CLINICAL COMPENDIUM

Advancing the Care of Patients With Type 2 Diabetes and Chronic Kidney Disease: Role of the Glucagon-Like Peptide-1 Receptor Agonists

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Key Concepts

Diabetes & Kidney Disease Overview

Diabetes is a chronic metabolic disorder that is the seventh leading cause of death in the United States of America.[1] Diabetes is expected to rise by 51% in the next 20 years and is linked to a host of complications that can negatively impact patients.[2] One of the most burdensome complications is kidney disease, which affects 40% of patients with diabetes.[3] Chronic kidney disease (CKD) is an abnormality in structure (persistent albuminuria) and/or function (reduced estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73m2) for at least 3 months.

Diabetic Kidney Disease's Burden

From the years 2010 to 2030, the number of people with end-stage kidney disease requiring renal replacement therapy is projected to double.[4] This is of major concern because a declining eGFR is associated with a multifold increase in all-cause mortality and cardiovascular events,[5] including heart failure, myocardial infarction, and stroke, compared to patients without chronic kidney disease.[6] The burden of CKD, particularly in those with diabetes, is a key reason why timely and routine screening, appropriate staging, and treatment, are crucial to optimize patient care and prevent cardiorenal disease.[7]

Diabetic Kidney Disease Standard of Care

Over the last 20 years, robust evidence and experience have provided a variety of pharmacotherapeutic options to treat patients with CKD. Angiotensin-converting enzyme inhibitors (ACE-I), angiotensin II receptor blockers (ARBs), and mineralocorticoid receptor antagonists, all of which block the renin-angiotensin-aldosterone-system (RAAS), and more recently the sodium glucose cotransporter-2 inhibitors (SGLT-2i) and nonsteroidal mineralocorticoid receptor antagonists (ns-MRA), have been proven to slow kidney disease progression and reduce kidney events.[7] In addition to these therapies, the 2022 American Diabetes Association (ADA) and Kidney Disease Improving Global Outcomes (KDIGO) consensus recommendations also highlight a potential fourth pillar – glucagon-like peptide-1 receptor agonists (GLP-1 RAs).[7] (Figure 1)

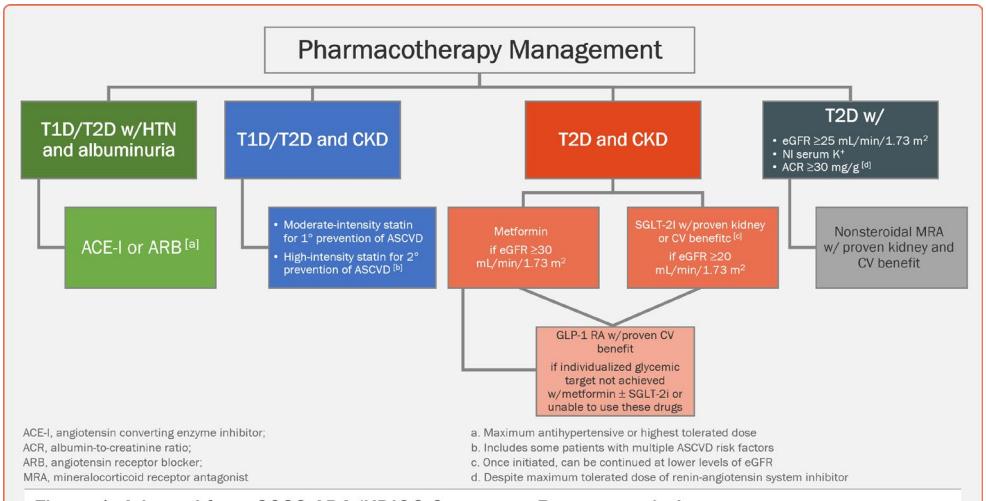

Figure 1: Adapted from 2022 ADA/KDIGO Consensus Recommendations

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Glucagon-Like Peptide-1 Receptor Agonists

