THE UNIVERSITY OF CHICAGO
MEDICINE & BIOLOGICAL SCIENCES

37 y/o man with hypertriglyceridemia and DKA

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Objectives

- Review the etiology and classification of hypertriglyceridemia
- To understand the relationship between hypertriglyceridemia, DKA and pancreatitis
- To learn about acute and chronic management of hypertriglyceridemia

Chief complaint

- 37 y/o man with PMH significant for T2DM presents with 4 days of abdominal pain and poor oral intake

HPI

- He presented to the ED with 4 days of epigastric pain. He reported initially feeling bloated but later develop pain, got progressively worse to the point he was not tolerating liquid diet. He had very poor intake for about 4 days. Denies nausea but had a forceful vomit to "try to feel better".

- He had hot flashes but no fevers, chills, cough or diarrhea. Denied recent alcohol use.

- He reported running out his medications for ~ 2 months.

- **PMH:**

  T2DM

  Hypertriglyceridemia

  Pancreatitis

- **PSH:** Adenoidectomy

- **FH:** father, mother and brother with T2DM

- **Medications:** Metformin 1000 mg BID, glipizide 10 mg BID, Niacin, statin

- Originally: Portugal. Parents are from the same village (unclear if there is some consanguinity)

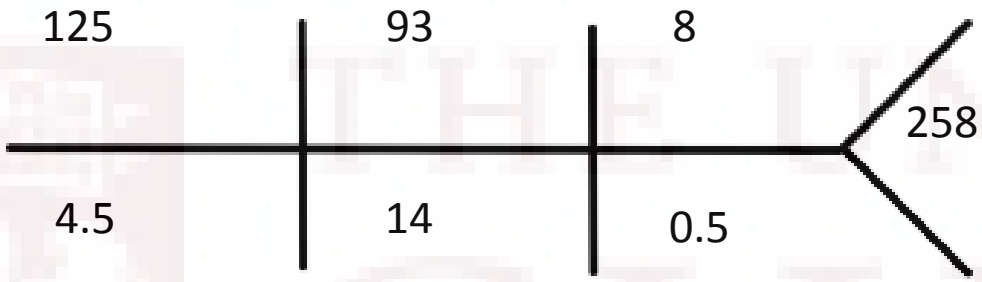
Physical exam

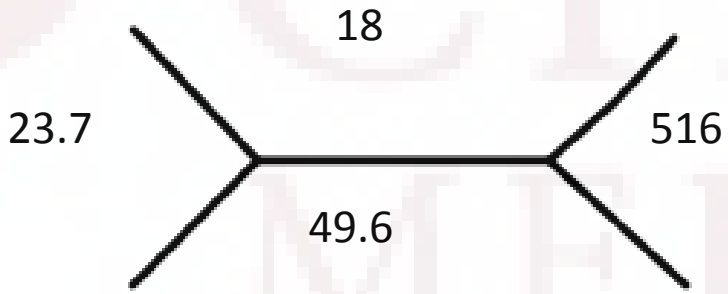
- **Vitals:** Afebrile, BP: 131/78, HR: 126, RR: 17, SpO2: 94%, Height: 182.8 cm, Weight 150 kg, BMI: 44.85 kg/m^2

General: obese man, awake in NAD
Skin: no rash
HEENT: EOM intact, anicteric, clear sclera.
Neck: non tender, no lymphadenopathy appreciated.

Cardio: tachycardic, regular rhythm. S1, S2 no murmur/gallop/rub. No S3, S4.
Pulmonary: CTAB. No wheezes/rales/crackles.
Abdomen: soft, non-tender, non-distended.
Extremities: no cyanosis, clubbing or edema. No rash or lesions.
Neuro: Alert and oriented, no focal deficits.

Admission labs





Beta-Hydroxybutyrate: 3.53

AST/ALT: normal

Lipase: hemolyzed

A1c: 11.4%

Triglycerides: 1150
Total cholesterol: 266
HDL: 15

Causes?

Primary [1, 2]		
Genetic syndromes presenting as chylomicronemia (rare)	Other genetic syndromes with hypertriglyceridemia (relatively common)	Primary genetic susceptibility
Lipoprotein lipase (LPL) deficiency Apolipoprotein C-II (apoC2) deficiency Apolipoprotein AV deficiency Dysbetalipoproteinemia Glycosylphosphatidylinositol-anchored high-density lipoprotein–binding protein 1 (GPIHBP1) deficiency (expressed in childhood)	Familial hypertriglyceridemia (FHTG) likely polygenic (high TG due to excess hepatic VLDL production, normal cholesterol levels) Familial combined hyperlipidemia (FCHL) (polymorphisms in molecules and enzymes participating in lipoprotein metabolism; (*e.g.*: apoC2, apoC3)	Metabolic syndrome
Secondary [1, 2, 18]		
Diseases	**Medications**	**Diet**
Hypothyroidism Diabetes mellitus (Poorly controlled, insulinopenic) Central obesity Renal diseases Nephrotic syndrome Autoimmune disorders *e.g.*, systemic lupus erythematosus (SLE) HIV- associated dyslipidemia Chronic idiopathic utricaria Pregnancy (the third trimester)	Beta-blockers (nonselective) Thiazides Corticosteroids Tamoxifen Raloxifene Estrogens (oral, not transdermal) (*e.g.* Contraceptives, Postmenopausal hormone therapy) Protease inhibitors Retinoic acid Isotretinoin Sirolimus L-Asparaginase Bile acid resins Phenothiazines Antipsychotics (second generation) Immunosuppressants	Alcohol excess Positive-energy balanced diet with saturated fat or high glycemic index/load content

Rygiel K. Hypertriglyceridemia - Common Causes, Prevention and Treatment Strategies. Curr Cardiol Rev. 2018;14(1):67-76.

