Management of chronic kidney disease: a Hong Kong consensus recommendation

Sydney CW Tang *, Kelvin KL Ho, Welchie WK Ko, Albert Lee, CB Leung, WK Lo, Ronald CW Ma, SL Pang, Kathryn CB Tan, MW Tsang, Martin CS Wong, William CW Wong, Francis KM Wong, CC Szeto

ABSTRACT

Chronic kidney disease (CKD) imposes a significant burden on healthcare systems worldwide, and diabetes is a major risk factor for CKD. There is currently no consensus in Hong Kong regarding the prioritisation of early identification and intervention for CKD. A comprehensive and Hong Kong–specific diabetes and CKD treatment guideline is also lacking. A multidisciplinary group of experts discussed issues surrounding the current management of CKD and reviewed evidence in the context of local experience to support recommendations. The experts used a modified Delphi approach to finalise recommendations. Consensus was regarded as ≥75% acceptability among all expert panel members. The panel members finalised 14 CKD-focused consensus statements addressing disease definition, screening, disease monitoring, lifestyle management, and treatment strategies. The recommendations provided are relevant to the Hong Kong healthcare setting and can be used as a guide by physicians across various specialties to facilitate the appropriate management of CKD.

Hong Kong Med J 2024;30:Epub
https://doi.org/10.12809/hkmj2311309

[1] **SCW Tang *,** MD, PhD
[2] **KKL Ho,** FRCP (Edinburgh), FHKAM (Medicine)
[3] **WWK Ko,** FHKAM (Family Medicine)
[4] **A Lee,** MD, FHKAM (Family Medicine)
[5] **CB Leung,** FRCP, FHKAM (Medicine)
[6] **WK Lo,** MD, FHKCP
[7] **RCW Ma,** FRCP, FHKCP
[6] **SL Pang,** MB, BS, FHKAM (Family Medicine)
[8] **KCB Tan,** MBBCh, MD
[9] **MW Tsang,** FRCP
[4] **MCS Wong,** MD, FHKAM (Family Medicine)
[10] **WCW Wong,** MPH, MD
[6] **FKM Wong,** FRCP
[11] **CC Szeto,** MD, FRCP

[1] *Division of Nephrology, Department of Medicine, School of Clinical Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China*
[2] *Department of Nephrology, Virtus Medical Group, Hong Kong SAR, China*
[3] *Department of Family Medicine and Primary Healthcare, Queen Mary Hospital, Hong Kong SAR, China*
[4] *The Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China*
[5] *Central Administration Office, Hong Kong Baptist Hospital, Hong Kong SAR, China*
[6] *Private Practice, Hong Kong SAR, China*
[7] *Division of Endocrinology and Diabetes, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China*
[8] *Division of Endocrinology and Metabolism, Department of Medicine, School of Clinical Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China*
[9] *United Medical Practice, Hong Kong SAR, China*
[10] *Department of Family Medicine and Primary Care, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China*
[11] *Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China*

* Corresponding author: scwtang@hku.hk

This article was published on 27 Aug 2024 at www.hkmj.org.

This version may differ from the print version.

Introduction

Chronic kidney disease (CKD) is a leading cause of mortality that affects >800 million people worldwide, and its burden is the greatest among individuals with a lower socio-economic status.[1] In Hong Kong, survey data from 2020 to 2022 showed that 0.7% of the general population aged ≥15 years had a confirmed diagnosis of renal impairment.[2]

Chronic kidney disease is classified into five stages; stages 4 and 5 have a considerably increased risk of death or risk of cardiovascular events.[3] Early detection of CKD in adults can prevent progression to kidney failure, while early identification by screening provides an opportunity to stratify patients according to risk, thereby enabling treatment that can modify the disease course.[3] Diabetes is a leading risk factor for CKD; >40% of people with diabetes will develop CKD, and many of these people will require dialysis and transplantation.[4] Considering the increasing prevalence of diabetes,[4] it is important to develop comprehensive guidelines for the treatment of diabetes and CKD.

香港慢性腎病管理共識建議

鄧智偉、何繼良、高煒杰、李大拔、梁誌邦、盧維基、馬青雲、彭少良、陳俊明、曾文和、黃至生、黃志威、黃劍明、司徒卓俊

慢性腎病在全球醫療系統中造成重大負擔，而糖尿病是該病的主要危險因素。目前，香港對慢性腎病的早期識別和干預優先排序尚無共識，亦缺乏一套全面和針對性的糖尿病及慢性腎病治療指南。我們成立了一個由多個專業組成的專家小組討論當前慢性腎病管理方面的問題，並根據本地專家的經驗審查科學證據以支持慢性腎病管理方面相關建議。專家採用改良的德爾菲法確定最終建議。所有小組成員中至少75%專家接受所提出的建議則被視為達成共識。專家小組最終確定了14項以慢性腎病為中心的建議，其中涵蓋疾病定義、篩查、疾病監測、生活方式管理和治療策略。專家小組所提供的建議與香港醫療環境相關，可供不同專科醫生用作指南，以促進對慢性腎病的適切管理。

In Hong Kong, there has been no consensus on prioritising early identification and intervention for CKD. Guidelines for early CKD evaluation and management have not been universally adopted, due to a lack of incentives.[5] This article documents the findings of an expert panel established to formulate the first consensus recommendations for CKD screening and management in Hong Kong, with the intention of providing practical guidance to local healthcare practitioners based on evidence and expert opinion.

