The prevention and management of chronic kidney disease among patients with metabolic syndrome

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Treatment of patients with chronic kidney disease (CKD) requires implementation of prevention and management strategies that reduce the risk of kidney failure and CKD-associated cardiovascular risk. Metabolic syndrome is characterized by obesity, high blood pressure, dyslipidemia, and hyperglycemia, and it is common among patients with CKD. Large-scale randomized trials have led to significant advances in the management of CKD, with 5 pharmacotherapies now proven to be nephroprotective and/or cardioprotective in certain types of patients. Renin-angiotensin system inhibitors and sodium-glucose cotransporter 2 inhibitors slow kidney disease progression and reduce heart failure complications for most patients with CKD. In addition, statin-based regimens lower low-density lipoprotein cholesterol and reduce the risk of atherosclerotic disease (with no clinically meaningful effect on kidney outcomes). For patients with type 2 diabetes and albuminuric CKD, the nonsteroidal mineralocorticoid receptor antagonist finerenone and the glucagon-like peptide-1 receptor agonist semaglutide also confer cardiorenal benefits, with semaglutide additionally effective at reducing weight. Together, these randomized data strongly suggest that metabolic syndrome mediates some of the cardiorenal risk observed in CKD. Considered separately, the trials help elucidate which components of metabolic syndrome influence the pathophysiology of kidney disease progression and which separately modify risk of atherosclerotic and nonatherosclerotic cardiovascular outcomes. As we predict complementary and different mechanisms of nephroprotection and cardioprotection for these different interventions, it seems logical that they should be deployed together to maximize benefits. Even when combined, however, these therapies are not a cure, so further trials remain important to reduce the residual cardiorenal risks associated with CKD.

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Editor's Note

Obesity, metabolic syndrome, and diabetes are commonly associated with chronic kidney disease (CKD) and cardiovascular disease (CVD). The management of these patients with high morbidities and mortality has been challenging. However, recent clinical trials have shown that several new classes of medications have both renal and cardiac protective effects, and some of them could also induce weight loss and improve lipid and metabolic profile in this patient population. In this first mini review of this series on "Metabolic disorder–associated kidney diseases," the authors provide an updated review on the current prevention and treatment of patients with metabolic dysfunction–associated CKD and CVD based on the recently published randomized clinical trials.

Metabolic syndrome is characterized by a cluster of interconnected metabolic abnormalities that include obesity, high blood pressure, dyslipidemia (high triglycerides and low high-density lipoprotein cholesterol), and hyperglycemia (Table 1).[1–4] The global prevalence of metabolic syndrome is estimated to be between 13%−31% in adults and has increased almost in parallel with the global obesity epidemic.[5,6] There is a strong association of metabolic syndrome with cardiovascular disease and an increasingly studied association of metabolic syndrome (and its components) with chronic kidney disease (CKD).[7,8] Indeed, the American Heart Association recently proposed the cardiovascular-kidney-metabolic syndrome and developed risk prediction equations that highlight the pathophysiological interactions of CKD, cardiovascular disease, and