Genetics

The Role of Genetics in Cardiovascular Risk Reduction: Findings From a Single Lipid Clinic and Review of the Literature☆

Lane B. Benes [a,*], Kent Brummell [b], Mendel Roth [c], Li Shen [c], Michael H. Davidson [a]

[a] The University of Chicago Medicine, Section of Cardiology, 5841 S Maryland Avenue, MC 6080, Chicago, IL 60637, USA
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[c] Genben Lifesciences, 6370 Lusk Blvd, Ste F205, San Diego, CA 92121, USA

- 82 patients (97.6%) were found to have a known pathogenic, likely pathogenic, variant of uncertain significance (VUS) or variant (s) associated with polygenic abnormal lipid metabolism or increased risk of CAD.

- Pathogenic/likely pathogenic variants identified included LDL receptor variants that cause FH and lipoprotein lipase variants that are associated with increased risk of hypertriglyceridemia.

Benes LB, Brummell K, Roth M, Shen L, Davidson MH. The Role of Genetics in Cardiovascular Risk Reduction: Findings From a Single Lipid Clinic and Review of the Literature. Cardiovasc Revasc Med. 2020 Feb;21(2):200-204

Classification

Table 1 Classification of fasting triglyceride concentration (mg/dL) by guideline[2,5–7]

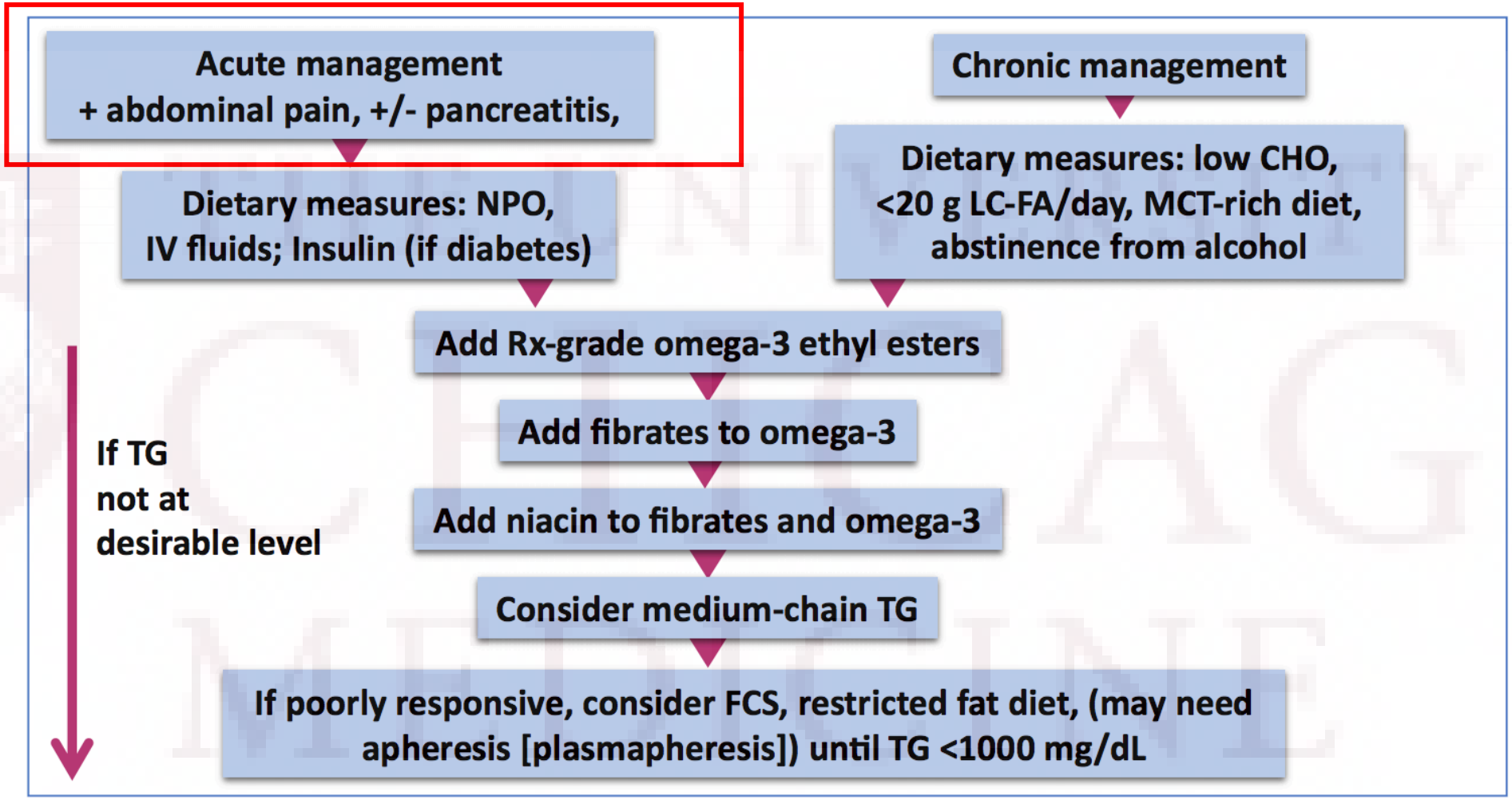
NCEP ATP III	Normal <150	Borderline 150–199	High 200–499	Very high ≥500	
AHA 2011	Normal <150	Borderline 150–199	High 200–499	Very high ≥500	
Endocrine Society 2012	Normal <150	Mild HTG 150–199	Moderate HTG 200–999	Severe HTG 1000–1999	Very severe HTG ≥2000
NLA 2014	Normal <150	Borderline 150–199	High 200–499	Very high ≥500	

AHA, American Heart Association; HTG, hypertriglyceridemia; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; NLA, National Lipid Association.

Journal of Clinical Lipidology. July-August 2017


Next Step

Algorithm for Managing Severe Hypertriglyceridemia (TG>1000 mg/dL)



CHO=carbohydrate; FCS=familial chylomicronemia syndrome; HDL-C=high-density lipoprotein cholesterol; IV=intravenous; LC-FA=long-chain fatty acid; IV=intravenous; LDL-C=low-density lipoprotein cholesterol; LDL-P=low-density lipoprotein particle; MCT=medium-chain triglycerides; NPO=nothing by mouth; Rx=prescription; SHTG= severe hypertriglyceridemia; TG=triglyceride.

