DYSLIPIDEMIA

Based on KDIGO & KDOQI guidelines for the care of kidney transplant recipients:[1]

Measure a complete lipid profile in all adults (≥18 years old) and adolescent (puberty to 18 years old) KTRs.

- → 2–3 months after transplantation;
- → 2–3 months after a change in treatment or other conditions known to cause dyslipidaemias;
- → At least annually, thereafter.

Evaluate KTRs with dyslipidaemias for secondary causes.

For KTRs with fasting triglycerides ≥500 mg/dL (≥5.65mmol/L) that cannot be corrected by removing an underlying cause, treat with:

- → Adults: therapeutic lifestyle changes and a triglyceride lowering agent
- → Adolescents: therapeutic lifestyle changes

For KTRs with elevated LDL-C:

- → Adults: If LDL-C ≥100 mg/dL (≥2.59 mmol/L), treat to reduce LDL-C to <100 mg/dL (<2.59 mmol/L)
- → Adolescents: If LDL-C ≥130 mg/dL (≥3.36 mmol/L), treat to reduce LDL-C to <130 mg/dL (<3.36 mmol/L)

For KTRs with normal LDL-C, elevated triglycerides and elevated non-HDL-C:

- → Adults: If LDL-C <100 mg/dL
- → (<2.59 mmol/L), fasting triglycerides ≥200 mg/dL (≥2.26 mmol/L), and nonHDL-C ≥130 mg/dL (≥3.36mmol/L), treat to reduce non-HDL-C to <130 mg/dL (<3.36 mmol/L)
- → Adolescents: If LDL-C <130 mg/dL (<3.36 mmol/L), fasting triglycerides ≥200 mg/dL (≥2.26 mmol/L), and nonHDL-C ≥160 mg/dL (≥4.14mmol/L), treat to reduce nonHDL-C to <160 mg/dL (<4.14mmol/L)