Table 1 | Summary table of 4 key definitions of metabolic syndrome

Definition	Criteria						
	Requirements	Obesity	Hypertension	Dyslipidemia		Hyperglycemia	Other
World Health Organization 1998[1]	***Insulin resistance and any 2 other criteria***	BMI >30 kg/m^2 and/or WHR >0.9 (M), >0.85 (F)	≥140/90 mm Hg	Triglycerides ≥150 mg/dl[a]	HDL-C <35 (M), <39 (F) mg/dl	**Evidence of insulin resistance (e.g., impaired glucose tolerance or type 2 diabetes)**	Evidence of albuminuria (e.g., uACR ≥30 mg/g)
IDF 2005[2]	***Central obesity and any 2 other criteria***	**Elevated waist circumference with ethnicity-specific cut points**	≥130/≥85 mm Hg or treatment of previously diagnosed hypertension	Triglycerides ≥150 mg/dl[a] or treatment for this lipid abnormality	HDL-C <40 (M), <50 (F) mg/dl[b] or treatment for this lipid abnormality	Fasting glucose ≥100 mg/dl or previously diagnosed diabetes	
AHA/NHLBI 2005[3]	***Presence of ≥3 of the following 5 criteria***	Waist circumference ≥102 (M), ≥88 (F) cm in Europids	≥130/≥85 mm Hg or treatment of hypertension	Triglycerides ≥150 mg/dl[a] or treatment for this lipid abnormality	HDL-C <40 (M), <50 (F) mg/dl[b] or treatment for this lipid abnormality	Fasting glucose ≥100 mg/dl or treatment for elevated glucose	
Harmonized definition incorporating IDF and AHA/NHLBI definitions 2009[4]	***Presence of ≥3 of the following 5 criteria***	Elevated waist circumference with population- and country-specific cut points	≥130/≥85 mm Hg or treatment of previously diagnosed hypertension	Triglycerides ≥150 mg/dl[a] or treatment for this lipid abnormality	HDL-C <40 (M), <50 (F) mg/dl[b] or treatment for this lipid abnormality	Fasting glucose ≥100 mg/dl or treatment for elevated glucose	

AHA, American Heart Association; BMI, body mass index; Europids, people of European origin; F, female; HDL-C, high-density lipoprotein cholesterol; IDF, International Diabetes Federation; M, male; NHLBI, National Heart, Lung, and Blood Institute; uACR, urinary albumin-to-creatinine ratio; WHR, waist-to-hip ratio.
[a]Triglycerides ≥1.7 mmol/l.
[b]HDL-C <1.0 (M), <1.3 (F) mmol/l.
Bold and italicized text indicate xxx.

metabolic risk factors.[9,10] Large-scale, high-quality, randomized trials in the past decade have led to significant advances in the management of patients with CKD and help elucidate which components of metabolic syndrome influence the pathophysiology of kidney disease progression and cardiovascular outcomes. This review provides an updated overview of how the components of metabolic syndrome modify the risk of kidney failure and different types of cardiovascular disease, focusing on the randomized data.

Risk prediction

Albuminuria is one of the earliest signs of kidney damage, and there is a steep association between level of albuminuria and future risk of kidney failure and cardiovascular events.[11–13] Despite this knowledge, rates of albuminuria screening in general are low.[14] Clinical practice guidelines recommend urine albumin-to-creatinine ratio measurements alongside estimated glomerular filtration rate (eGFR) as part of the routine assessment of patients with metabolic syndrome to enable health care professionals to recognize onset of kidney disease early, and quantify risk of kidney failure once diagnosed with CKD.[13] Moreover, the indications for some risk-modifying therapies are currently restricted to patients with type 2 diabetes and CKD with evidence of albuminuria (finerenone and semaglutide).

The Kidney Disease: Improving Global Outcomes (KDIGO) heat map risk stratification of CKD reinforces the importance to health professionals of using both eGFR and urine albumin-to-creatinine ratio for assessing severity and prognosis of CKD at a population level but does not enable individual risk prediction.[13] Several risk prediction tools have been developed for patients with CKD that allow health care professionals to estimate absolute risk for individuals and for specific outcomes. The kidney failure risk equation is a risk prediction tool for the progression of CKD stage 3 to 5 to kidney failure in the next 2 or 5 years.[15] Although the kidney failure risk equation was not specifically developed for patients with metabolic syndrome (and does not include the components of metabolic syndrome as variables), the models have been extensively validated in diverse populations with CKD stages 3 to 5, including patients with metabolic syndrome.[16,17] Patients with metabolic syndrome and CKD stages 1 to 2 may be at risk of rapid progression but low risk of kidney failure in the next 5 years, and alternative risk prediction equations have been developed for predicting progression (e.g., based on ≥40% eGFR decline).[18]