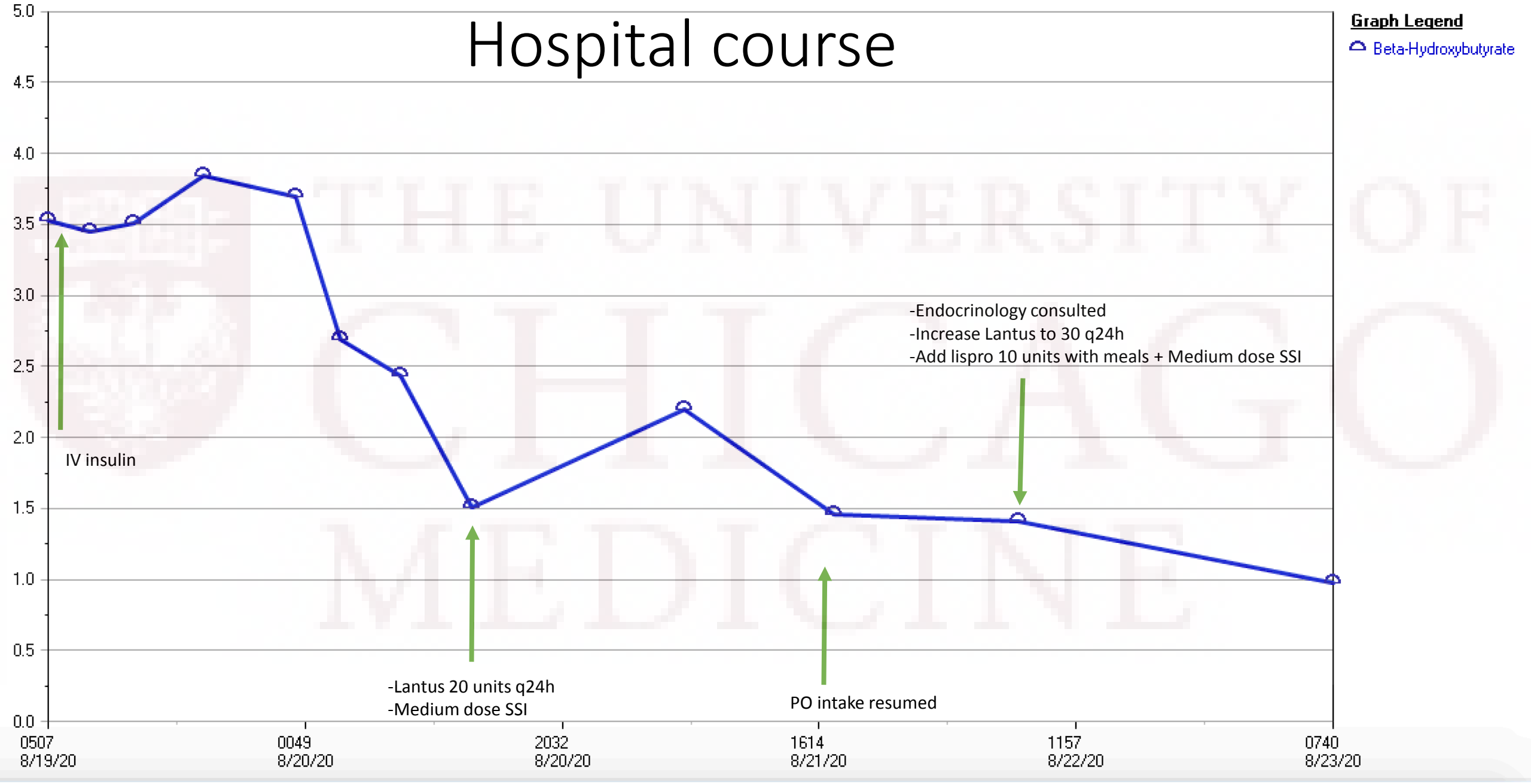
Ewald N, et al. *Clin Res Cardiol Suppl*. 2012;7:31-35; Bays HE, et al. *J Clin Lipidol*. 2016 Jan-Feb;10(1 Suppl):S1-43.

Laboratory test or imaging study?

- Lipase: 17

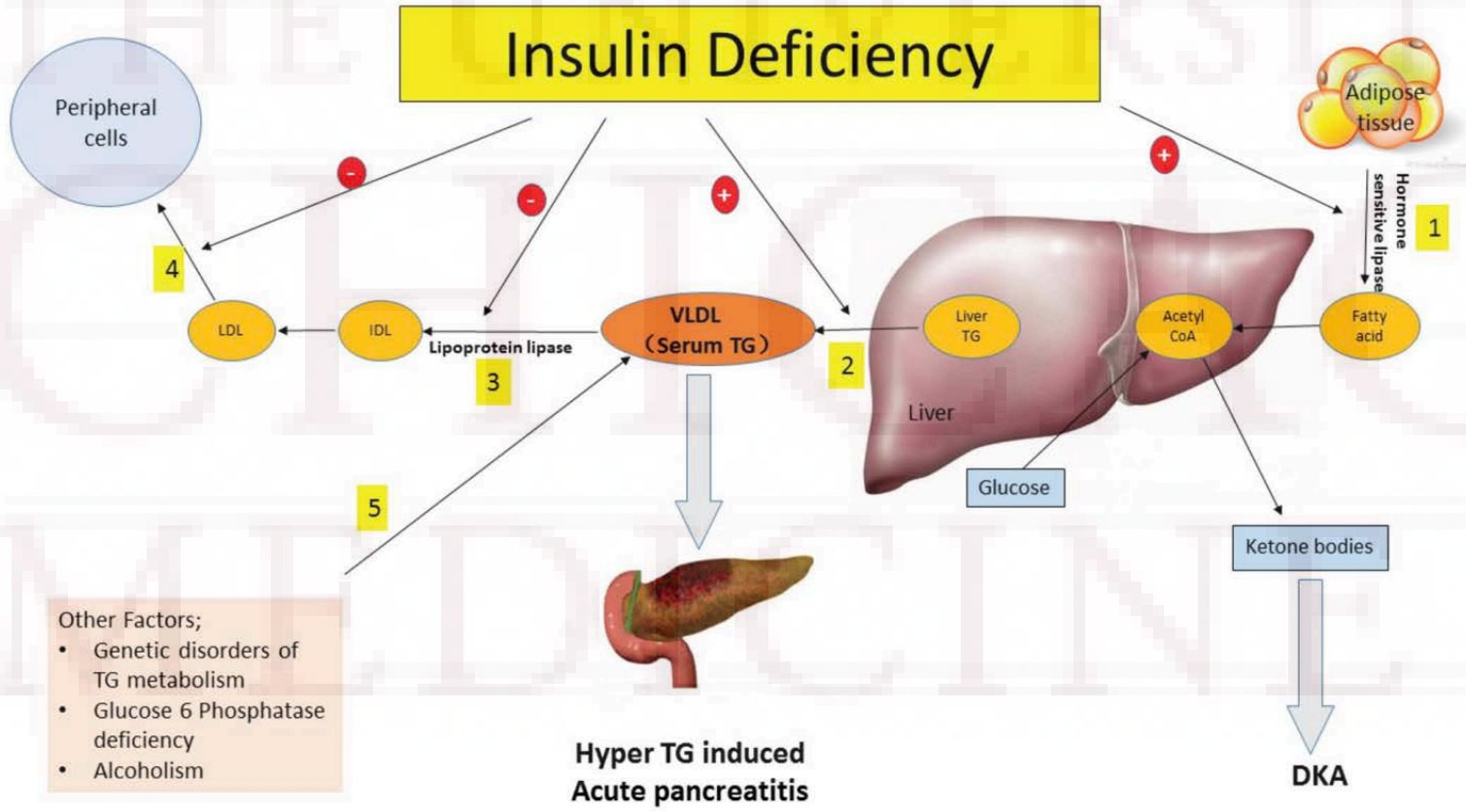
- Abdominal xray: Normal bowel gas pattern, no pathologic calcifications seen anywhere, pancreas normal.