Methods

Literature search

A search of PubMed was conducted to identify peer-reviewed articles regarding CKD screening and treatment. Local (ie, Hong Kong or Chinese study populations) English-language publications from January 2017 to September 2022 were retrieved. Publication types were limited to clinical trials (ie, randomised controlled or controlled clinical trials), practice guidelines, and meta-analyses or systematic reviews.

Consensus method

In accordance with published international guidelines[4,6-8] and literature search results, consensus development leaders (first author and last author) drafted a set of preliminary statements concerning the definition, screening, and management of CKD. Twelve Hong Kong experts (nephrologists, endocrinologists, and family medicine specialists from public hospitals and private clinics) were invited to join the development leaders to form a 14-member consensus expert panel. All panel members were tasked with reviewing the draft statements in the context of current local practice and available evidence, and then discussed those statements during two expert meetings held in October and November 2022.

The consensus statements were developed through a modified Delphi process. Panellists evaluated each draft statement using a 5-point Likert scale (A: accept completely; B: accept with some reservations; C: accept with major reservations; D: reject with reservations; E: reject completely). When necessary, statements were modified, and a second vote was conducted. A consensus was recorded if ≥75% of the group accepted a statement completely or with reservations. When applicable, the level of evidence was evaluated using the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence.[9,10]

Consensus statements

In total, 14 statements met the threshold for consensus; these are summarised in Table 1.

Disease definition

Statement 1: Chronic kidney disease is defined as abnormalities of kidney structure or function with health implications, which are present for ≥3 months.

Chronic kidney disease stages 1 and 2 are characterised by structural abnormalities and persistent proteinuria, albuminuria, or haematuria. Patients present with a normal to mildly decreased estimated glomerular filtration rate (eGFR) of ≥60 mL/min/1.73 m^2, as well as other markers of kidney disease. Stage 3 is characterised by impaired kidney function, defined as an eGFR between 30 and 59 mL/min/1.73 m^2 on at least two occasions ≥3 months apart, irrespective of other markers of kidney disease. Stage 4 is defined as a severely reduced eGFR (15-29 mL/min/1.73 m^2), and stage 5 is considered kidney failure (eGFR <15 mL/min/1.73 m^2).[3]

Most patients with early CKD are asymptomatic and unaware of their disease. Diagnosis is often based on incidental findings during routine medical examinations. The detection of CKD in its early stages could lead to timely interventions, avoid inappropriate exposure to nephrotoxic agents, and delay CKD progression.[3]

Screening

Statement 2: People with hypertension, diabetes or cardiovascular disease should be screened for chronic kidney disease.

The screening of patients with higher CKD risk provides an opportunity to modify the disease course. Hypertension, diabetes, and cardiovascular diseases each has a single intermingled cause-and-effect relationship with CKD.[1] Hypertension is a common cause of CKD, particularly in older adults, as well as a risk factor for faster progression of

TABLE 1. Summary of Hong Kong consensus recommendations on the management of chronic kidney disease

	Statement	Evidence quality	Consensus level (responses)*
	Disease definition		
1	Chronic kidney disease is defined as abnormalities of kidney structure or function with health implications, which are present for ≥3 months.	1	93% (A: 57%, B: 36%, C: 7%, D: 0%, E: 0%)
	Screening		
2	People with hypertension, diabetes or cardiovascular disease should be screened for CKD.	1	100% (A: 100%, B: 0%, C: 0%, D: 0%, E: 0%)
3	Chronic kidney disease screening and risk stratification must consist of a combined assessment of eGFR and albuminuria (ie, uACR). If uACR assessments are not feasible or available, screening with spot urine albumin concentration, urine protein-creatinine ratio, or urine protein dipstick test may be regarded as alternatives.	3	100% (A: 71%, B: 29%, C: 0%, D: 0%, E: 0%)
	Disease monitoring		
4	Estimated glomerular filtration rate and albuminuria/proteinuria level should be monitored at least annually in patients with early stages of CKD and more often in patients with later stages of CKD or with a higher risk of progression.	1	100% (A: 93%, B: 7%, C: 0%, D: 0%, E: 0%)
5	Early recognition and treatment of CKD require awareness and involvement of clinicians, including (but not restricted to) nephrologists, endocrinologists, cardiologists, and primary care physicians.	1	93% (A: 79%, B: 14%, C: 7%, D: 0%, E: 0%)
	Lifestyle management		
6	Patients with CKD should not smoke, should maintain a normal body mass index, and should avoid processed foods with high salt and phosphate contents.	1	100% (A: 86%, B: 14%, C: 0%, D: 0%, E: 0%)
7	Patients with diabetes and CKD are advised to engage in moderate-intensity physical activity for a cumulative duration of ≥150 minutes per week or at a level compatible with their cardiovascular and physical tolerance.	1	100% (A: 100%, B: 0%, C: 0%, D: 0%, E: 0%)
	Treatment strategies		
8	In patients with type 2 diabetes, CKD, and an eGFR of ≥30 mL/min/1.73 m^2, metformin can be used as first-line pharmacological treatment for glycaemic control.	1	100% (A: 93%, B: 7%, C: 0%, D: 0%, E: 0%)
9	In patients with diabetes and hypertension or albuminuria, ACEis or ARBs should be initiated as first-line pharmacological treatment for renal protection and blood pressure control, and the maximum tolerated dose should be titrated.	1	100% (A: 79%, B: 21%, C: 0%, D: 0%, E: 0%)
10	In patients with T2DM and CKD who have an eGFR of ≥20 mL/min/1.73 m^2, a SGLT2i can be initiated as first-line pharmacological treatment for glycaemic control, renal protection, and cardiovascular protection.	1	93% (A: 64%, B: 29%, C: 7%, D: 0%, E: 0%)
11	Patients with T2DM who have an eGFR of ≥25 mL/min/1.73 m^2, normal serum potassium concentration, and uACR of ≥30 mg/g (≥3 mg/mmol) despite receiving the maximum tolerated dose of a RAS inhibitor can be treated with a nonsteroidal MRA for renal and cardiovascular protection, depending on accessibility.	1	86% (A: 50%, B: 36%, C: 14%, D: 0%, E: 0%)
12	Patients with T2DM and CKD who have not achieved individualised glycaemic targets despite metformin and SGLT2i treatment or who cannot use those medications can be treated with GLP-1 RAs.	1	100% (A: 64%, B: 36%, C: 0%, D: 0%, E: 0%)
13	Non-diabetic CKD patients with hypertension and a uACR of ≥200 mg/g (≥20 mg/mmol) should be treated with the maximum tolerated dose of an ACEi or an ARB for blood pressure control and renal protection.	2	100% (A: 93%, B: 7%, C: 0%, D: 0%, E: 0%)
14	Non-diabetic CKD patients with an eGFR of ≥20 mL/min/1.73 m^2 and a uACR of ≥200 mg/g (≥ 20 mg/mmol) can be treated with a SGLT2i for renal and cardiovascular protection.	1	100% (A: 71%, B: 29%, C: 0%, D: 0%, E: 0%)

