who was recently diagnosed with T2DM, who had a normal cIMT followed by a coronary calcium score that was abnormal, and who was told by his primary care physician that his LDL-C of 130 mg/dL and high-density lipoprotein cholesterol (HDL-C) of 35 mg/dL were "ok." Should we screen the patient with T2DM who is already taking 81 mg of aspirin and a statin and has an LDL-C of 65 mg/dL? Probably not, because an abnormal score would not lead to an intensification of therapy.

A powerful argument can be made that screening modalities can enhance our ability to risk stratify patients beyond the Framingham Risk Score. They can also be a powerful tool to motivate patients and the treating physician. Because a stress test only screens for obstructive coronary artery disease, it would not seem to be an appropriate approach in the presence of any coronary artery disease. ■

Dyslipidemia

Treatment in Patients With Chronic Kidney Disease

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Table 1
Dosing Modifications for Lipid-Lowering Drugs in CKD

Agent	GFR 60-90 mL/min/1.73 m^2	GFR 15-59 mL/min/1.73 m^2	GFR < 15 mL/min/1.73 m^2	Notes
Statins				
Atorvastatin	No	No	No	
Fluvastatin	No	Not defined	Not defined	↓ dose to one-half at GFR < 30 mL/min/1.73 m^2
Lovastatin	No	↓ to 50%	↓ to 50%	↓ dose to one-half at GFR < 30 mL/min/1.73 m^2
Pravastatin	No	No	No	Start at 10 mg/d for GFR < 60 mL/min/1.73 m^2
Rosuvastatin	No	5-10 mg	5-10 mg	Start at 5 mg/d for GFR < 30 mL/min/1.73 m^2, maximum dose 10 mg/d
Simvastatin	No	No	5 mg	Start at 5 mg if GFR < 10 mL/min/1.73 m^2
Nonstatins				
Nicotinic acid	No	No	↓ to 50%	34% kidney absorption
Cholestyramine	No	No	No	Not absorbed
Colesevelam	No	No	No	Not absorbed
Ezetimibe	No	No	No	
Fenofibrate	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Gemfibrozil	No	No	No	NLA recommends a dose of 600 mg/d for GFR 15-59 mL/min/1.73 m^2 and avoiding use for GFR < 15 mL/min/1.73 m^2
Omega-3 fatty acids	No	No	No	

CKD, chronic kidney disease; GFR, glomerular filtration rate; NLA, National Lipid Association.
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Managing Dyslipidemia in Chronic Kidney Disease

Harper CR, Jacobson TA.

J Am Coll Cardiol. 2008;51:2375-2384.

Harper and Jacobson[10] do a masterful job of helping us navigate the therapeutic nuances of treatment of dyslipidemia in patients with CKD. These patients represent nearly 11% of the entire adult US population and carry a heavy predisposition to develop cardiovascular disease. Because of the impact of CKD on the pharmacokinetics of lipid therapies, it is very important that physicians be tuned into these issues to avoid complications and maximize clinical benefit.[11]

In their lipid profile, CKD patients are more likely to have greater elevations of triglyceride and very-low-density lipoprotein and lower levels of HDL-C than patients who do not have CKD. The data supporting the use of statins in reducing cardiovascular events are solid in patients with CKD, with the exception being those on hemodialysis. Harper and Jacobson[10] provide dosing modifications for lipid-lowering drugs in CKD (Table 1) and propose a treatment algorithm for management of lipids in patients with CKD (Table 2).

The Die Deutsche Diabetes Dialyze Studie (4D) trial is the only prospectively randomized trial of statins in dialysis patients comparing 20 mg of atorvastatin with placebo. It did not show a significant reduction in the combined primary endpoint of cardiac death, nonfatal

Table 2
Proposed Treatment Algorithm for Lipid Management in Patients With CKD (Stage 3 to 5)

Lipid Disorder	Therapeutic Option*
Moderate to severe CKD, stages 3 to 4 (GFR 15-59 mL/min/1.73 m^2)	
Elevated LDL-C	1. Atorvastatin, add ezetimibe if not at LDL-C goal
	2. Fluvastatin, add ezetimibe if not at LDL-C goal
Mixed dyslipidemia† (not at non-HDL‡ goal)	1. Atorvastatin or fluvastatin + ezetimibe
	2. Fluvastatin + gemfibrozil 600 mg/d + ezetimibe if not at non-HDL goal
	3. Statin + omega-3 fatty acids, add ezetimibe if not at non-HDL goal
	4. Statin + fenofibrate 48 mg/d, add ezetimibe if not at non-HDL goal
Very high triglycerides (⩾ 500 mg/dL)	1. Gemfibrozil 600 mg/d
	2. Omega-3 fatty acids 3-4 g/d
	3. Fenofibrate 48 mg/d
CKD stage 5 (hemodialysis or GFR < 15 mL/min/1.73 m^2)	
Elevated LDL-C	Atorvastatin (10-80 mg/d) or fluvastatin 40 mg/d, add ezetimibe if not at LDL-C goal
Mixed dyslipidemia	Atorvastatin or fluvastatin 40 mg/d, add ezetimibe 10 mg/d or omega-3 fatty acids 3-4 g/d if not at non-HDL goal
Very high triglycerides	Omega-3 fatty acids 3-4 g/d or gemfibrozil 600 mg/d

*See Table 1 for dose adjustments.
†Mixed dyslipidemia refers to elevated triglycerides and low HDL with or without elevated LDL.
‡Non-HDL refers to total cholesterol minus HDL cholesterol.
CKD, chronic kidney disease; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL-C, low-density lipoprotein cholesterol.
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Table 3
Clinical Pharmacokinetics of Statins

	Rosuvastatin	Atorvastatin	Simvastatin	Lovastatin	Pravastatin	Fluvastatin
Half Life (h)	20.8	15-30	2-3	2.9	1.3-2.8	0.5-2.3
Urinary Excretion (%)	10	< 2	13	10	20	6
CYP3A4 Metabolism	No	Yes	Yes	Yes	No	No
CYP Metabolism	2CY9	3A4	3A4	3A4	Sulfation	2CY9

CYP, cytochrome P450.
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Table 4
Statin/Fibrate Pharmacokinetic Interactions

	Gemfibrozil	Fenofibrate
Atorvastatin	↑ C_{max} by 1.8-fold	No effect
Simvastatin	↑ C_{max} by 2-fold	No effect
Pravastatin	↑ C_{max} by 2-fold	No effect
Rosuvastatin	↑ C_{max} by 2-fold	No effect
Fluvastatin	No effect	No effect
Lovastatin	↑ C_{max} by 2.8-fold	Not available
Cerivastatin	↑ C_{max} by 2-fold to 3-fold	No effect

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MI, or stroke.[12] In fact, the rates of stroke were nearly doubled in the atorvastatin group. Interestingly, more deaths were attributed to an arrhythmic etiology (sudden cardiac death) than to acute MI. The Omega-3 Fatty Acids as Secondary Prevention Against Cardiovascular Events in Patients Who Undergo Chronic Hemodialysis (OPACH) trial did show a 70% reduction in the incidence of MI.[13]

Of the currently available statins, atorvastatin and fluvastatin have the lowest fraction of active metabolites excreted in the urine, and pravastatin has the highest (Table 3). Fluvastatin has the additional benefit of not being metabolized via the cytochrome P450-3A4 and thus is less likely to interact with other drugs (Table 4). ■

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