Hospital course



What is the association between DKA, pancreatitis and hypertriglyceridemia?

The large diameter of triglyceride-rich lipoproteins especially chylomicrons may impair the circulatory flow in the pancreatic capillary beds resulting in ischemia.



Wang, Yuchen MD.; Attar, Bashar M. MD, PhD, FACG; Siddamsetti, Sisir MD.; Rivas-Chicas, Oscar MD.; Trick, William MD.; Simons-Linares, Carlos Roberto MD.; Fogelfeld, Leon MD Diabetes Ketoacidosis with Hypertriglyceridemia Induced Acute Pancreatitis as Initial Presentation of Diabetes Mellitus: A Report of Three Cases. AACE Clinical Case Reports 2017

What is the treatment for severe hypertriglyceridemia and pancreatitis?

- Aggressive intravenous hydration
- Initial bowel rest
- Pain control

- IV Insulin
- IV Heparin
- Plasmapheresis

Is there a role for IV insulin?

- Has been used for more than a decade to lower TG.
- Insulin activates LPL activity which in turn accelerates chylomicron degradation.
- Insulin lowers TGs levels by 50-75% over 2-3 days
- While there are many case reports and series demonstrating TG lowering effect, there are no comparison studies evaluating insulin versus conservative therapy

Garg R, Rustagi T. Management of Hypertriglyceridemia Induced Acute Pancreatitis. Biomed Res I

Is there a role for IV heparin?

- Heparin releases stored lipoprotein lipase from the endothelial cell thus lowering TGs levels.
- Combination of insulin and heparin has been used to lower TGs level in case reports and case series with mean decrease of TGs level by 50% within 24 hours.
- There is a concern of rebound hypertriglyceridemia as long term or continuous heparin infusion has been shown to deplete LPL, leading to reduction of chylomicrons catabolism and increase in TGs levels.
- Due to concern of rebound hypertriglyceridemia and risk of hemorrhage into the pancreas during acute attack on continuous heparin infusion, heparin should preferably be avoided.

Yang AL, McNabb-Baltar J. Hypertriglyceridemia and acute pancreatitis. Pancreatology. 2020 Jul;20(5):79
Garg R, Rustagi T. Management of Hypertriglyceridemia Induced Acute Pancreatitis. Biomed Res Int. 201

Case series: Insulin + heparin

Table 2. Baseline characteristics of the cases

Parameters	Case 1	Case 2	Case 3	Case 4
Age (years)/ Gender	32/M	38/M	28/F	46/M
Weight (kg)	103	88	63	82
BMI (kg/m^2)	35.0	31.1	25.0	28.7
Blood glucose at presentation (mg/dL)	540	232	96	298
HbA1c (%) at presentation	11.2	9.2	5.2	10.8
Diabetes duration	3 years	3 years	ND	4 years
History of pancreatitis	Recurrent (third episode)	First episode	First episode	Recurrent (second episode)
Antidiabetic drugs/day	Metformin 2 g/d Glimepiride 4 mg/d	Metformin 1 g/d Gliclazide 80 mg/d	None	Metformin 1 g/d
Antilipidemic drugs	Fenofibrate 145 mg/d	None	None	Atorvastatin 10 mg/d

BMI: body mass index; M: male; F: female; HbA1c: glycated hemoglobin; ND: no diabetes.

Table 1. Laboratory parameters of the patients

	Parameter	Admission	24 hours	48 hours	72 hours	Day 12
Case 1	TG (mg/dL)	5,860	3,416	2,280	1,578	501
	VLDL (mg/dL)	249	260	256	239	100
Case 2	TG (mg/dL)	3,891	1,851	979	686	320
	VLDL (mg/dL)	262	219	157	142	96
Case 3	TG (mg/dL)	1,820	1,011	876	534	221
	VLDL (mg/dL)	202	180	120	84	42
Case 4	TG (mg/dL)	2,430	1,121	992	601	252
	VLDL (mg/dL)	235	192	143	110	82

To convert triglycerides from mg/dL to mmol/L, divide the value by 88.5.