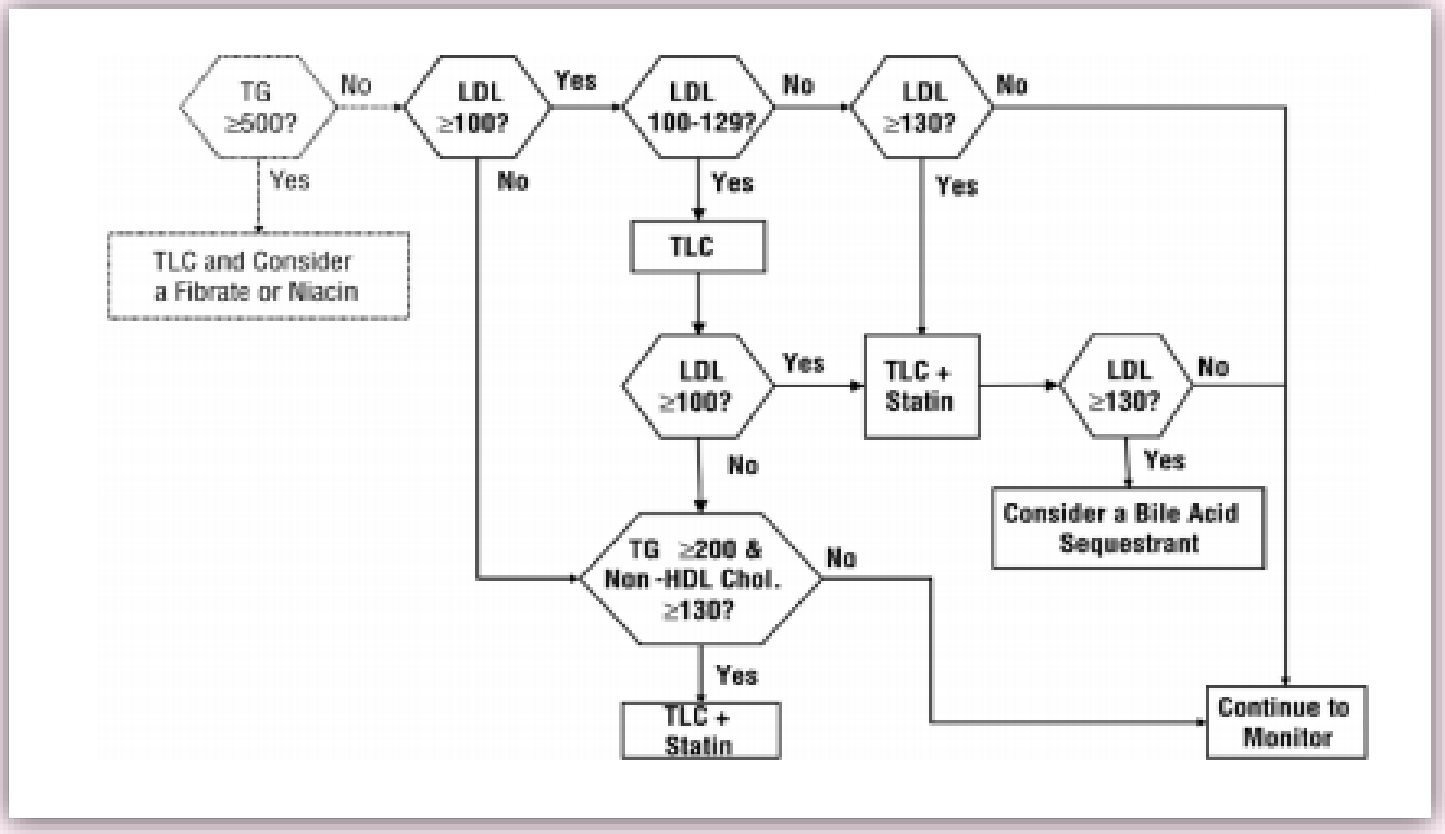

Table 15: The management of dyslipidemias in adult kidney transplant recipients

Dyslipidemia	Goal	Initiate	Increase	Alternative
TG ≥500 mg/dL	TG <500 mg/dL	TLC	TLC + Fibrate or niacin	Fibrate or niacin
LDL 100–129 mg/dL	LDL <100 mg/dL	TLC	TLC + low dose statin	Bile acid seq. or niacin
LDL ≥130 mg/dL	LDL <100 mg/dL	TLC + low dose statin	TLC + max. dose statin	Bile acid seq. or niacin
TG ≥200 mg/dL and non-HDL ≥130 mg/dL	Non-HDL <130 mg/dL	TLC + low dose statin	TLC + max. dose statin	Fibrate or niacin

To convert mg/dL to mmol/L, multiply triglycerides by 0.01129, and cholesterol by 0.02586. TG, triglycerides; LDL, low-density lipoprotein cholesterol; TLC, therapeutic lifestyle changes; seq., sequestrant; max.,maximum

Table 19: Recommended daily statin dose ranges.

	Level of GFR (ml/min/1.73m²)		
Statin	≥30	>30 or dialysis	With cyclosporine
Atorvastatin	**10-80**	**10-80**	**10-40**
Fluvastatin	**20-80**	**10-40**	**10-40**
Pravastatin	**20-40**	**20-40**	**20-40**

Adult Treatment Panel III recommendations for GFR ≥30 ml/min/1.73m². Most manufacturers recommend once daily dosing, but consider giving 50% of the maximum dose twice daily

Table 18: Lipid-lowering medication dose adjustments for reduced kidney function.

	Adjust for reduced GFR (ml/min/1.73m²)			
Agent	60-90	15-59	<15	Notes
Atorvastatin(205)	**No**	**No**	**No**	
Fluvastatin	**?**	**?**	**?**	
Pravastatin(206,207)	**No**	**No**	**No**	
Nicotinic acid	**No**	**No**	**↓to 50%**	**34% kidney excretion**
Cholestipol	**No**	**No**	**No**	**Not absorbed**
Cholestyramine	**No**	**No**	**No**	**Not absorbed**
Fenofibrate (217)	**↓to 50%**	**↓to 25%**	**Avoid**	**May ↑ Serum creatinine**

GFR, glomerular filtration rate; USFDA, United States Food and Drug Administration

For kidney transplant recipients with LDL 100 mg/dL (2.59 mmol/L), despite optimum medical management: [2]

Change the immunosuppression protocol to one that is less likely to exacerbate high LDL levels, if this can be done without causing undue risk to the allograft. Options to consider include:

(i) tapering and discontinuing prednisone, with or without adding or increasing the dose of azathioprine or mycophenolate mofetil

(ii) replacing cyclosporine with tacrolimus.

(iii) tapering and discontinuing cyclosporine, with or without adding or increasing the dose of azathioprine or mycophenolate mofetil.

(iv) discontinuing or replacing sirolimus with an alternative immunosuppressive agent.

→ Cyclosporine has been shown to increase the blood levels of virtually every statin that has been investigated (Table 20). [2]

→ Most medications that are well-documented as increasing statin blood levels are also metabolized by the hepatic cytochrome P450 enzyme superfamily. [2]

→ Statins can be used safely with cyclosporine if the dose of the statin is reduced (Table 20). It is recommended that the maximum doses of statins be reduced in patients receiving either cyclosporine or tacrolimus (Table 20). [2]

→ The addition of a third agent that is also metabolized by the **cytochrome P450** system increases the risk of myositis and rhabdomyolysis, and therefore such combinations should be avoided. [2]

→ Avoid the use of a fibrate together with a statin, at least until additional studies are conducted in patients with reduced GFR to establish the safety of this. [2]

Table 20: Effects of cyclosporine on blood vessels of statins in kidney transplant recipients

Statin	Increase in AUC (-fold)
Atorvastatin (226)	**6**
Simavastatin (228)	**3**
Simavastatin (229)	**8**
Lovastatin (230)	**2**
Lovastatin (231)	**3**
Lovastatin (232)	**20**
Pravastatin (232)	**5**
Fluvastatin (233)	**2[b]**

[b]P>0.05; Abbreviation: AUC, area under the concentration-time curve.

[1]- Special Issue: KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. (2009). *American Journal Of Transplantation*, *9*, S1-S155. doi: 10.1111/j.1600-6143.2009.02834.x

[2]- Kasiske, B., Cosio, F., Beto, J., Bolton, K., Chavers, B., & Grimm, R. et al. (2004). Clinical practice guidelines for managing dyslipidemias in kidney transplant patients: a report from the Managing Dyslipidemias in Chronic Kidney Disease Work Group of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative. *American Journal Of Transplantation*, *4*(s7), 13-53. doi: 10.1111/j.1600-6135.2004.0355.x

[3]- Catapano, A., Graham, I., De Backer, G., Wiklund, O., Chapman, M., & Drexel, H. et al. (2016). 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. *European Heart Journal*, *37*(39), 2999-3058. doi: 10.1093/eurheartj/ehw272

[4]- Kaplan, B., Qazi, Y., & Wellen, J. (2014). Strategies for the management of adverse events associated with mTOR inhibitors. *Transplantation Reviews*, *28*(3), 126-133. doi: 10.1016/j.trre.2014.03.002