Implementation of the KDIGO guideline on lipid management requires a substantial increase in statin prescription rates

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The KDIGO guideline on lipid management in adult patients with chronic kidney disease (CKD) reflects a paradigm shift as proposals for statin use are based on cardiovascular risk rather than cholesterol levels. Statin use is now universally recommended in CKD patients 50 years and older, assuming a 10-year risk of coronary heart disease (CHD) of over 10%. Specific comorbidities or formal risk calculation are required for younger patients. It is unknown to which extent these new guidelines differ from previous practice. Here we analyzed statin use in the German Chronic Kidney Disease study of 5217 adult patients with moderately severe CKD under nephrological care enrolled shortly before publication of the new guideline. Accordingly, 407 patients younger than 50 years would be eligible for statins compared with the 277 patients treated so far, and all 4224 patients 50 years and older would be eligible compared with the 2196 already treated. Overall, guideline implementation would almost double statin prescription from 47 to 88%. Among patients 50 years and older currently not on a statin, an estimated 10-year CHD and atherosclerotic event risks over 10% were present in 68% and 82%, respectively. Thus, implementation of the new lipid guideline requires a substantial change in prescription practice, even in CKD patients under nephrological care. Based on comorbidities and risk estimates, the universal recommendation for statin use in CKD patients 50 years and older appears justified.

Kidney International advance online publication, 2 September 2015; doi:10.1038/ki.2015.246

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Received 8 March 2015; revised 23 June 2015; accepted 25 June 2015

KEYWORDS: cardiovascular diseases; cholesterol; kidney diseases; practice guideline; risk assessment

Dyslipidemia is highly prevalent and contributes to the high rate of cardiovascular (CV) complications in patients with chronic kidney disease (CKD).[1–3] In 2003, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) published the first guideline addressing lipid therapy in CKD patients. This guideline recommended a low-density lipoprotein (LDL) cholesterol target of <100 mg/dl in CKD patients on the basis that CKD was viewed as a coronary heart disease (CHD) risk equivalent. It was recommended to treat with a statin whenever this LDL cholesterol target could not be reached with lifestyle changes. However, at the time of publication, solid evidence from clinical trials that such an approach would improve outcomes in CKD patients was not available. In fact, two large randomized trials failed to demonstrate a benefit from statin therapy in patients on dialysis.[4,5] For some time, this created uncertainty regarding lipid therapy in CKD patients. However, the subsequent Study of Heart and Renal Protection (SHARP) showed a clear benefit of a combined treatment with simvastatin and ezetimibe in a large cohort of CKD patients, with renal function ranging from mildly impaired to dialysis-dependent.[6] This study reinstated statin therapy as one of the few means demonstrated to improve outcomes in CKD patients.[7]

Recently, the American College of Cardiology (ACC) and the American Heart Association (AHA) jointly published their new guideline on lipid therapy.[8] This guideline represents a paradigm shift away from a 'lipid-focused' view, towards a risk-based approach deriving the decision to use a statin from individualized CV risk assessment. Statin therapy is now recommended for patients with already established atherosclerotic CV disease (considered at high risk for future events),