Kuchay MS, Farooqui KJ, Bano T, Khandelwal M, Gill H, Mithal A. Heparin and insulin in the management of hypertriglyceridemia-associated pancreatitis: case series and literature review. Arch Endocrinol Metab. 2017

Case series: IV Insulin alone or IV insulin + IV heparin

Table 1 Use of insulin in treatment of severe hypertriglyceridemia in nondiabetic patients

Patient and reference	Triglyceride level at presentation	Method of insulin administration	Results
39-year-old woman "on contraception" for 5 years presenting with acute pancreatitis [3]	7699 mg/dL (87.5 mmol/L)	Insulin intravenous drip 3-9 units/h for 4 days, and maintain blood glucose 120-160 mg/dL (6.7-8.9 mmol/L)	Triglyceride levels decreased to ~4000 mg/dL (45.4 mmol/L) by day 1, and 246 mg/dL (2.8 mmol/L) by day 4
13-year-old adolescent [4]	1893 mg/dL (21.5 mmol/L)	Single dose of regular insulin (0.1 units/kg)	Triglyceride levels decreased to 1015 mg/dL (11.5 mmol/L) in 4 hours
Present case: 39-year-old woman on estrogen-containing contraceptive patch presenting with acute pancreatitis	10 560 mg/dL (120 mmol/L)	10% dextrose infusion at 200 mL/h and insulin lispro 4 units subcutaneously every 4 hours for every 50 mg/dL of blood-glucose increment above 150 mg/dL	Triglyceride levels decreased to 1479 mg/dL (16.8 mmol/L) by day 1, and 712 mg/dL (8.1 mmol/L) by day 2, 718 mg/dL (8.1 mmol/L) by day 3, and 656 mg/dL (7.4 mmol/L) by day 4

Table 2 Use of insulin in conjunction with heparin in treatment of severe hypertriglyceridemia in nondiabetic patients

Patient and reference	Triglyceride levels at presentation	Protocol of insulin and heparin therapy	Results
41-year-old woman with history of alcohol abuse [3]	7037 mg/dL (80 mmol/L)	Regular insulin intravenous drip 1-5 units/h for 5 days, and intravenous heparin 500-900 units/h for 3 days	Triglyceride levels decreased to 511 mg/dL (5.8 mmol/L) by day 3
51-year-old man with history of alcohol abuse [6]	7900 mg/dL (90 mmol/L)	Intravenous infusion of 12 units of regular insulin in 5% dextrose, and heparin 5000 units IV BID	Triglyceride levels decreased to 2260 mg/dL 25.7 mmol/L) by day 2, and 670 mg/dL (7.6 mmol/L) by day 4
31-year-old women at 30-week gestation, and 47-year-old man with history of alcohol abuse [7]	4445 mg/dL (50.5 mmol/L) and 7280 mg/dL (80.4 mmol/L), respectively	Intravenous infusion of 20 units of insulin in 1 L of 20% dextrose per 24 hours, and heparin 10 000 units IV per 24 hours	Triglyceride levels decreased to less than 880 mg/dL (10 mmol/L), within ~3 days

All patients presented with acute pancreatitis.

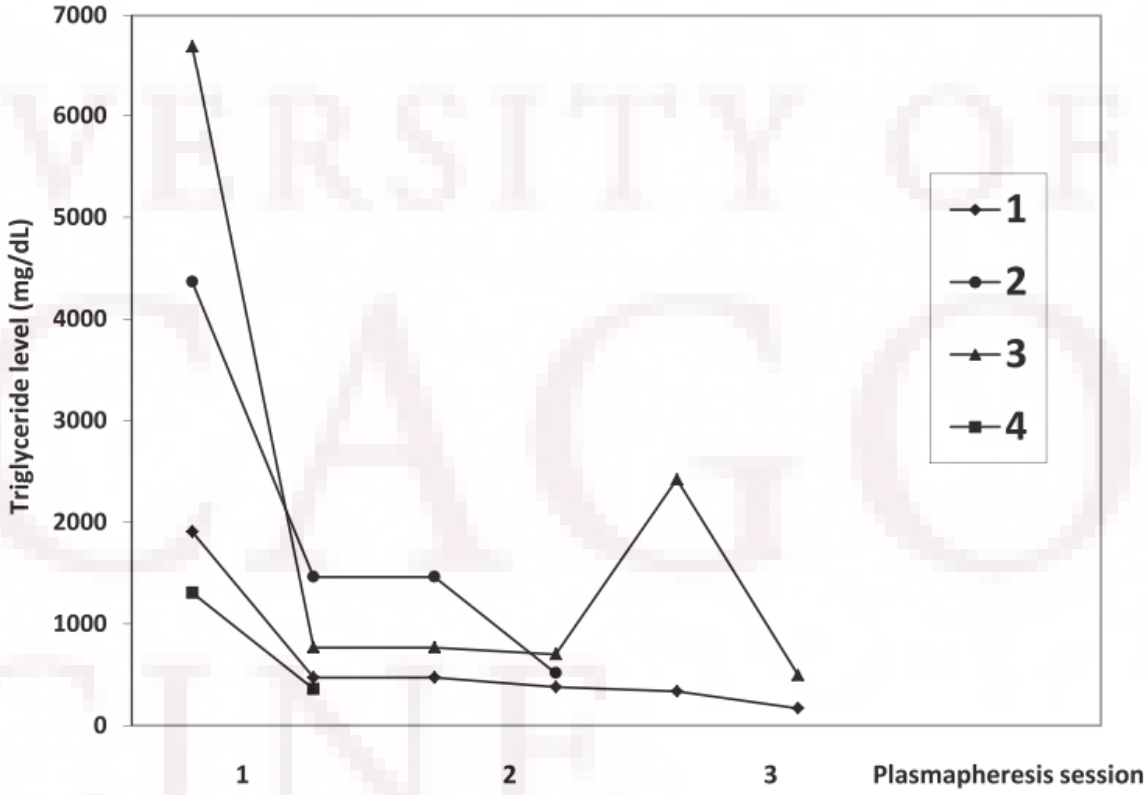
No randomized controlled trials available.

Insulin should only be administered in uncontrolled Type 2 diabetes or in patients with Type 1 diabetes with diabetic ketoacidosis.