Abbreviations: ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; MRA = mineralocorticoid receptor antagonist; RAS = renin-angiotensin system; SGLT2i = sodium-glucose cotransporter-2 inhibitor; T2DM = type 2 diabetes mellitus; uACR = urine albumin-creatinine ratio

* Likert scale responses: A: accept completely; B: accept with some reservations; C: accept with major reservations; D: reject with reservations; E: reject completely

kidney disease.[3] The Hong Kong Renal Registry lists hypertension as the third most common cause of renal replacement therapy in Hong Kong.[11]

In Hong Kong, diabetes is the most common primary aetiology leading to renal replacement therapy (49.6%).[11] It has also been identified as

a risk factor for CKD; most patients with stages 1 and 2 CKD are asymptomatic (36.0% and 47.1%, respectively).[12] This recommendation is consistent with the 2019 Hong Kong College of Physicians Clinical Practice Guidelines for the Provision of Renal Services in Hong Kong.[13]

Statement 3: Chronic kidney disease screening and risk stratification must consist of a combined assessment of estimated glomerular filtration rate and albuminuria (ie, urine albumin-creatinine ratio). If urine albumin-creatinine ratio assessments are not feasible or available, screening with spot urine albumin concentration, urine protein-creatinine ratio, or urine protein dipstick test may be regarded as alternatives.

Measurements of renal function are complex, and no single method provides an accurate overall assessment of renal function. Combined evaluation of GFR and albuminuria is the gold standard for CKD screening.[14] Glomerular filtration rate screening detects existing kidney damage, whereas albuminuria screening detects kidney damage occurring before substantial loss of nephron mass.[14] A change in albuminuria level also serves as a surrogate endpoint for CKD progression.[15]

In clinical practice, eGFR is used.[14] The Kidney Disease: Improving Global Outcomes (KDIGO) guideline defines CKD as an eGFR of <60 mL/min/1.73 m^2 or the detection of markers associated with kidney damage, or both, that persists for ≥3 months, regardless of the underlying cause.[14] Estimated glomerular filtration rate–based CKD detection can accurately assess kidney function.[16] In clinical practice, the eGFR is often derived from the serum creatinine concentration using the Chronic Kidney Disease Epidemiology Collaboration equation or the Modification of Diet in Renal Disease Study equation. Recent studies suggest that the Chronic Kidney Disease Epidemiology Collaboration equation predicts prognosis more accurately than the Modification of Diet in Renal Disease Study equation.[3,17,18]

Although urinary albumin excretion is an important prognostic biomarker for CKD, various methodologies are currently used to measure urinary albumin concentrations; these methodologies are not standardised in clinical practice.[14] The gold standard for urinary albumin measurement is the urine albumin-creatinine ratio (uACR). The normal range of uACR is <30 mg/g (<3 mg/mmol); values above this range indicate kidney damage. The KDIGO 2012 guideline provided the reference ranges for eGFR and uACR categories (Table 2; see Disclaimer at the end of this article).[3]

The expert panel recognised that uACR testing is not available to all clinicians. Therefore, spot screening for urinary albumin concentration, urine protein-creatinine ratio (uPCR), or a urine protein dipstick test may be regarded as alternatives. A cohort study of Indo-Asian patients showed that spot screening for urinary albumin concentration and the uACR could be considered comparable to screening for albuminuria.[19] Another study has also shown that the uPCR is positively correlated with the uACR.[20] A uPCR of >200 mg/g (>20 mg/mmol) indicates a high risk of kidney damage[21]; a dipstick protein reading of ≥1+ also indicates kidney damage. The expert panel noted that a diagnosis should be confirmed by repeated testing.