To complement the kidney outcome risk prediction tools, the cardiovascular-kidney-metabolic staging construct incorporates the KDIGO heat map and reflects the spectrum of cardiovascular risk.[9,10] PREVENT are risk prediction equations that enable 10- and 30-year risk estimates for total cardiovascular disease and include eGFR as a predictor with an option to add urine albumin-to-creatinine ratio.[19] The particular inclusion of heart failure risk alongside atherosclerotic cardiovascular disease means this is a useful new tool to facilitate identification of those at increased cardiovascular risk in CKD, where heart failure and structural heart disease are increasingly prevalent as eGFR decreases.[20]

Excess adiposity

Measures of adiposity (body mass index, waist-to-hip ratio, and waist circumference) have been positively associated with risk of CKD.[21,22] Genetic analyses suggest that the effect of increased adiposity on CKD risk is largely causal and partially mediated by diabetes and blood pressure (BP).[23] However, other mechanisms not linked to diabetes or BP could still be responsible for some of the adiposity-CKD associated risk. KDIGO recommends patients with CKD to achieve an optimal body mass index and undertake physical activity compatible with cardiovascular health, tolerance, and level of frailty.[13] This seems reasonable given that physical inactivity is a modifiable risk factor for cardiovascular disease and mortality in the general population, and regular exercise training is associated with improved health outcomes in individuals with CKD.[24,25] Moreover, the Look AHEAD trial demonstrated that an intensive lifestyle intervention (compared with diabetes support and education) reduced the incidence of very-high-risk CKD by 31% over a median of 9.6 years in 5145 overweight and obese patients with diabetes.[26] This was partially attributable to reductions in hemoglobin A_{1c}, weight, and BP, with a 1.6 (range, 1.1–2.0) mm Hg reduction in systolic BP per 1-kg/m^2 decrease in body mass index.[27,28]

Recently, glucagon-like peptide-1 receptor agonists (GLP-1RAs) have revolutionized the management of excess adiposity.[29] GLP-1 receptor stimulation increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, decelerates gastric emptying, and increases satiety while decreasing prospective food consumption. The SELECT trial demonstrated that allocation to the high "weight-loss dose" of semaglutide (2.4 mg weekly s.c.) versus placebo over 2.8 years led to a 20% reduction in its primary cardiovascular composite outcome (hazard ratio [HR], 0.80; 95% confidence interval [CI], 0.72–0.90) in 17,604 patients who are overweight or obese with preexisting cardiovascular disease, but *without* diabetes.[30] In addition to the benefit on risk of recurrent atherosclerotic disease, there was an 18% reduction in risk of a heart failure composite outcome (HR, 0.82; 95% CI, 0.71–0.96). Subanalyses of SELECT also suggest possible renoprotection in this population, with a lower incidence of a composite kidney outcome with semaglutide versus placebo (1.8% versus 2.4%; HR, 0.78; 95% CI, 0.63–0.96).[31] To complement this, the FLOW trial demonstrated that allocation to the lower "glycemic control dose" of semaglutide (1.0 mg weekly s.c.) versus placebo over 3.4 years led to a 24% lower risk of major kidney disease events or death from kidney-related or cardiovascular causes (HR, 0.76; 95% CI, 0.66–0.88) in 3533 patients with type 2 diabetes and CKD with albuminuria.[32] Gastrointestinal adverse effects do lead to permanent discontinuation of semaglutide in a minority of patients (the absolute excess was 8.0% in SELECT and 3.4% in FLOW), but the safety data from large trials provide considerable reassurance on use of

GLP-1RAs in overweight/obese patients with type 2 diabetes and CKD.[30,32] Taken altogether, there is now substantial evidence that the GLP-1RA semaglutide should be implemented alongside other first-line treatments for patients overweight with preexisting cardiovascular disease, and for patients with type 2 diabetes and CKD with albuminuria.