Mikhail N, Trivedi K, Page C, Wali S, Cope D. Treatment of severe hypertriglyceridemia in nondiabetic patients with insulin. Am J Emerg Med. 2005 May;23(3):415-7.

Plasmapheresis

- Lower the lipid levels drastically within hours compared to conservative therapy that usually takes several days. Most patients require only 1 session.
- Reported to lower TG levels by 50-80%.
- Improves hypertriglyceridemia-pancreatitis outcomes by lowering TG levels but also by removing proinfammatory markers and cytokines to downregulate the inflammatory process.
- The only prospective study to date with a historic control (60 versus 34 patients) failed to show any mortality benefit compared to conservative management.



Galán Carrillo I, Demelo-Rodriguez P, Rodríguez Ferrero ML, Anaya F. Double filtration plasmapheresis in the treatment of pancreatitis due to severe hypertriglyceridemia. J Clin Lipidol. 2015 Sep-Oct;9(5):698-702

More history…

- He reported being diagnosed with hypertriglyceridemia and pancreatitis (Tg in the 3000 during that time) and diabetes during same admission 5 years ago, he was initially on insulin but was able to lose weight and was transitioned to metformin and glipizide.

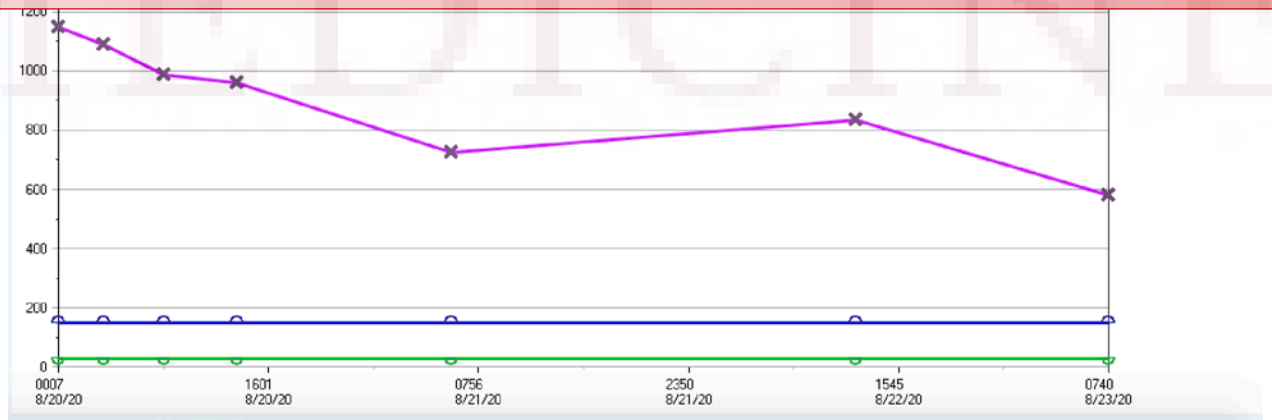
- Reported high alcohol intake when young (he drank VERY heavily to the point of blacking out), no alcohol use for past 2 years.

- Gained weight as eating processed foods and frozen dinners, sweets and snacks.

Hospital course

	8/20/2020 0331	8/20/2020 0807	8/20/2020 1338	8/21/2020 0555	8/22/2020 1234	8/23/2020 0740
CV & CARDIAC MARKERS						
Cholesterol	434 ▲				311 ▲	266
HDL Cholesterol	16 ▼				16 ▼	15
LDL Cholesterol,Calc	Calculation of... *				Calculation of... *	Calculation of... *
Triglycerides ▲	1,088 ▲	987 ▲	962 ▲	725 ▲	835 ▲	582

Patient will be discharged, what will you recommend?



Interventions to treat hypertriglyceridemia

Intervention	Lowering of TG	Remarks	Evidence level
Lifestyle modification	Variable; up to 70%	– Alcohol abstinence and reduced intake of rapidly metabolizable carbohydrates have the greatest effect (e6, e7) – Increasing physical activity; the goal is >2.5 h (better 5 h) of aerobic exercise of moderate intensity spread over the week (e8) – Very variable effect: depends on the baseline condition and the underlying predisposition – Nutritional counseling should be offered to all patients	A
Weight loss	Variable; up to 70%	– Particularly effective in patients with abdominal obesity or with other factors related to metabolic syndrome (e9) – Variable effect: in some patients very pronounced lowering of TG levels after losing only a few kilograms of weight; in other patients minor effect despite significant weight loss	A
Blood glucose control	Variable; up to 70%	– In type 2 diabetes mellitus: in many cases significant improvement, but usually no return to normal blood glucose levels; largely independent of the antidiabetic agent used – In type 1 diabetes mellitus: hypertriglyceridemia usually only if blood glucose is uncontrolled; return to normal after control has been achieved	A
Administration of fibrates	30–50%	– As monotherapy or in combination with non-statins (old studies): minor positive effect on cardiovascular endpoints (25, e13) – In combination with statins: no positive effects in endpoint studies, but potential benefits in subgroups (26, 27) – Consider use in patients with very high cardiovascular risk and persistent hypertriglyceridemia (5) – Try fibrates in patients with severe hypertriglyceridemia	A
Administration of omega-3 fatty acids	30–50%	– Low-dose (1–2 g daily) omega-3 fatty acids show no clinical benefits (31) – High-dose (3–4 g daily) omega-3 fatty acids should be considered in patients with high cardiovascular risk and persistent hypertriglyceridemia (4) – Try omega-3 fatty acids in patients with severe hypertriglyceridemia – In one study (REDUCE-IT), treatment with eicosapentaenoic acid ethyl ester at a dose of 4 g daily showed significant clinical benefits in high-risk patients with statin therapy; the mechanism of action is unclear (32)	A