GLP-1 RAs are highly efficacious agents for glucose-lowering and weight reduction, however, there are many variances in glycemic and nonglycemic effects within the class. The pharmacokinetics and structure of short-acting GLP-1 RAs (exenatide twice-daily and lixisenatide) give rise to the differences in effects compared to long-acting GLP-1 RAs (dulaglutide, exenatide once-weekly, liraglutide, semaglutide). Short-acting GLP-1 RAs have a more prominent effect on gastric emptying and postprandial glucose-lowering, and long-acting GLP-1 RAs on lowering the fasting plasma glucose level, hemoglobin A1C level, and body weight. Per ADA/KDIGO, the use of specific long-acting GLP-1 RAs (dulaglutide, liraglutide, injectable semaglutide) is strongly supported in patients with type 2 diabetes and CKD or atherosclerotic cardiovascular disease, due to their primary cardiovascular and secondary kidney benefits, including patients with stage 3b-stage 5 CKD.[7] Similar to the ADA/KDIGO recommendations, the 2022 ADA/EASD Consensus Report features a GLP-1 RA with proven cardiovascular benefit as an alternative/adjunct to SGLT-2i in patients with diabetes and CKD (Figure 2).[8] However, clinicians should be able to manage safety issues (eg, gastrointestinal adverse events) and avoid prescribing in patients with contraindications (eg, medullary thyroid cancer, multiple endocrine neoplasia, or family history).

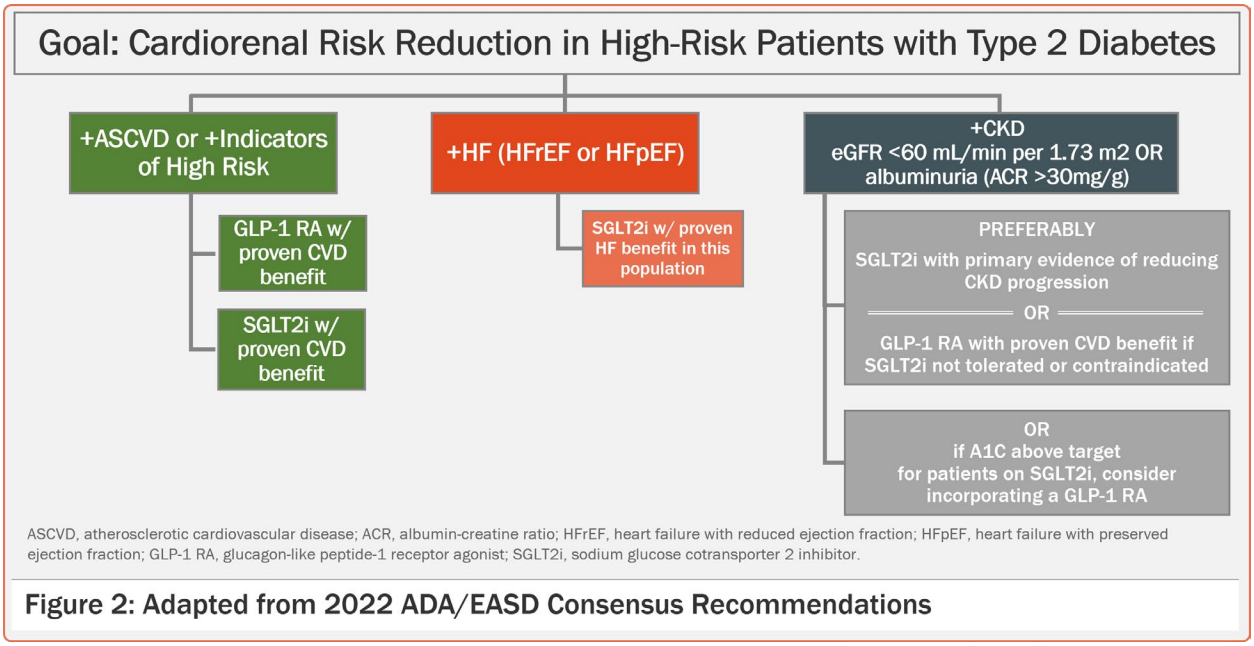

Figure 2: Adapted from 2022 ADA/EASD Consensus Recommendations

Multidisciplinary Management

Collaboration and teamwork among physicians, advanced practice providers, pharmacists, and others is recommended by both the 2022 ADA/EASD and 2022 ADA/KDIGO consensus reports to provide the holistic care needed for patients with diabetes and CKD. Collaborative care is beneficial to patients, the care team, and health systems, by increasing efficient use of resources, improving health outcomes, and enhancing patient and team member satisfaction.

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