# Managing Diabetes and Cardiovascular Risk in Chronic Kidney Disease Patients

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**KEYWORDS**

• Diabetes mellitus • Chronic kidney disease • Cardiovascular risk factors
• Glycated albumin • Fructosamine • A1C • Dyslipidemia of chronic kidney disease

**KEY POINTS**

- Treatment of CKD-associated dyslipidemia decreases CVD mortality; statins have a positive effect in mild-moderate CKD; however, statin are less effective in dialysis dependent patients. Addition of Ezetimibe to a statin may be effective in preventing CVD events in patients with CKD.
- Diabetes is the leading cause of CKD; glycemic goals in CKD population are similar to non-CKD patients to prevent microvascular complications, while avoiding hypoglycemia.
- Pharmacologically, the goal in CKD population, should be to focus on treatment that targets multiple risk factors with low risk for side effects.

Disclosure Statement: V.A. Fonseca has served as a paid consultant to Eli Lilly, Takeda, Novo Nordisk, Sanofi- Aventis, Astra- Zeneca, Abbott, Boehringer Ingelheim, and. Tulane University Endocrinology has also received grants and Research Support from Novo- Nordisk, Asahi, Abbott, Sanofi, and Bayer. Dr D. Lovre-has received research grant (to Tulane) from Lexicon. Dr A. Sihota, and Dr S. Shah have nothing to disclose.
Dr V.A. Fonseca is supported in part by the Tullis Tulane Alumni Chair in Diabetes, the Patient Centered Outcomes Research Institute (through Louisiana Clinical Data Research Network [LACDRN]) and grant 1 U54 GM104940 from the National Institute of General Medical Sciences of the National Institutes of Health, which funds the Louisiana Clinical and Translational Science Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
Author Contributions: All authors contributed to the literature search and writing of the article. V.F. designed the search strategy, supervised study implementation and reviewed/edited the article.
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Endocrinol Metab Clin N Am ■ (2017) ■–■
https://doi.org/10.1016/j.ecl.2017.10.006 **endo.theclinics.com**

## INTRODUCTION

Cardiovascular disease (CVD) is a major clinical problem contributing to significant mortality worldwide, especially in populations with chronic kidney disease (CKD) and diabetes.[1,2] According to the US Renal Data System (USRDS) and the adult National Health and Nutrition Examination Survey (NHANES), the prevalence of CVD in patients with CKD is as high as 63% compared with only 5.8% for patients without CKD, and is directly related to the severity of CKD.[3] Because CVD mortality rates are 10 to 30 times higher in patients on dialysis than in the general population,[4] patients with CKD are more likely to die of CVD than reach end-stage renal disease (ESRD).[5–7] USRDS 2016 data showed that 41% of deaths in dialysis patients are due to CVD. A recent systematic review and meta-analysis of global CKD showed mean CKD prevalence of 13.4% for all 5 stages, and 10.6% for stages 3 to 5.[8] According to the World Health Organization, diabetes had an estimated prevalence of 8.5% in 2014, and evidence suggests that CKD may be even more common.[9]

Diabetes mellitus is the leading cause of CKD in the United States, with estimates suggesting that close to 50% of patients with diabetes show evidence of CKD.[10,11] Diabetes is also often difficult to control in the CKD population; several antihyperglycemic agents are contraindicated in patients with CKD, and the pharmacokinetics of others, including insulin, change with declining glomerular filtration rate (GFR).

In this review, we discuss mechanisms of increased CVD in patients with CKD and strategies for managing cardiovascular (CV) risk in patients with CKD. Our focus is mainly on decreasing cardiovascular events (CVEs) and progression of microvascular complications by reducing levels of glucose and lipids. We recognize the importance of blood pressure (BP) control in the management of CKD and prevention of CVD events in this population, but a detailed discussion of blood pressure is beyond the scope of this review. We searched PubMed using the terms “mechanisms of increased CVD in CKD,” “CVD and CKD and hyperlipidemia,” “CKD and CVD and diabetes,” “dyslipidemia and CKD,” “ezetimibe and CKD,” “statins and CKD/ESRD,” “glycemic control and CKD,” “glycemic markers,” and “glycosylated albumin and fructosamine and CKD” with no limit on the date of the article. All articles were discussed among all authors. We chose pertinent articles, and searched their references in turn for additional relevant publications.

## MECHANISMS OF INCREASED CARDIOVASCULAR DISEASE IN CHRONIC KIDNEY DISEASE

The complex relationship between CKD and CVD involves a combination of cardiovascular risk factors, comprising “traditional factors” (eg, advanced age, hypertension, diabetes mellitus, and dyslipidemia) and “nontraditional factors” specific to CKD (eg, anemia, volume overload, mineral metabolism abnormalities, proteinuria, oxidative stress, and inflammation).[12]

An analysis of NHANES data from 2001 to 2010 encompassing (1) the prevalence of CV-related comorbidities and CV risk factors, (2) the utilization of lipid-lowering and BP-lowering agents, and (3) rates of low-density lipoprotein cholesterol (LDL-C) or BP goal attainment in US adults stratified by CKD stage[13] demonstrated that despite a reported increase in lipid and BP treatment, treatment remains suboptimal. Greater efforts are required to improve CVD reduction in the CKD population.[13]

### *Left Ventricular Dysfunction*

The leading cardiac abnormality in patients with CKD and ESRD is left ventricular (LV) dysfunction.[12] One study showed that approximately 74% of patients with ESRD starting dialysis suffer from LV hypertrophy, 32% show LV dilatation, and another