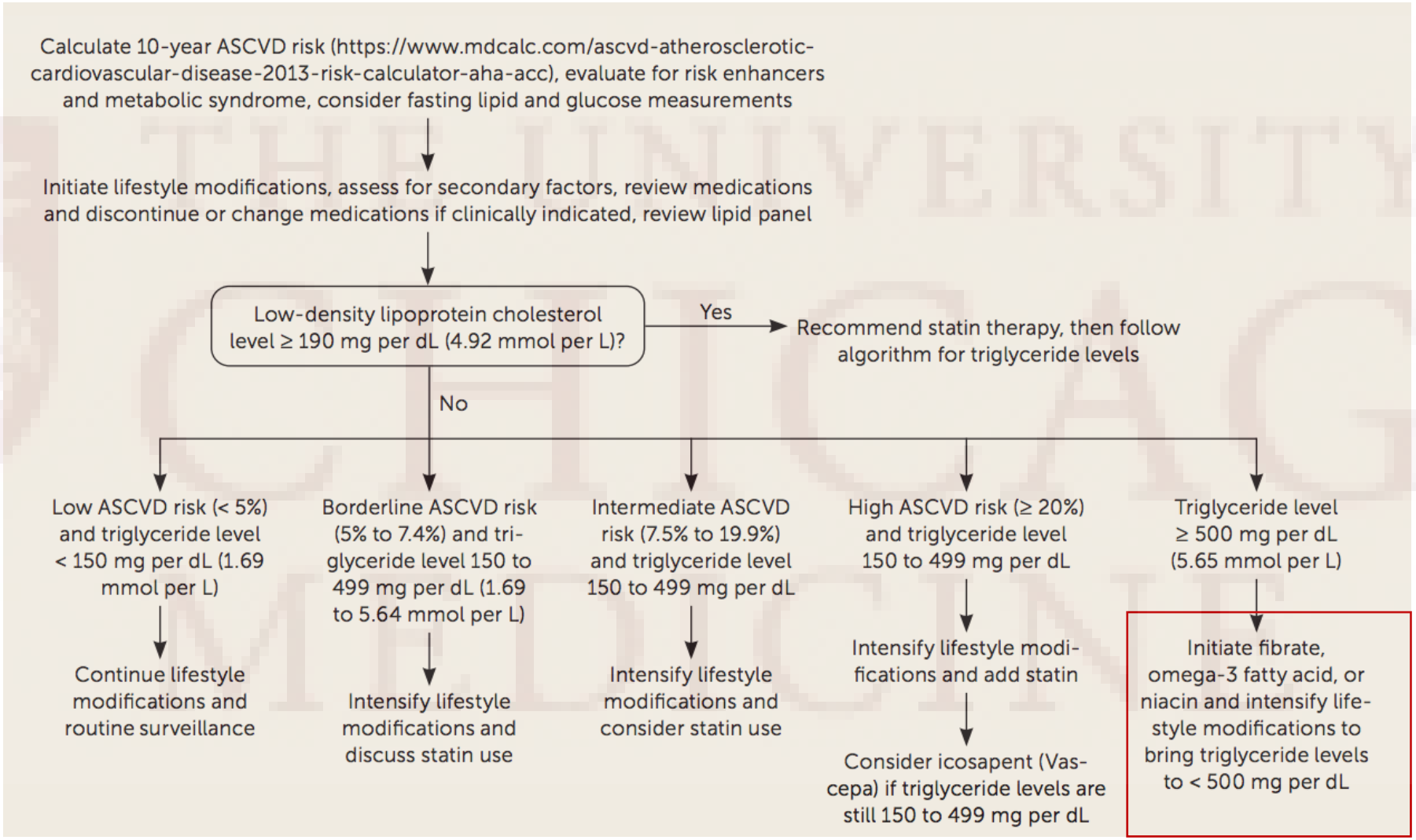
Parhofer KG, Laufs U. The Diagnosis and Treatment of Hypertriglyceridemia. Dtsch Arztebl Int. 2019

Interventions to treat hypertriglyceridemia

Administration of MCT fats	Variable	– As a replacement for other fats; hardly any effect on fasting lipids, but no postprandial TG increase; in the medium term, in most patients improved fasting TG levels (because postprandial lipoproteins can also be detected in fasting blood specimens of patients with severe hypertriglyceridemia) – Consider use in patients with high uncontrolled TG levels (4)	B
Administration of statins	10–20%	– Used to reduce cardiovascular risk depending on overall risk and LDL-cholesterol, minor direct effect on TG (21)	A
Administration of ezetimibe	5–10%	– Used to reduce cardiovascular risk in addition to statins depending on overall risk and LDL-cholesterol; no direct effect on TG (e10)	B
Administration of PCSK9 inhibitors	10–20%	– Used to reduce cardiovascular risk in addition to maximum oral treatments depending on overall risk and LDL-cholesterol, minor direct effect on TG (e11, e12)	A
Administration of bile acid sequestrants	Increase	– Contraindicated; bile acid sequestrants can increase TG levels in patients with hypertriglyceridemia	B

Parhofer KG, Laufs U. The Diagnosis and Treatment of Hypertriglyceridemia. Dtsch Arztebl Int. 2019

Algorithm



Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on clinical practiceguidelines [published correction appears in J Am Coll Cardiol. 2019

2019 ESC/EAS Guidelines

Recommendations for drug treatment of patients with hypertriglyceridaemia

Recommendations	Class[a]	Level[b]
Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)].[355]	I	B
In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin.[194]	IIa	B
In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	B
In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	C

CVD = cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; PUFA = polyunsaturated fatty acids; TG = triglyceride.
[a]Class of recommendation.
[b]Level of evidence.