BP and the renin-angiotensin-aldosterone system

Accelerated phase hypertension can cause severe kidney injury, but the extent to which moderate increases in BP affect kidney outcomes is unclear. Studies have not been able to disentangle the complex interrelationship and establish definitively if the increase in BP caused by CKD creates a vicious cycle of further declines in kidney function.[33] Genetic association studies have yielded conflicting results regarding the causal relationship between high BP and kidney outcomes.[34,35] Furthermore, meta-analyses of intensive versus standard BP-lowering trials that tested an average BP difference of ≈7 mm Hg (down to 130 mm Hg) revealed no clear benefit on kidney outcomes.[36,37]

There is a well-documented log-linear relationship between higher BP and increased cardiovascular mortality in apparently healthy adults, without evidence of a threshold down to at least 115/75 mm Hg.[38] The SPRINT trial showed that a systolic BP target of <120 mm Hg (compared with a target of <140 mm Hg) reduced the risk of major adverse cardiovascular events by 25% (HR, 0.75; 95% CI, 0.64–0.89) in 9361 patients with a systolic BP of ≥130 mm Hg and an increased cardiovascular risk, but *without* diabetes.[39] There was no difference in the main kidney outcome between the 2 randomized groups in the participants with CKD at baseline, perhaps not surprising given the relatively mild CKD with a low risk of progression (66% had a baseline eGFR ≥45 ml/min per 1.73 m^2) in the selected population.[40] However, the relative cardiovascular benefits were similar in people with and without CKD, and although the SPRINT trial excluded patients with diabetes, the cardiovascular benefits of BP lowering (particularly the reduced risk of stroke) are apparent in patients with diabetes in meta-analysis of intensive versus standard BP-lowering trials.[41,42] KDIGO therefore recommends targeting a systolic BP to <120 mm Hg, when tolerated, using standardized office BP measurement (with recommended preparation procedures to ensure the patient is relaxed) to reduce cardiovascular risk in patients with CKD.[43] Routine office BP measurements (without preparation procedures) are generally higher, and their sole use could lead to a higher incidence of hypotension-related adverse events when an intensive strategy is implemented.

The renin-angiotensin-aldosterone system has a key role in the development of high BP and has been implicated in the etiology of obesity, dyslipidemia, and insulin resistance, suggesting it could be a common thread linking the components within metabolic syndrome.[44] In addition to reducing BP, renin-angiotensin system inhibitors (RASis) reduce the risk of kidney failure in patients with diabetes and albuminuria, with some evidence of renoprotection in patients with proteinuric nondiabetic kidney diseases.[45–47] KDIGO recommends RASi treatment for patients with CKD and moderate-to-severe albuminuria and patients with CKD and normal-to-mild albuminuria with specific indications (e.g., to treat hypertension or heart failure with reduced ejection fraction).[13]

Aldosterone acts downstream of the RAS, forming the last effector of the renin-angiotensin-aldosterone system, and has profibrotic and inflammatory effects in the heart, vasculature, and kidney.[48] Although patients taking RASis are partially protected against increased aldosterone levels, chronic use of them can still result in mineralocorticoid receptor overactivation because of an incomplete suppression of serum aldosterone (i.e., aldosterone breakthrough).[49] Targeting residual aldosterone overactivity is desirable and has led to the development of nonsteroidal mineralocorticoid receptor antagonists (nsMRAs) and, more recently, aldosterone synthase inhibitors (ASis). For patients with type 2 diabetes and CKD with albuminuria, the nsMRA finerenone has been shown in 2 large trials (FIDELIO-DKD [Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease] and FIGARO-DKD [Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease]) to confer reductions in cardiorenal risk when taken in addition to RASis. In pooled analyses of these trials with the FINEARTS-HF trial conducted in patients with heart failure with preserved ejection fraction, finerenone was shown to reduce the composite kidney outcome by 20% (HR, 0.80; 95% CI, 0.72–0.90) and the risk of hospitalization from heart failure by 17% (HR, 0.83; 95% CI, 0.75–0.92) in 18,991 participants over 2.9 years.[50] Both nsMRAs and ASis increase serum potassium levels, and findings from currently reported finerenone and ASi trials have limited their generalizability because of a serum potassium screening visit eligibility criterion requiring potassium of ≤4.8 mmol/l. Ongoing and future large trials will help determine if nsMRAs and ASis can also offer kidney and cardiovascular benefits for patients with nondiabetic kidney disease and those without significant albuminuria.[51–53]

