

Hypertriglyceridemia: A review of the evidence



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Objectives

- Discuss diagnosis and screening mechanisms associated with hypertriglyceridemia
- Discuss complications and primary/secondary causes of hypertriglyceridemia
- Identify therapeutic interventions to treat hypertriglyceridemia



Hypertriglyceridemia

A clinical conundrum?




Diagnosis

Triglyceride Levels

Diagnosis made with FASTING lipid levels


- < 150 mg/dL- Normal
- 150-199 mg/dL- Borderline High
- 200-499 mg/dL- High
- ≥ 500 mg/dL- Very High



Screening

Screen using fasting or non-fasting lipid levels

- Starting at age 20 years- every 5 years
- Every 1-2 years for males ≥ 45 years, females ≥ 55 years
- At time of diagnosis for diabetics
- More frequent screenings with family history of ASCVD or multiple risk factors




Primary Causes

Genetic

Rare

Lipid Disorder	Molecular Defect	Incidence	Lipid Profile	Presentation
Familial Chylomicronemia syndrome	LPL/ Apo CIII deficiency	1:1,000,000	TG > 1,000 mg/dL	Early onset, eruptive xanthomas, recurrent pancreatitis
*Familial Combined Dyslipidemia	Unknown	1:200	↑ TG ↑ LDL-C ↓ HDL-C	Seen with obesity, insulin resistance, and HTN
*Familial Hypertriglyceridemia	Unknown	1:500	TG 200-1,000 mg/dL	Family members usually affected
*Dysbeta-lipoproteinemia	Abnormal Apo E	1:5,000	TG 250-1,000mg/dL ↑ TC	Palmar and tuberoeruptive xanthomas



* Generally present in adulthood unless precipitated by secondary cause (obesity, insulin resistance, etc)



Secondary Causes

Metabolic Causes



- Metabolic Syndrome
- Estrogen
- Pregnancy- 3rd Trimester- up to 200% increase
- Hypothyroidism
- Chronic Kidney Disease

Secondary Causes

Medication Side Effects



- Oral estrogen
- Tamoxifen
- Diuretics
- Beta-blockers- > atenolol, metoprolol, propranolol
- Corticosteroids
- Antiretroviral therapy
- Isotretinoin
- Immunosuppressants
- Antipsychotics- > clozapine, risperidone, quetiapine, < aripiprazole or ziprasidone
- SSRI- Sertraline

Secondary Causes

Dietary Causes



- Alcohol ingestion- dose dependent
- Simple carbohydrates

Complications

TG levels > 500 mg/dL

- Pancreatitis
- Lipemia Retinalis
- Eruptive Xanthomas





Lifestyle Interventions

Nutritional Practices to Lower TG

Nutritional Practice	TG-Lowering Response
Weight Loss (5-10% of body weight)	20%
Implement Mediterranean-style diet vs Low-fat diet	10-15%
Add marine-derived polyunsaturated fatty acids (per gram)	5-10%
Decrease carbohydrates (1% energy replacement with mono or polyunsaturated fatty acids)	1-2%
Eliminate trans fat (1% energy replacement with mono or polyunsaturated fatty acids)	1%
Total optimal TG lowering effect	49%


Adapted from Jacobson TA, Maki KC, Orringer CE, et al. "National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2." *Journal of Clinical Lipidology* 9, no. 6 (n.d.): S1-S122.e1. <https://doi.org/10.1016/j.jacl.2015.09.002>.



Lifestyle Interventions

Nutritional Practices

- Limit ETOH- (abstain if TG> 500 mg/dL)
- Limit total dietary fat-
 - If TG > 1,000 mg/dL, intake should be no more than 15% daily caloric intake
 - If pts remain on very low-fat diets, may need essential fatty acid supplementation- walnut/sunflower oil.
- Limit sugar consumption
- Limit refined grains



Lifestyle Interventions

Physical Activity



- ↑ Physical Activity lowers TG 4-37%
- TG ↓ immediately after endurance exercise
- If no reduction in visceral adiposity, TG reduction not persistent
- High intensity exercise reduces post prandial TG more effectively than moderate intensity exercise



Medical Interventions

Statins

- Primarily indicated to lower LDL-C
- Can lower TG 30%- based on dose/ potency of statin
- High dose/High potency statins required for optimal TG lowering





Medical Interventions

Fibrates

May decrease TG up to 62%

- Adverse Effects
 - Myopathy
 - Cholelithiasis
 - Creatinine elevation
 - Rhabdomyolysis
- Drug-drug Interactions
 - Statin
 - Increased area under curve





Medical Interventions

Omega-3 fatty acids

OTC supplements/ Prescription drugs

- Both lower TG in a dose dependent manner
- Exact MOA unknown
- Pleiotropic benefits
- No serious safety issues
- Tolerated well
- May increase LDL-C (up to 45%)



 

Medical Interventions

Niacin

Nicotinic acid/ Vitamin B3



- 3 different forms
- Dose dependent lipid effects
- Side effects often preclude use
- "Flush-free" niacin doesn't lower lipids

Medical Interventions

Others



- PCSK9i- may reduce TG up to 17.7%
- Pioglitazone- may reduce TG up to 25%
- DPP 4 inhibitors- may reduce TG up to 15%

Medical Interventions

In Development



- Pemafibrate
- Volanesorsen
- Multiple drugs in phase I or II trials



Moving Forward

Hypertriglyceridemia is increasingly common

Be proactive
Encourage lifestyle modification
Understand cultural diversity



Questions?

