CLINICAL IMPACT RATINGS

GM ★★★★★★☆ Np ★★★★★★☆

KDIGO made 12 recommendations for managing diabetes with CKD

Navaneethan SD, Zoungas S, Caramori ML, et al. **Diabetes management in chronic kidney disease: synopsis of the 2020 KDIGO Clinical Practice Guideline.** Ann Intern Med. 2020. [Epub ahead of print].

Guideline scope: Management of patients with diabetes and chronic kidney disease (CKD).

Methods: The Kidney Disease: Improving Global Outcomes (KDIGO) Work Group developed recommendations based on systematic reviews that searched multiple databases from Oct 2018 to Feb 2020 for studies that assessed comprehensive care, glycemic monitoring and targets, lifestyle interventions, antihyperglycemic therapies, and management approaches in patients with diabetes and CKD. 244 randomized controlled trials (approximately $n = 150\,000$), 31 observational studies, and 50 reviews met the inclusion criteria.

Funding: No external funding.

Results: Grade 1A and 1B recommendations for management of patients with diabetes and CKD*

Treat patients with diabetes, hypertension, and albuminuria with an ACE inhibitor or ARB and titrate to the highest tolerated, approved dose. (Grade 1B) Key evidence: ACE inhibitor or ARB therapy reduces severely increased albuminuria (RR, 0.45 [95% CI, 0.29 to 0.69] and 0.37 [CI, 0.20 to 0.68], respectively) or doubling of serum creatinine (RR, 0.68 [CI, 0.47 to 1.00] and 0.84 [CI, 0.72 to 0.98], respectively).
Treat patients with T2DM, CKD, and eGFR ≥30 mL/min/1.73 m^2 with metformin. (Grade 1B) Key evidence: Metformin reduces HbA_{1c}, with low risk for hypoglycemia; prevents weight gain or reduces weight in obese patients; and reduces cardiovascular events.
Treat patients with T2DM, CKD, and eGFR ≥30 mL/min/1.73 m^2 with an SGLT2 inhibitor. (Grade 1A) Key evidence: Meta-analyses showed that in patients with an eGFR of 30 to <60 mL/min/1.73 m^2, SGLT2 inhibitors reduce heart failure hospitalizations (HR, 0.60 [CI, 0.47 to 0.77]) and major adverse cardiac events (HR, 0.82 [CI, 0.70 to 0.95]).
Treat patients with T2DM and CKD who have not achieved individualized glycemic targets despite use of metformin and an SGLT2 inhibitor, or who are unable to use those medications, with a long-acting GLP-1 RA. (Grade 1B) Key evidence: GLP-1 RA vs. placebo reduces cardiovascular death (HR, 0.88 [CI, 0.81 to 0.96]); all-cause mortality (HR, 0.88 [CI, 0.83 to 0.95]); and, in patients with or without CKD, a composite kidney outcome (HR, 0.83 [CI, 0.78 to 0.89]).

ACE = angiotensin-converting enzyme, ARB = angiotensin II receptor blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; GRADE = Grading of Recommendations, Assessment, Development and Evaluations; HbA_{1c} = glycated hemoglobin; HR = hazard ratio; RR = relative risk; SGLT2 = sodium–glucose cotransporter-2; T2DM = type 2 diabetes mellitus; CI defined in Glossary.
*Table includes only strong, level 1 recommendations ("we recommend": most people in the situation would want the recommended course of action, and only a small proportion would not; most patients should receive the recommended course of action) based on Grade A (there is confidence that the true effect is close to the estimate of the effect) or Grade B (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) quality evidence assessed by the GRADE approach. The guideline includes 12 recommendations and 48 practice points.

Bottom line:
Based on current best evidence, the KDIGO Work Group made several recommendations for managing patients with diabetes and CKD.

Commentary: The KDIGO guidelines highlight the importance of treating patients who have diabetes, hypertension, and albuminuria with an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. Among glucose-lowering drugs, metformin and sodium–glucose cotransporter-2 (SGLT2) inhibitors are recommended as first-line treatment, whereas glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are second-line options for patients with type 2 diabetes mellitus (T2DM) and CKD. The recommendation for metformin is based on its established efficacy and safety profile (even in patients with an estimated glomerular filtration rate [eGFR] as low as 30 mL/min/1.73 m^2), low cost, and potential cardioprotective benefits. The recommendations for SGLT2 inhibitors and GLP-1 RAs are supported by meta-analyses of cardiovascular outcomes trials that included patients with CKD (1-3) and a dedicated kidney outcome trial for canagliflozin in patients with T2DM and CKD (4).

Despite inherent limitations of subgroup analyses, the consistency of findings for patients with T2DM and CKD across trials suggests that chance is an unlikely explanation for the observed beneficial cardiovascular and kidney effects of SGLT2 inhibitors and long-acting GLP-1 RAs. The credibility of the subgroup meta-analyses based on kidney disease is enhanced by the fact that the analyses synthesized within-trial subgroup differences from well-designed and executed trials. The evidence is particularly strong for canagliflozin because it is also based on data from a dedicated kidney outcome trial (4). Of note, a kidney outcome trial for dapagliflozin has been recently published (5), whereas studies are ongoing for empagliflozin and semaglutide.

The KDIGO Work Group is committed to update its recommendations with data from these ongoing trials and from cardiovascular outcomes trials for ertugliflozin, finerenone, and sotagliflozin. This underscores the value of a living systematic review process to ensure that guidelines keep up with emerging evidence as soon as it becomes available (6).

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