Lipid-modifying treatments

In patients with CKD, dyslipidemia is a common complication, and the lipid abnormalities mirror that of metabolic syndrome: high triglycerides, low high-density lipoprotein cholesterol, and an increased proportion of low-density lipoprotein particles that are small and oxidized.[54] However, among 6245 participants with CKD not on dialysis at randomization, lowering low-density lipoprotein cholesterol (LDL-C) by 0.96 mmol/l with simvastatin, 20 mg, and ezetimibe, 10 mg, for 5 years had no significant effect on the progression of kidney disease.[55] There was no excess risk of hepatitis, gallstones, or cancer, and the excess risk of myopathy was only 2 per 10,000 patients with CKD per year of this statin-based treatment.[56] Although lowering LDL-C using statin-based therapies has no clinically meaningful effect on risk of kidney failure, the beneficial effects on the risk of atherosclerotic cardiovascular disease are well established in

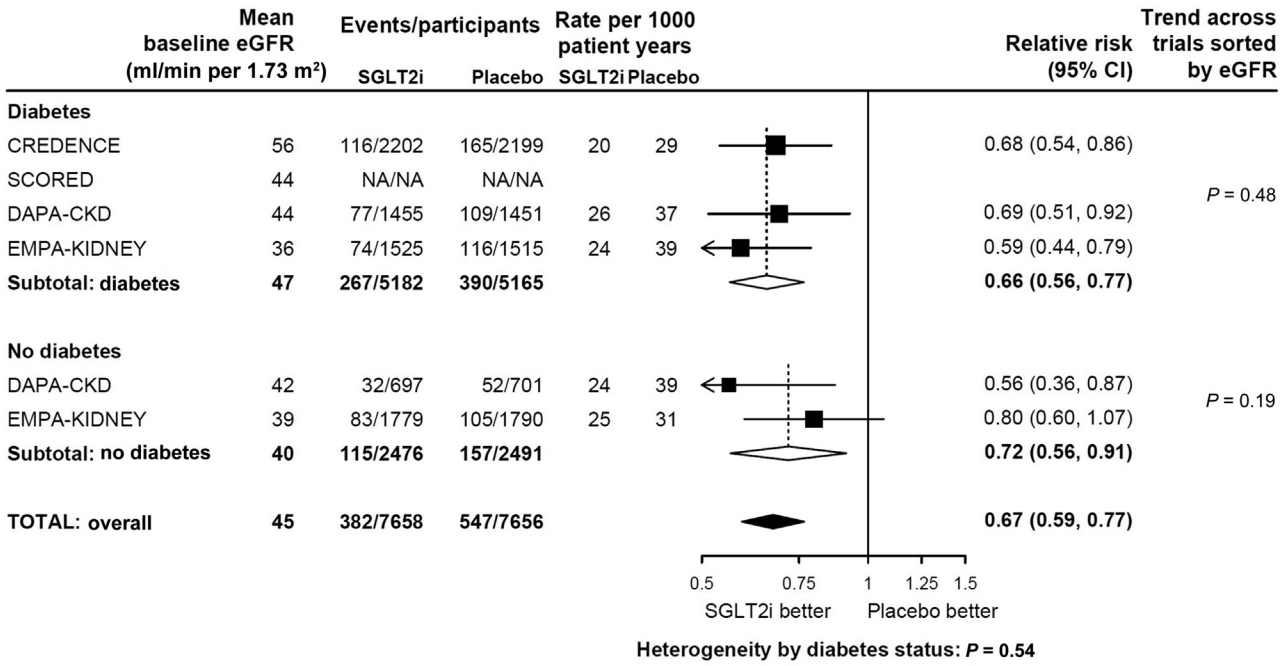

Figure 1 | Effect of sodium-glucose cotransporter-2 inhibition (SGLT2i) on kidney failure by diabetes status in the 4 dedicated chronic kidney disease trials. Kidney failure, defined as composite of sustained estimated glomerular filtration rate (eGFR) <15 ml/min per 1.73 m^2 (or eGFR <10 ml/min per 1.73 m^2 in EMPA-KIDNEY [The Study of Heart and Kidney Protection With Empagliflozin]), maintenance dialysis, or kidney transplantation. Data for kidney failure not available for SCORED. Adapted from *The Lancet*, Volume 400, Issue 10365, The Nuffield Department of Population Health Renal Studies Group, SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium, Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials, pages 1788–1801.[68] CI, confidence interval; CREDENCE, Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation; DAPA-CKD, Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease.

people with and without CKD.[57] Therefore, KDIGO recommends statin-based regimens for patients with CKD not treated with dialysis or kidney transplantation if aged ≥50 years or 18 to 49 years and at risk of atherosclerotic cardiovascular disease.[13,58]