TABLE 2. Prognosis of chronic kidney disease according to glomerular filtration rates and albuminuria categories: Kidney Disease: Improving Global Outcomes (KDIGO) 2012[3] *

GFR categories (mL/min/1.73 m^2) Description and range			Persistent albuminuria categories Description and range		
			A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30-300 mg/g 3-30 mg/mmol	A3 Severely increased >300 mg/g >30 mg/mmol
G1	Normal or high	≥90	Low risk	Moderate risk	High risk
G2	Mildly decreased	60-89	Low risk	Moderate risk	High risk
G3a	Mildly to moderately decreased	45-59	Moderate risk	High risk	Very high risk
G3b	Moderately to severely decreased	30-44	High risk	Very high risk	Very high risk
G4	Severely decreased	15-29	Very high risk	Very high risk	Very high risk
G5	Kidney failure	<15	Very high risk	Very high risk	Very high risk

Reproduced with permission from KDIGO

Abbreviation: GFR = glomerular filtration rates

* See Disclaimer at the end of this article

Disease monitoring

Statement 4: Estimated glomerular filtration rate and albuminuria/proteinuria level should be monitored at least annually in patients with early stages of chronic kidney disease and more often in patients with later stages of chronic kidney disease or with a higher risk of progression.

Patients with CKD are often asymptomatic, especially in the early stages of disease.[22] Risk factors contributing to CKD progression include the underlying cause of CKD, reduced eGFR, albuminuria level, age, sex, race/ethnicity, elevated blood pressure, hyperglycaemia, dyslipidaemia, smoking, obesity, and history of cardiovascular disease.[3] The panel agreed that frequent (at least annual) monitoring of eGFR and albuminuria or proteinuria levels is important to ensure early detection of disease progression and prevent worsening. Nonetheless, uACR/proteinuria measurements may not be meaningful for patients with advanced CKD, kidney failure, or nephrotic syndrome.

Statement 5: Early recognition and treatment of chronic kidney disease require awareness and involvement of clinicians, including (but not restricted to) nephrologists, endocrinologists, cardiologists, and primary care physicians.

A CKD management programme should integrate CKD screening, patient risk stratification, and treatment within existing health services and processes.[23] Many international guidelines recommend a multidisciplinary approach for CKD screening and management.[4,6-8]

Patient risk stratification enabling appropriate referral to speciality care and increased follow-up frequency (when needed) can improve treatment efficiency.[24] A survey of primary care physicians in the United States showed that a robust multidisciplinary care team composed of dietitians, case managers, pharmacists, and health educators is desirable for enhancing patient education and facilitating self-management of risk factors for CKD progression.[25] Primary care physicians with access to multidisciplinary care teams agreed that this approach was extremely helpful.[25] Strategies to improve patient awareness of CKD, adherence to treatment, and achievement of CKD care goals should include greater access to effective self-management support within primary care.[25]

Lifestyle management

Statement 6: Patients with chronic kidney disease should not smoke, should maintain a normal body mass index, and should avoid processed foods with high salt and phosphate contents.

Smoking has been identified as a risk factor for CKD in Chinese and other populations,[26,27] and a cohort study from Taiwan revealed that obesity was associated with an increased risk of kidney failure, consistent with international data.[28] This recommendation is aligned with the Asian Pacific Society of Nephrology recommendation that people with diabetic kidney disease undergo smoking cessation interventions, maintain a healthy body mass index, and consume a diet rich in plant-based proteins and free of processed meats with high salt and phosphate contents.[8]

Statement 7: Patients with diabetes and chronic kidney disease are advised to engage in moderate-intensity physical activity for a cumulative duration of ≥150 minutes per week or at a level compatible with their cardiovascular and physical tolerance.

Improvements in physical activity levels offer cardiometabolic, kidney, and musculoskeletal benefits to the general population, including patients with diabetes.[29] A systematic review identified exercise training as a potential strategy to improve eGFR and body mass index while reducing conventional blood pressure (as measured by auscultation or oscillometric methods) in patients with CKD.[30] The expert panel agreed that clinicians should encourage patients with CKD to engage in moderate-intensity activities such as brisk walking, water aerobics, cycling, tennis, ballroom dancing, or general gardening.[29]

Treatment strategies

Statement 8: In patients with type 2 diabetes mellitus, chronic kidney disease, and an estimated glomerular filtration rate of ≥30 mL/min/1.73 m^2, metformin can be used as first-line pharmacological treatment for glycaemic control.

An evaluation of the effectiveness of common medications used to treat type 2 diabetes mellitus (T2DM) showed that metformin is superior to dipeptidyl peptidase-4 inhibitors and comparable to thiazolidinediones and sulfonylureas in terms of reducing glycated haemoglobin levels (with pooled mean differences in glycated haemoglobin levels of -0.37%, -0.07%, and 0.07%, respectively).[31] A meta-analysis concluded that metformin is superior to sulfonylureas in reducing the risk of hypoglycaemia among patients with normal kidney function (odds ratio [OR]=0.11; 95% confidence interval [CI]=0.06-0.20) and among patients with impaired kidney function (OR=0.17; 95% CI=0.11-0.26).[4] This recommendation is aligned with KDIGO guidance for patients with mild to moderate loss of kidney function and an eGFR of ≥30 mL/min/1.73 m^2.[4]

Statement 9: In patients with diabetes and hypertension or albuminuria, angiotensin-

converting enzyme inhibitors or angiotensin II receptor blockers should be initiated as first-line pharmacological treatment for renal protection and blood pressure control, and the maximum tolerated dose should be titrated.

