Maine Medical Center
Maine Transplant Program
Policies and Procedures
Dyslipidemia and Kidney Transplantation Management Recommendations

Cardiovascular disease is the leading cause of mortality in kidney transplant recipients. Dyslipidemia is a major risk factor for development of heart disease. Preexisting dyslipidemia may be exacerbated after transplantation by immunosuppressive medications including sirolimus, cyclosporine, steroids and tacrolimus.

Lipid screening recommendations

Check fasting lipid profiles within 3 months of transplant, at 1-year post-transplant, and annually thereafter. Repeat testing 2-3 months after treatment change or with the development of other conditions known to cause or worsen dyslipidemia.

Treatment options for dyslipidemia include therapeutic lifestyle changes (TLC) and lipid lowering therapy. Statins are the best studied lipid lowering agents and are considered the agents of choice in solid organ transplantation (SOT). Drug-drug interactions may complicate their use therefore careful selection and monitoring is required (see Table 3).

Table 1: Current target lipid levels in transplant recipients and treatment recommendations

Dyslipidemia	Goal	Initiate	Increase
TG>500 mg/dL with LDL <100 mg/dL	TG<500 mg/dL	TLC	TLC + statin
LDL 100–129 mg/dL	LDL< 100 mg/dL	TLC	TLC + low-intensity statin
LDL>130 mg/dL	LDL<100 mg/dL	TLC + Low or moderate-intensity statin	TLC + moderate OR high intensity statin with dose based on LDL reduction required

Table 2: Overview of statin therapy based on LDL lowering potential

High-Intensity Statin	Moderate-Intensity Statin	Low-Intensity Statin
Lowers LDL by ≥ 50%	**Lowers LDL by 30-49%**	**Lowers LDL by<30%**
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg†	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg twice daily Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

† Can cause proteinuria and renal failure in <1% of patients

Drug Interactions

Drug interactions between statins and various immunosuppressive medications may be associated with increased risk of serious adverse events. See Table 3 for summary of drug interactions between statins and immunosuppressant medications.

Table 3: Drug interaction risk and max doses of select statins in kidney transplant recipients

Agent	CsA	Tac	Siro	Ever	Steroids	MMF	AZA
Atorvastatin	10mg max	Compatible	Compatible	Compatible	Compatible	Compatible	Compatible
Simvastatin	Avoid	40 mg max	40 mg max	40 mg max	Compatible	Compatible	Compatible
Rosuvastatin	5 mg max	Compatible	Compatible	Compatible	Compatible	Compatible	Compatible
Pravastatin	40mg max	Compatible	Compatible	Compatible	Compatible	Compatible	Compatible
Lovastatin	Avoid	Monitor	Monitor	Monitor	Compatible	Compatible	Compatible
Fluvastatin	40mg max	Compatible	Compatible	Compatible	Compatible	Compatible	Compatible
Pitavastatin	Avoid	Monitor	Monitor	Monitor	Compatible	Compatible	Compatible

Adverse Effects

Adverse effects are uncommon though may include muscle weakness, pain and liver problems. These problems can be readily detected using screening blood tests and generally resolve without long-term adverse consequence if the medication is stopped.

Adjunctive and/or alternative lipid lowering agents

PCSK9 Inhibitors: alirocumab and evolocumab have limited data but are reasonable choice in SOT in patients with inadequate response to standard lipid lowering therapies. Based on the data in from the clinical cases series in SOT with hypercholesterolemia, reduction in LDL of 60% was achieved and was comparable to the 50-60% reduction in non-SOT patients. Of note, no clinically significant drug interactions identified with immunosuppressive therapy. Mild adverse drug events may occur (i.e. injection site reactions, rhinorrhea and nausea).
Evolocumab dosing: 140mg subcutaneously every 2 weeks or 420mg once monthly.
Alirocumab dosing: 75-150mg subcutaneously every 2 weeks or 300 mg once monthly.

ACL Inhibitor: Bempedoic Acid has no data in SOT to date. This agent is a prodrug that works similarly to statins but without causing muscle pain which leads to statin intolerance in many patients. Based on the data from CLEAR OUTCOMES trial of 4206 statin intolerant patients, bempedoic acid when used for primary prevention resulted in LDL reduction of 22 % compared with placebo.
Bempedoic acid dosing: 180mg orally once daily

Ezetimibe has limited data but is reasonable adjunctive choice in SOT and lowers LDL by 15-20% with or without statin. Of note, drug interaction exists with cyclosporine but not with other immunosuppressant medications. Ezetimibe 5mg is max dose when used with cyclosporine, but a full dose of 10 mg can be used in patients on noncyclosporine based immunosuppression.

Omega-3 fatty acids have demonstrated variable efficacy in mitigating hypertriglyceridemia, however do appear relatively safe to use in without significant interactions with immunosuppressive medications.

Fibrates (i.e. gemfibrozil and fenofibrate), niacin and bile acid sequestrants (i.e. cholestyramine and colesevelam) are generally discouraged in SOT and should be avoided in transplanted patients due to limited efficacy, significant drug interactions and high rate of adverse effects.

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