The proportional benefits of lowering LDL-C are determined by the absolute LDL-C reduction, and so in CKD, the data suggest we should aim to maximize the reduction in LDL-C. Proprotein convertase subtilisin kexin 9 inhibitors are a promising alternative or additional LDL-C–lowering therapy to statins with the potential to provide further reductions in risk of atherosclerotic cardiovascular disease for patients with mild-moderate CKD.[59,60] In addition, bempedoic acid also lowers LDL-C and is associated with a reduced risk of major cardiovascular events among statin-intolerant patients, including those with mild-moderate CKD.[61,62] Currently, there is no evidence that high-density lipoprotein cholesterol–increasing pharmacotherapies and insufficient evidence that triglyceride-lowering (e.g., fibrates) pharmacotherapies improve clinical outcomes in patients with CKD.[58]

Glycemic targets and modifying glucose metabolism

KDIGO recommends that patients with CKD and diabetes should have an individualized hemoglobin A_{1c} target ranging from <6.5% to <8.0%, with higher targets in those with a high risk of hypoglycemia.[13,63] The effect of more intensive glycemic control compared with less intensive glycemic control on the risk of kidney failure is uncertain, but such an approach reduces risk of developing or worsening of diabetic nephropathy based on measures of albuminuria.[64–66] More intensive glycemic control in patients with type 2 diabetes is also associated with a reduced risk of progression of retinopathy and perhaps may modestly reduce risk of atherosclerotic cardiovascular events (but not heart failure).[64,67]

The notable kidney and cardiovascular protective effects of sodium-glucose cotransporter-2 inhibitors (SGLT2is) mean that these agents should be prioritized in patients with CKD irrespective of diabetes status, glycemic control, or level of albuminuria. A meta-analysis of all of the 13 large SGLT2i randomized control trials included 90,413 participants and demonstrated that the proportional benefits on a standardized kidney disease progression outcome were large (HR, 0.63; 95% CI, 0.58–0.69). In the 3 dedicated CKD progression trials, SGLT2 inhibition reduced the risk of kidney failure by 34% (HR, 0.66; 95% CI, 0.56–0.77) compared with placebo (Figure 1).[68] There were also significant effects on risk of nonatherosclerotic cardiovascular outcomes, with a 23% reduction in the risk of the composite outcome of cardiovascular death or hospitalization for heart failure (HR, 0.77; 95% CI, 0.74–0.81). These cardiorenal benefits were similar