A review by Strippoli et al[32] demonstrated the impacts of angiotensin-converting enzyme inhibitors (ACEis) and angiotensin II receptor blockers (ARBs) in terms of preventing kidney disease progression; both classes of medications significantly reduced the risk of progression to end-stage kidney disease compared with placebo or no treatment (relative risk [RR]=0.60; 95% CI=0.39-0.93 and RR=0.78; 95% CI=0.67-0.91, respectively). Angiotensin-converting enzyme inhibitors and ARBs also significantly reduced the risk of progression from microalbuminuria to macroalbuminuria (RR=0.45; 95% CI=0.29-0.69 and RR=0.49; 95% CI=0.32-0.75, respectively) and reduced the risk of serum creatinine doubling (RR=0.68; 95% CI=0.47-1.00 and RR=0.79; 95% CI=0.67-0.93, respectively).[32] Evaluation of ACEi or ARB efficacy in a Chinese population revealed that patients taking ACEis or ARBs had a lower mortality risk compared with untreated patients (OR=0.77; 95% CI=0.58-0.90).[33]

Although combination therapy with an ACEi and an ARB is superior to either medication as monotherapy in terms of reducing proteinuria and blood pressure,[34] such combination therapy can lead to higher incidences of hyperkalaemia and hypotension, especially in patients with advanced CKD.[35] Individualised patient management involving potassium binders may expand the applications of combined therapy[34]; however, the panel noted that some hypotensive patients may not tolerate ACEis or ARBs, and this approach is less popular because of emerging treatment options for CKD. Combined therapy should only be considered by experienced clinicians after careful assessment and discussion with the patient.

Statement 10: In patients with type 2 diabetes mellitus and chronic kidney disease who have an estimated glomerular filtration rate of ≥20 mL/min/1.73 m^2, a sodium-glucose cotransporter-2 inhibitor can be initiated as first-line pharmacological treatment for glycaemic control, renal protection, and cardiovascular protection.

Sodium-glucose cotransporter-2 inhibitors (SGLT2is) deliver glycaemic control while conferring cardiovascular[36-39] and renal[40-45] benefits to patients with T2DM and CKD who have an eGFR between 25 and 90 mL/min/1.73 m^2. In patients with T2DM and various levels of cardiovascular and renal risk, SGLT2i lowered all-cause mortality (OR=0.85; 95% CI=0.79-0.92), cardiovascular mortality (OR=0.84; 95% CI=0.76-0.92), non-fatal myocardial infarction (OR=0.87; 95% CI=0.79-0.97), and kidney failure (OR=0.71; 95% CI=0.57-0.89) compared with placebo.[46] The inhibitors are expected to reduce the incidence of kidney failure per 1000 patients over 5 years for patients with very low (1 case), low (3 cases), moderate (6 cases), high (25 cases), and very high (38 cases) baseline risk.[46] The effectiveness of SGLT2is in terms of glycaemic control is attenuated among patients with an eGFR of <45 mL/min/1.73 m^2.[47] Thus, additional therapy for glycaemic control may be needed in this population.

Statement 11: Patients with type 2 diabetes mellitus who have an estimated glomerular filtration rate of ≥25 mL/min/1.73 m^2, normal serum potassium concentration, and urine albumin-creatinine ratio of ≥30 mg/g (≥3 mg/mmol) despite receiving the maximum tolerated dose of a renin-angiotensin system inhibitor can be treated with a nonsteroidal mineralocorticoid receptor antagonist for renal and cardiovascular protection, depending on accessibility.

Multiple studies have demonstrated the renal and cardiovascular protective effects of mineralocorticoid receptor antagonists in patients with diabetes and CKD.[48-50] In the FIDELIO-DKD study (Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease), a lower incidence (18% vs 21%; P=0.001) compared with placebo was observed for the primary composite outcome of kidney failure, a sustained 40% decline in eGFR, or death from renal causes among T2DM patients with an eGFR of ≥25 mL/min/1.73 m^2 who received finerenone.[48] The trial showed that finerenone reduced the risk of the primary cardiovascular composite outcome of death from cardiovascular causes, non-fatal myocardial infarction, non-fatal stroke, or hospitalisation for heart failure in T2DM patients with an eGFR of ≥25 mL/min/1.73 m^2 (12.4% vs 14.2% in the placebo group; P=0.03).[49]

A meta-analysis of the efficacy and safety of finerenone in patients with CKD concluded that, compared with placebo, finerenone significantly reduced the uACR (mean difference: -0.30; P<0.05) while decreasing the risk of cardiovascular disorders and increasing the risk of hyperkalaemia (RR=0.92; 95% CI=0.85-0.99; P<0.05 and RR=2.04; 95% CI=1.77-2.34; P<0.00001, respectively).[50]

Statement 12: Patients with type 2 diabetes mellitus and chronic kidney disease who have not achieved individualised glycaemic targets despite metformin and sodium-glucose cotransporter-2 inhibitor treatment or who cannot use those medications can be treated with glucagon-like peptide-1 receptor agonists.

