Address CKD risk, Modify CVD management, and Plan health services. Implementation of this new ESC Guideline should be fostered not only by using educational tools developed by the ESC, but also by integrating them into national electronic health record systems and digital-based healthcare solutions. Validated equations (i.e. KFRE) now exist to help estimate an individual's 5-year risk of kidney failure

once eGFR and uACR are measured. Laboratories could encourage uACR measurement when decreased eGFR is reported and calculate risk alongside test results. This will facilitate timely referral to nephrology and support patient communication about kidney failure risk.

CVD and CKD are major burdens on patients, healthcare systems, and society. The key messages should be distributed to all relevant healthcare stakeholders and policymakers, and the gaps in evidence distributed to research funders. Awareness should be raised, respectively, at both national and European parliamentary levels, including the responsible EU Commission. This will help realize the hope that this ESC Guideline will lead to important individual and societal improvement for those with or at risk of CVD and CKD.

16. Key messages

The key messages of the guideline are summarized according to the **STAMP on CKD** acronym—**S**creen, **T**riage, and **A**ddress CKD risk, **M**odify CVD management, and **P**lan health services.

Screen

- A key aim of the guideline is to facilitate early diagnosis of CKD in patients with CVD (and *vice versa*)
- Screen for CKD by measuring eGFR and albuminuria in all patients with CVD
- Stage CKD using eGFR and a spot uACR, and consider chronicity
- At least annual re-screening/re-testing for eGFR and uACR is recommended in patients with diabetes, CKD, and CVD.

Triage and staging of CKD

- In CKD categories G3–5, use the KFRE to assess an individual's absolute risk for progression to needing KRT to allow timely referral for nephrology evaluation and management
- CVD risk scores that include eGFR and/or albuminuria should be preferentially used to establish accurate CVD risk in patients with CKD

Addressing CKD and CVD risk

- A key aim of the guideline is to ensure appropriate early use of kidney failure and CVD risk-modifying therapy in patients with CVD and CKD
- Suitably intensive statin-based therapy with or without ezetimibe should be routinely and widely offered to patients with CKD (not on dialysis) irrespective of lipid levels, to reduce risk of ASCVD
- An ACEI or ARB, and SGLT2 inhibitor are recommended for most patients with CKD to reduce the risk of CKD progression and CVD risk
- SGLT2 inhibitors can safely be initiated at eGFR $\geq$20 mL/min/1.73 $m^2$and can be continued when eGFR progresses below 20 mL/min/1.73 m^2 until initiation of KRT (hence it would be reasonable to start them at eGFR <20 mL/min/1.73 m^2)
- Non-steroidal MRA (finerenone) and GLP-1RA (semaglutide) therapy are recommended for patients with CKD with type 2 diabetes and albuminuria to further reduce risk of CKD progression and cardiovascular events
- Extra biochemical monitoring after initiation of SGLT2 inhibitors or GLP-1RAs is not routinely required, but 1–4 weeks after initiation of RAAS blockade serum potassium and eGFR should be re-checked
- When initiating RAAS blockade/SGLT2 inhibitors for CKD and/or HF, a modest decrease in eGFR (typically <30%) is expected, which does not diminish the beneficial treatment effects
- Blood glucose lowering and blood pressure management in CKD should prioritize agents also shown to reduce risk of kidney disease progression and/or cardiovascular events

Modifying approaches to CVD management

The guideline aims to highlight key areas where the presence of decreased GFR necessitates changes to CVD management.

(i) *HF*
- Foundational medical therapies for treating HF are similarly effective in terms of relative treatment effects in patients with and without CKD. High absolute risk in CKD predicts large absolute treatment benefits
- In patients with evidence of volume overload, sufficiently high loop diuretic dosing, measuring diuretic response, and employing combination diuretic therapy in decompensated HF and CKD should achieve maximal decongestion

(ii) *CCS and ACS*
- An individualized approach to diagnostic coronary imaging is recommended in patients with CKD. Management of CCS in patients with CKD generally follows a standard approach where an initial conservative approach of optimal medical therapy is recommended
- If revascularization is indicated, individualized decision-making is required regarding type of revascularization (PCI vs CABG)
- Abbreviated DAPT duration (1–3 months vs conventional 6 months) should be considered for patients with CKD and CCS undergoing elective PCI, to reduce the risk of bleeding
- Serial assessment of troponin levels in patients with CKD and suspected ACS is important
- Patients with ACS and CKD have a higher risk of bleeding and this may impact choice, type, intensity, and duration of (dual) antiplatelet therapy