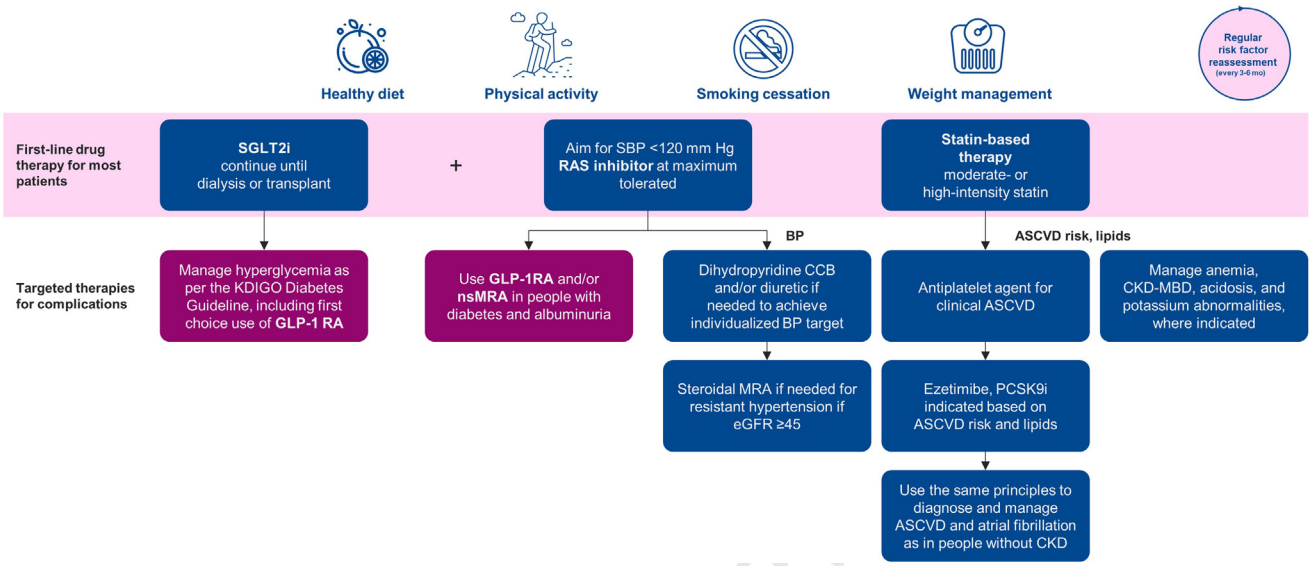

Figure 2 | Proposed updates of 2024 Kidney Disease: Improving Global Outcomes (KDIGO) chronic kidney disease (CKD) management guideline following results of FLOW. We suggest the glucagon-like peptide-1 receptor agonist (GLP-1RA) semaglutide should be considered (in addition to the nonsteroidal mineralocorticoid receptor antagonist [nsMRA] finerenone) alongside other first-line drug therapies for patients with type 2 diabetes and albuminuria.[32] In addition, GLP-1RAs should be a first choice consideration to manage hyperglycemia. ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; MBD, mineral and bone disorder; MRA, mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RASi, renin-angiotensin system inhibitor; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter 2 inhibitor. Adapted from *Kidney International*, Volume 105, Issue 4S, Kidney Disease: Improving Global Outcomes (KDIGO) CKD Working Group, KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, Chapter 3: Delaying CKD progression and managing its complications, pages S117–S314,.[13]