A 2022 trial compared the effectiveness of four commonly used glucose-lowering medications in patients with T2DM, namely, insulin glargine U-100, glimepiride (sulfonylurea), liraglutide (glucagon-like peptide-1 receptor agonist [GLP-1 RA]), and sitagliptin (dipeptidyl peptidase-4 inhibitor).[51] All four medications reduced glycated haemoglobin levels in combination with metformin, although glargine and liraglutide were modestly more effective in terms of achieving and maintaining glycaemic targets.[51] Severe hypoglycaemia was rare in all treatment groups: glimepiride (2.2% of participants), glargine (1.3%), liraglutide (1.0%), and sitagliptin (0.7%).[51] There were no differences in the rates of major adverse cardiac events, hospitalisation for heart failure, cardiovascular mortality, and all-cause mortality.[51]

A meta-analysis of randomised trials concluded that GLP-1 RAs are effective for cardiovascular and renal protection.[52] Similarly, Sattar et al[52] reported that GLP-1 RAs significantly reduced major adverse cardiac events by 14% (P<0.0001), all-cause mortality by 12% (P=0.0001), hospital admission for heart failure by 11% (P=0.013), and composite renal outcomes by 21% (P<0.0001), without increasing the risks of severe hypoglycaemia, retinopathy, or pancreatic adverse effects. The cardiovascular and renal protective effects of GLP-1 RAs in patients with T2DM were confirmed by a second meta-analysis.[46]

The expert panel noted that all available evidence regarding the renal protective effects of GLP-1 RAs was derived from secondary analyses of cardiovascular outcome trials. However, there is an ongoing renal outcome–specific trial involving semaglutide to further investigate its effects on renal outcomes.

Statement 13: Non-diabetic chronic kidney disease patients with hypertension and a urine albumin-creatinine ratio of ≥200 mg/g (≥20 mg/mmol) should be treated with the maximum tolerated dose of an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker for blood pressure control and renal protection.

Angiotensin-converting enzyme inhibitors produce antihypertensive and renal protective effects while reducing proteinuria in non-diabetic nephropathy patients.[53] The strong and consistent effects of ACEis in terms of slowing non-diabetic renal disease progression and decreasing blood pressure were confirmed in a meta-analysis of 11 randomised controlled trials.[53]

Coronel et al[54] showed that irbesartan usage in non-diabetic patients with advanced CKD had effects on disease progression and blood pressure control similar to those of ACEis. Irbesartan also showed a stronger antiproteinuric effect compared with ACEis.[54]

Statement 14: Non-diabetic chronic kidney disease patients with an estimated glomerular filtration rate of ≥20 mL/min/1.73 m^2 and a urine albumin-creatinine ratio of ≥200 mg/g (≥20 mg/mmol) can be treated with a sodium-glucose cotransporter-2 inhibitor for renal and cardiovascular protection.

There is increasing evidence of the renal and cardiovascular protective effects of SGLT2is in non-diabetic patients with CKD. The renal protective effects of SGLT2is in patients with CKD were demonstrated in the DAPA-CKD (Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease)[41] and EMPA-KIDNEY (Study of Heart and Kidney Protection with Empagliflozin) trials.[55] In the DAPA-CKD trial, dapagliflozin conferred a composite renal benefit (sustained eGFR decline of ≥50%, end-stage kidney disease, or death from renal causes; hazard ratio [HR]=0.56; 95% CI=0.45-0.68) in CKD patients with or without T2DM, an eGFR of 25 to 75 mL/min/1.73 m^2, and an uACR of 200 to 5000 mg/g (20-500 mg/mmol).[41] Dapagliflozin also reduced all-cause mortality (HR=0.69; 95% CI=0.53-0.88).[41] In the EMPA-KIDNEY trial, empagliflozin lowered the risk of kidney disease progression (defined as end-stage kidney disease, sustained eGFR decline to <10 mL/min/1.73 m^2, sustained eGFR decline of ≥40% from baseline, or death from renal causes; HR=0.71; 95% CI=0.62-0.81).[55]

Cardiovascular outcome trials showed that SGLT2is lowered the risks of heart failure hospitalisation and cardiovascular death by 30% to 35%.[56] The results of the DAPA-CKD[36] and EMPA-KIDNEY trials[55] confirmed that SGLT2is can benefit patients with CKD, regardless of T2DM status. Dapagliflozin is the only SGLT2i with evidence of reducing all-cause mortality in a clinical trial (ie, DAPA-CKD) specifically focused on patients with CKD, with or without T2DM. In the DAPA-CKD trial,[41] dapagliflozin lowered the composite risk of death from cardiovascular causes or hospitalisation for heart failure (HR=0.71; 95% CI=0.55-0.92).

Conclusion

Chronic kidney disease is a major health problem worldwide and in Hong Kong. Our consensus group developed this initial set of recommendations to familiarise Hong Kong clinicians with strategies for early CKD management. In this article, we discussed the current status of CKD management in Hong Kong; based on the limited local evidence and international evidence, we also highlighted the need for early diagnosis and treatment of CKD. Finally, we recommended appropriate treatment strategies for patients with CKD who present with co-morbid diabetes or hypertension.