Table 1 | Characteristics of patients with and without statin therapy

Parameter	Patients with statin, $N = 2473$	Patients without statin, $N = 2744$
Age (median, IQR) (years)	66 (58–70)	61 (49–69)
Male sex, *n* (%)	1644 (66.5%)	1488 (54.2%)
Hypertension, *n* (%)	2445 (98.9%)	2571 (93.7%)
Diabetes mellitus, *n* (%)	1139 (46.1%)	703 (25.6%)
BMI (median, IQR) (kg/m^2)	29.9 (26.6–34.2)	28.1 (24.8–32.2)
Current smoking, *n* (%)	371 (15.0%)	457 (16.7%)
Coronary heart disease, *n* (%)	796 (32.2%)	243 (8.9%)
Prior MI, *n* (%)	471 (19.1%)	112 (4.1%)
CABG, *n* (%)	302 (12.2%)	45 (1.6%)
PCI, *n* (%)	573 (23.2%)	170 (6.2%)
Cerebrovascular disease, *n* (%)	354 (14.3%)	156 (5.7%)
Prior stroke, *n* (%)	291 (11.8%)	139 (5.1%)
Carotid surgery, *n* (%)	93 (3.8%)	25 (0.9%)
Carotid intervention, *n* (%)	47 (1.9%)	13 (0.5%)
Peripheral vascular disease, *n* (%)	323 (13.1%)	170 (6.2%)
Heart failure, *n* (%)	576 (23.3%)	352 (12.8%)
Atrial fibrillation, *n* (%)	268 (10.9%)	212 (7.7%)
Diabetic nephropathy, *n* (%)	874 (35.3%)	534 (19.5%)
Vascular nephropathy, *n* (%)	1165 (47.1%)	992 (36.2%)
Systemic disease, *n* (%)	238 (9.6%)	374 (13.6%)
Primary glomerulopathy, *n* (%)	560 (22.6%)	625 (22.8%)
eGFR (median, IQR) (ml/min per 1.73 m^2)	45 (36–55)	48 (38–60)
Cystatin C (median, IQR) (mg/l)	1.49 (1.24–1.81)	1.38 (1.15–1.73)
UACR (median, IQR) (mg/g)	38.7 (36.4–41.0)	38.8 (36.5–41.1)
Total cholesterol (mg/dl)	196 ± 52	225 ± 50
HDL cholesterol (mg/dl)	51 ± 17	53 ± 19
LDL cholesterol (mg/dl)	103 ± 41	132 ± 41
Triglycerides (mg/dl)	210 ± 131	189 ± 125
CRP (median, IQR) (mg/l)	2.29 (1.04–4.82)	2.29 (1.02–5.23)
Phosphate (median, IQR) (mg/l)	1.10 (0.96–1.24)	1.10 (0.97–1.23)
Uric acid (median, IQR) (mg/dl)	7.22 (6.12–8.47)	6.96 (5.75–8.1)
Hemoglobin (median, IQR) (g/dl)	13.6 (12.6–14.7)	13.6 (12.6–14.7)
HbA1c (median, IQR) (%)	6.2 (5.6–6.8)	5.9 (5.6–6.3)

Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; CKD-EPI, Chronic Kidney Disease-Epidemiology; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; MI, myocardial infarction; PCI, percutaneous coronary intervention, UACR, urinary albumin-to-creatinine ratio.
Values are mean ± s.d., unless indicated otherwise. Missing values were <5% for all parameters presented.

or an estimated 10-year risk for an atherosclerotic CV event >7.5%. For estimation of risk, new risk equations were developed using data pooled from several large cohort studies.[9]

In parallel, Kidney Disease: Improving Global Outcomes (KDIGO) also developed a new 'Clinical Practice Guideline for Lipid Management in CKD'.[10,11] Similar to the ACC-AHA guideline, the new KDIGO guideline on lipid management adopts a risk-based approach for statin indication and refrains from recommending specific LDL cholesterol targets. The KDIGO guideline even goes a step further in simplifying treatment decisions: CKD patients ⩾50 years of age are considered at sufficiently high risk for a CV event (>10% risk of manifest CHD over 10 years) to justify statin therapy without the need for applying any formal risk calculation in individual patients. In patients 18–49 years of age, statin therapy is recommended for those with known CHD (prior myocardial infarction or coronary revascularization), diabetes mellitus, or prior ischemic stroke. Only if none of these comorbidities are present, formal risk assessment is recommended to guide therapy in CKD patients 18–49 years of age, with a 10-year risk of CHD >10% justifying statin therapy. By simplifying the decision processes, the guideline workgroup aimed to facilitate implementation of the recommendations into clinical practice.

How these recommendations differ from practice and the impact this new KDIGO guideline should have on statin prescription rates is currently unknown. We therefore analyzed statin use before publication of the novel KDIGO lipid guideline in the German CKD (GCKD) study, the worldwide largest cohort study of CKD patients under nephrological care.[12,13] Implementation of the new KDIGO lipid guideline was simulated based on prevalent comorbidities and CV risk estimates.

RESULTS

Clinical characteristics of patients with versus without statin therapy

In the GCKD cohort, 2473 (47%) out of the 5217 patients received statins, whereas 2744 (53%) did not receive statin therapy. Clinical characteristics of patients with and without statin therapy are presented in Table 1. Patients who received statin therapy were older, were more frequently male, had higher body mass index, slightly higher rate of hypertension,