(iii) *AF*
- Existing stroke and bleeding risk-prediction tools in AF perform poorly in CKD
- DOACs are preferred over VKAs for patients with AF and CKD with eGFR >30 mL/min/1.73 m^2
- Oral factor Xa inhibitors may be considered in preference over VKAs for patients with eGFR 15–29 mL/min/1.73 m^2
- Cardioversion success appears to be unaffected by CKD stage, but AF recurrence is high. Catheter ablation may be an effective alternative
- Both rate- and rhythm-control strategies in CKD patients need individualized approaches, with considerations for drug pharmacokinetics, electrolyte imbalance, prevalence of structural heart disease, and AF recurrence risks

(iv) *CI-AKI*
- Permanent harm directly from CI-AKI (i.e. death, dialysis, or sustained important reduction in eGFR after 6 months)

is relatively rare and therefore risk of CI-AKI is nearly always outweighed by the benefits of diagnostic imaging and therapeutic interventions (and any potential harm of withholding or delaying procedures or therapies should be avoided)
- Use of iso-osmolar or low osmolar contrast media in combination with contrast-sparing protocols is indicated when eGFR is <30 mL/min/1.73 m^2, and peri-procedural intravenous hydration may also be considered

Planning health services for the complexities of CKD

- From a patient perspective, communication and education about CKD is important
- All clinicians should engage in managing risk of CVD and risk of CKD progression to reduce the global burden of both conditions
- Health services should be set up to recognize high-risk patients, taking into account special considerations in CKD, to minimize risks as well as any delay in treatment that such patients have

17. Gaps in evidence

In general, more RCTs are needed in patients with CKD at all stages as they have been historically understudied, and the high prevalence of multiple coexisting conditions and risk factors increases the chances of important residual confounding in observational non-randomized evidence.

Screening

- Clinical utility and cost effectiveness of targeted CKD screening in various high-risk populations, including the impact of community-based screening programmes in resource-limited settings
- The optimal frequency of re-screening for eGFR and albuminuria in various populations at risk for CKD

Addressing CKD and CVD risk

- Refinement of CVD risk scores to include albuminuria
- Optimal blood pressure targets and methods for measurement in patients with eGFR <30 mL/min/1.73 m^2 (and particularly <20 mL/min/1.73 m^2)
- The safety and efficacy of bempedoic acid and PCSK9 inhibitors in moderate-to-severe CKD
- Use of antithrombotic agents in patients with CKD without ASCVD, and particularly those with high coronary calcium score or subclinical atherosclerotic diseases; and CKD-specific bleeding risk scores
- Cost effectiveness of SGLT2 inhibitors at earlier stages of CKD (e.g. G3A1)
- Cardiorenal benefits and risks of aldosterone pathway inhibition and incretin-based therapies in CKD without diabetes or at lower levels of albuminuria

Modifying approaches to CVD management

- Risk-prediction tools for risk of primary and recurrent ASCVD and HF in patients on KRT

(i) *HF*
- The optimal natriuretic peptide cut-points to rule in and out HF in the setting of CKD
- RCTs of foundational HF therapies in patients with eGFR <20 mL/min/1.73 m^2

(ii) *CCS and ACS*
- The optimal duration of DAPT in patients with CCS and CKD
- Optimal assay-specific thresholds for cardiac troponin to rule in and out ACS in patients with CKD

(iii) *Peripheral arterial and aortic disease*
- Specific criteria for patients with CKD who should undergo standardized screening for PAD or AAA

(iv) *Anticoagulation in CKD*
- CKD-specific tools for ischaemic stroke and bleeding risk prediction in the setting of AF
- RCTs testing the safety and efficacy of DOACs and other anticoagulants for treatment of VTE, or for stroke and systemic thromboprophylaxis in AF, for patients with eGFR <15 mL/min/1.73 m^2

(v) *AF*
- RCTs assessing safety and efficacy of LAAO devices for preventing stroke in patients with AF and severe CKD (including those on KRT)
- RCTs comparing rate- vs rhythm-control strategies for AF
- Pharmacokinetic and safety data for AADs in patients with severe CKD including patients on KRT

(vi) *Valvular disease*
- Optimal approach to valve intervention compared with surgery or no intervention at different ages in patients with CKD

(vii) *Peri-procedural changes in kidney function*
- The optimum approach (volume and solution) for prophylactic hydration for CI-AKI (where indicated) in patients with eGFR <30 mL/min/1.73 m^2

(viii) *Specific to kidney transplantation*
- The benefits vs risks of more advanced screening and treatment strategies for CAD in kidney transplant candidates

Planning health services for the complexities of CKD

- Impact of routine screening and treatment for mental health conditions in CVD and CKD settings

18. Evidence tables

Evidence tables are available at *European Heart Journal* online.

19. Data availability

No new data were generated or analysed in support of this research.

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21. Appendix

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