Author contributions

All authors contributed to the concept or design, acquisition

of data, analysis or interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

RCW Ma has received research funding from AstraZeneca, Bayer, Merck Sharp & Dohme, Novo Nordisk, Pfizer, Roche Diagnostics, and Tricida Inc for carrying out clinical trials or studies, and from AstraZeneca, Bayer, Boehringer Ingelheim, and Merck for speaker honoraria or consultancy on advisory boards. All proceeds have been donated to The Chinese University of Hong Kong to support diabetes research. CC Szeto receives research support from AstraZeneca, Boehringer Ingelheim, and Otsuka Pharmaceutical. KCB Tan has participated in advisory boards and speakers bureaus for Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, and Sanofi. MCS Wong is an advisory committee member for Pfizer; an external expert for GlaxoSmithKline Limited, a member of the advisory board of AstraZeneca, and an honorary advisor of GenieBiome Limited. He was paid consultancy fees for providing research advice and delivering talks. Also, as an editor of the journal, he was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

Acknowledgement

English language editing and writing support, funded by an unrestricted educational grant from AstraZeneca Hong Kong Limited, was provided by Mr Poh Sien Ooi of MIMS Medica Sdn Bhd and Dr Mita Pabari of MIMS (Hong Kong) Limited. The funder had no role in study design, data collection, analysis, interpretation, or manuscript preparation.

Disclaimer

This article references the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Please note that the KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease[57] has been published during the development of this work. As such, readers are advised to consult the most recent KDIGO guideline for the latest recommendations and information on chronic kidney disease.

References

1. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney Int Supp (2011) 2022;12:7-11.
2. Non-communicable Disease Branch, Centre for Health Protection, Department of Health, Hong Kong SAR Government. Report of Population Health Survey 2020-22 (Part I). 2022. Available from: https://www.chp.gov.hk/files/pdf/dh_phs_2020-22_part_1_report_eng_rectified.pdf. Accessed 14 May 2023.
3. Kidney Disease: Improving Global Outcomes. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl 2013;3:1-150.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. Kidney Int 2022;102(5S):S1-127.
5. Shlipak MG, Tummalapalli SL, Boulware LE, et al. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int 2021;99:34-47.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. Kidney Int 2021;100(4S):S1-276.
7. Banerjee D, Winocour P, Chowdhury TA, et al. Management of hypertension in patients with diabetic kidney disease: summary of the Joint Association of British Clinical Diabetologists and UK Kidney Association (ABCD-UKKA) Guideline 2021. Kidney Int Rep 2022;7:681-7.
8. Liew A, Bavanandan S, Prasad N, et al. Asian Pacific Society of Nephrology clinical practice guideline on diabetic kidney disease—executive summary. Nephrology (Carlton) 2020;25 Suppl 2:3-11.
9. Howick J, Chalmers I, Glasziou P, et al. The 2011 Oxford CEBM Evidence Levels of Evidence (Introductory Document). 2011. Available from: https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence. Accessed 27 May 2024.
10. OCEBM Levels of Evidence Working Group. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. Available from: https://www.cebm.ox.ac.uk/files/levels-of-evidence/cebm-levels-of-evidence-2-1.pdf. Accessed 27 Aug 2024.
11. Leung CB, Cheung WL, Li PK. Renal registry in Hong Kong—the first 20 years. Kidney Int Suppl (2011) 2015;5:33-8.
12. Mok KY, Chan PF, Lai LK, Chow KL, Chao DV. Prevalence of diabetic nephropathy among Chinese patients with type 2 diabetes mellitus and different categories of their estimated glomerular filtration rate based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation in primary care in Hong Kong: a cross-sectional study. J Diabetes Metab Disord 2019;18:281-8.
13. Tang SC, Wong AK, Mak SK. Clinical practice guidelines for the provision of renal service in Hong Kong: general nephrology. Nephrology (Carlton) 2019;24 Suppl 1:9-26.
14. Seidu S, Barrat J, Khunti K. Clinical update: the important role of dual kidney function testing (ACR and eGFR) in primary care: identification of risk and management in type 2 diabetes. Prim Care Diabetes 2020;14:370-5.
15. Heerspink HJ, Greene T, Tighiouart H, et al. Change in albuminuria as a surrogate endpoint for progression of kidney disease: a meta-analysis of treatment effects in randomised clinical trials. Lancet Diabetes Endocrinol 2019;7:128-39.
16. Vassalotti JA, Centor R, Turner BJ, et al. Practical approach to detection and management of chronic kidney disease for the primary care clinician. Am J Med 2016;129:153-62.e7.
17. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
18. Earley A, Miskulin D, Lamb EJ, Levey AS, Uhlig K. Estimating equations for glomerular filtration rate in the era of creatinine standardization: a systematic review. Ann Intern Med 2012;156:785-95.