across different categories of CKD causes, and in patients with and without diabetes.[68,69] In the studied populations, SGLT2 inhibition was associated with approximately an 8% increased risk of urinary tract infections and 4 times increased risk of mycotic genital infections.[68] However, overall, the absolute benefits of SGLT2 inhibition substantially outweigh serious hazards, and risk of ketoacidosis and lower limb amputation are particularly low in patients without diabetes status. Importantly, 254 participants in the EMPA-KIDNEY (The Study of Heart and Kidney Protection With Empagliflozin) trial had an eGFR of 15 to 20 ml/min per 1.73 m^2 at randomization, and the benefits on the primary cardiorenal composite outcome did not appear to attenuate even as kidney failure approached.[68] KDIGO recommends treating patients with CKD and type 2 diabetes or heart failure with an SGLT2i down to at least an eGFR of 20 ml/min per 1.73 m^2 with continued use until the need for kidney replacement therapy (despite low eGFR substantially attenuating their hemoglobin A_{1c}–lowering effect).[13]

SGLT2is reduce plasma glucose by enhancing urinary excretion of glucose and have intermediate glycemic efficacy, with lower glycemic efficacy when eGFR is decreased. As their glucose-lowering effect is modest in CKD, other treatments should be considered to meet individualized glycemic targets in those with low eGFR.[70] The benefits of GLP-1RA therapy have been discussed earlier. KDIGO recommendations for GLP-1RA use predate the FLOW trial results. On the basis of FLOW, we consider semaglutide to be a first-line treatment, alongside RASis, statin-based therapy, and SGLT2is, in patients with albuminuric CKD and type 2 diabetes (Figure 2).

Inflammation

An important hallmark of metabolic syndrome is chronic low-grade inflammation characterized by the production of inflammatory cytokines and reactive oxygen species.[71] Trials of colchicine and more complex anti-inflammatory agents suggest that reducing inflammation modifies the risk of cardiovascular disease.[72–74] Ongoing studies (such as the ZEUS trial of ziltivekimab) are investigating whether targeting inflammatory pathways can provide additional benefit on atherosclerotic cardiovascular risk, as well as other cardiorenal outcomes.[75]

Implementation

KDIGO recommends treatment with an RASi, statin-based therapy, and SGLT2i for most patients with CKD to provide kidney and cardiovascular protection.[13] In patients with type 2 diabetes and albuminuric CKD, finerenone and semaglutide also offer additional cardiorenal benefits and should be implemented alongside other first-line therapies. These 5 drug classes are postulated to have different but complementary mechanisms of action, and the cardiorenal benefits

of SGLT2is are consistent regardless of background use of nsMRA or GLP-1RA, and vice versa.[76,77] There may be other features of their effects, which means they are tolerated well in combination. For example, the reduced risk of serious hyperkalemia conferred by SGLT2 inhibition could counteract hyperkalemia caused by RASis, nsMRAs, and ASis.[78,79] Therefore, combined use of risk-modifying therapies should be implemented for patients with CKD promptly, where tolerated, to optimize cardiovascular-kidney-metabolic health. If such treatment is discontinued during hospital admission, then particular attention to restarting treatment after discharge is needed as reported reinitiation rates are low and beneficial carryover effects are only short lived.[80,81] Coordination and collaboration with other specialties and primary care physicians harmonizes clinical management by reducing disparities and promotes effective implementation by reducing clinician inertia.[82]

Summary

There is a high growing burden of metabolic syndrome globally, and it is common among patients with CKD. Early detection of CKD and awareness of the different risk-modifying therapies will reduce the burden of kidney failure and CKD-associated cardiovascular disease. A key consideration moving forward is when and how to deploy an increasing array of pharmacotherapies with multisystem effects that slow kidney disease progression, offer cardioprotection, and/or improve metabolic control. For patients with type 2 diabetes and albuminuric CKD (many of whom will have features of metabolic syndrome), there are now 5 evidence-based therapies (RASis, statin-based therapy, SGLT2is, finerenone, and semaglutide) that improve cardiovascular-kidney-metabolic health. A holistic approach, integrating these therapies with early detection strategies, is essential to effectively reduce the cardiorenal risk of CKD among patients with metabolic syndrome, while ongoing and future trials identify further methods to reduce the burden of disease in this high-risk population.

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