19. Jafar TH, Chaturvedi N, Hatcher J, Levey AS. Use of albumin-creatinine ratio and urine albumin concentration as a screening test for albuminuria in an Indo-Asian population. Nephrol Dial Transplant 2007;22:2194-200.
20. Kulasooriya PN, Bandara SN, Priyadarshani C, et al. Prediction of microalbuminuria by analysing total urine protein-to-creatinine ratio in diabetic nephropathy patients in rural Sri Lanka. Ceylon Med J 2018;63:72-7.
21. Kamińska J, Dymicka-Piekarska V, Tomaszewska J, Matowicka-Karna J, Koper-Lenkiewicz OM. Diagnostic utility of protein-to-creatinine ratio (P/C ratio) in spot urine sample within routine clinical practice. Crit Rev Clin Lab Sci 2020;57:345-64.
22. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. Lancet 2017;389:1238-52.
23. Tsang JY, Blakeman T, Hegarty J, Humphreys J, Harvey G. Understanding the implementation of interventions to improve the management of chronic kidney disease in primary care: a rapid realist review. Implement Sci 2016;11:47.
24. Smekal MD, Tam-Tham H, Finlay J, et al. Patient and provider experience and perspectives of a risk-based approach to multidisciplinary chronic kidney disease care: a mixed methods study. BMC Nephrol 2019;20:110.
25. Sperati CJ, Soman S, Agrawal V, et al. Primary care physicians' perceptions of barriers and facilitators to management of chronic kidney disease: a mixed methods study. PLoS One 2019;14:e0221325.
26. Elihimas Júnior UF, Elihimas HC, Lemos VM, et al. Smoking as risk factor for chronic kidney disease: systematic review [in English, Portuguese]. J Bras Nefrol 2014;36:519-28.
27. Xue L, Lou Y, Feng X, Wang C, Ran Z, Zhang X. Prevalence of chronic kidney disease and associated factors among the Chinese population in Taian, China. BMC Nephrol 2014;15:205.
28. Lin YC, Lai YJ, Lin YC, et al. Effect of weight loss on the estimated glomerular filtration rates of obese patients at risk of chronic kidney disease: the RIGOR-TMU study. J Cachexia Sarcopenia Muscle 2019;10:756-66.
29. Milam RH. Exercise guidelines for chronic kidney disease patients. J Ren Nutr 2016;26:e23-5.
30. Mallamaci F, Pisano A, Tripepi G. Physical activity in chronic kidney disease and the EXerCise Introduction To Enhance trial. Nephrol Dial Transplant 2020;35 (Suppl 2):ii18-22.
31. Bennett WL, Maruthur NM, Singh S, et al. Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. Ann Intern Med 2011;154:602-13.
32. Strippoli GF, Bonifati C, Craig M, Navaneethan SD, Craig JC. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease. Cochrane Database Syst Rev 2006;2006:CD006257.
33. Song YH, Cai GY, Xiao YF, Liu JQ, Chen XM. The clinical characteristics and antihypertensive medications for mortality of elderly hospitalized hemodialysis patients: a multicenter retrospective study in China. Saudi J Kidney Dis Transpl 2021;32:637-44.
34. Zhao M, Qu H, Wang R, et al. Efficacy and safety of dual vs single renin-angiotensin-aldosterone system blockade in chronic kidney disease: an updated meta-analysis of randomized controlled trials. Medicine (Baltimore) 2021;100:e26544.
35. Palevsky PM, Zhang JH, Seliger SL, Emanuele N, Fried LF; VA NEPHRON-D Study. Incidence, severity, and outcomes of AKI associated with dual renin-angiotensin system blockade. Clin J Am Soc Nephrol 2016;11:1944-53.
36. McMurray JJ, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019;381:1995-2008.
37. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med 2020;383:1413-24.
38. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med 2017;377:644-57.
39. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2019;380:347-57.
40. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med 2019;380:2295-306.
41. Heerspink HJ, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med 2020;383:1436-46.
42. Bakris G, Oshima M, Mahaffey KW, et al. Effects of canagliflozin in patients with baseline eGFR <30 ml/min per 1.73 m^2: subgroup analysis of the randomized CREDENCE trial. Clin J Am Soc Nephrol 2020;15:1705-14.
43. Chertow GM, Vart P, Jongs N, et al. Effects of dapagliflozin in stage 4 chronic kidney disease. J Am Soc Nephrol 2021;32:2351-61.
44. Bhatt DL, Szarek M, Pitt B, et al. Sotagliflozin in patients with diabetes and chronic kidney disease. N Engl J Med 2021;384:129-39.
45. Li N, Zhou G, Zheng Y, et al. Effects of SGLT2 inhibitors on cardiovascular outcomes in patients with stage 3/4 CKD: a meta-analysis. PLoS One 2022;17:e0261986.
46. Palmer SC, Tendal B, Mustafa RA, et al. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. BMJ 2021;372:m4573.
47. Cherney DZ, Cooper ME, Tikkanen I, et al. Pooled analysis of phase III trials indicate contrasting influences of renal function on blood pressure, body weight, and HbA1c reductions with empagliflozin. Kidney Int 2018;93:231-44.
48. Bakris GL, Agarwal R, Anker SD, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. N Engl J Med 2020;383:2219-29.
49. Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. N Engl J Med 2021;385:2252-63.
50. Fu Z, Geng X, Chi K, et al. Efficacy and safety of finerenone in patients with chronic kidney disease: a systematic review with meta-analysis and trial sequential analysis. Ann Palliat Med 2021;10:7428-39.
51. GRADE Study Research Group; Nathan DM, Lachin JM, et al. Glycemia reduction in type 2 diabetes—glycemic outcomes. N Engl J Med 2022;387:1063-74.
52. Sattar N, Lee MM, Kristensen SL, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials. Lancet Diabetes Endocrinol 2021;9:653-62.

53. Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data. Ann Intern Med 2001;135:73-87.
54. Coronel F, Cigarrán S, García-Mena M, Herrero J, Calvo N, Pérez-Flores I. Irbesartan in hypertensive non-diabetic advanced chronic kidney disease. Comparative study with ACEi [in Spanish]. Nefrologia 2008;28:56-60.
55. The EMPA-KIDNEY Collaborative Group; Herrington WG, Staplin N, et al. Empagliflozin in patients with chronic kidney disease. N Engl J Med 2023;388:117-27.
56. Joshi SS, Singh T, Newby DE, Singh J. Sodium-glucose co-transporter 2 inhibitor therapy: mechanisms of action in heart failure. Heart 2021;107:1032-8.
57. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int 2024;105(4S):S117-314.