AACE guidelines 2017

- Physical activity - 30 minutes of moderate intensity physical activity (4 to 6 times weekly)
- Medical nutrition
- Pharmacologic treatment:
  - Fibrates should be used to treat severe hypertriglyceridemia (TG >500 mg/dL)
  - Omega-3 oil, 2 to 4 g daily, should be used to treat severe hypertriglyceridemia (TG >500 mg/dL).
  - Niacin therapy is recommended principally as an adjunct for reducing TG

Endo Society 2020 guidelines

- Tg > 500 mg/dL (5.6 mmol/L\) → pharmacologic treatment as adjunct to diet and exercise to prevent pancreatitis. (1⊕OOO)
- Patients with triglyceride levels over 1000 mg/dL (11.3 mmol/L) often do not get an adequate response to medications and, therefore, control of diabetes, modification of diet, and weight loss are essential.
- In patients with triglyceride-induced pancreatitis, we suggest against the use of acute plasmapheresis as a first-line therapy to reduce triglyceride levels. (2⊕OOO)
- In patients without diabetes and who have triglyceride-induced pancreatitis, we suggest against the routine use of insulin infusion. (2⊕OOO)
- In adults who are on statins and still have moderately elevated triglyceride levels >150 mg/dL (1.7 mmol/L), and who have either atherosclerotic cardiovascular disease or diabetes plus 2 additional risk factors, we suggest adding eicosapentaenoic acid ethyl ester to reduce the risk of cardiovascular disease. (2⊕⊕⊕O)

Newman CB, Blaha MJ, Boord JB, Cariou B, Chait A, Fein HG, Ginsberg HN, Goldberg IJ, Murad MH, Subramanian S, Tannock LR. Lipid Management in Patients with Endocrine Disorders: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2020

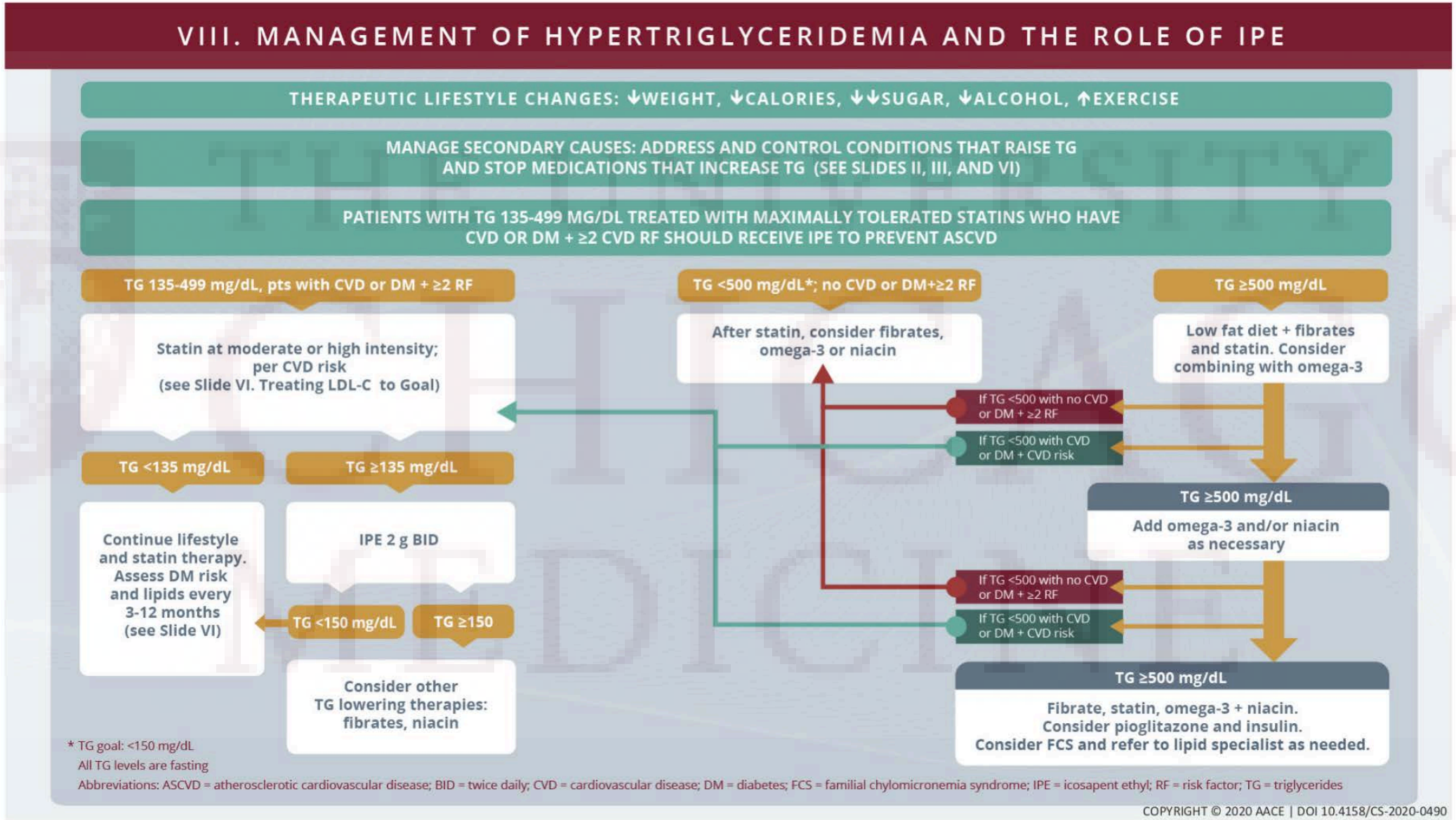
Novel and emerging therapies

- Pemafibrate: selective PPAR modulator that reduces TG levels by 35–45%, is being evaluated in **PROMINENT**, a Phase 3 ASCVD outcomes study of 10 000 patients with Type 2 diabetes and HTG.

- **STRENGTH** - Phase 3 trial of >13 000 patients evaluating ASCVD outcomes of 4 g daily of omega-3 carboxylic acids containing eicosapentaenoic acid and docosahexaenoic acid: Stopped earlier this year for futility. This suggests that the formulation of these omega-3 fatty acids was not as effective as EPA alone.

- 2019 **REDUCE-IT** trial - 4g icosapent ethyl (Vascepa®) in high risk patients with persistently elevated TGs despite statin therapy, demonstrated a dramatic risk reduction (HR 0.75) in ASCVD events over a mean of 4.9 years

Bhatt DL, Steg PG, Miller M, Brinton EA, Jacobson TA, Ketchum SB, Doyle RT Jr, Juliano RA, Jiao L, Granowitz C, Tardif JC, Ballantyne CM; REDUCE-IT Investigators. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med. 2019 Jan



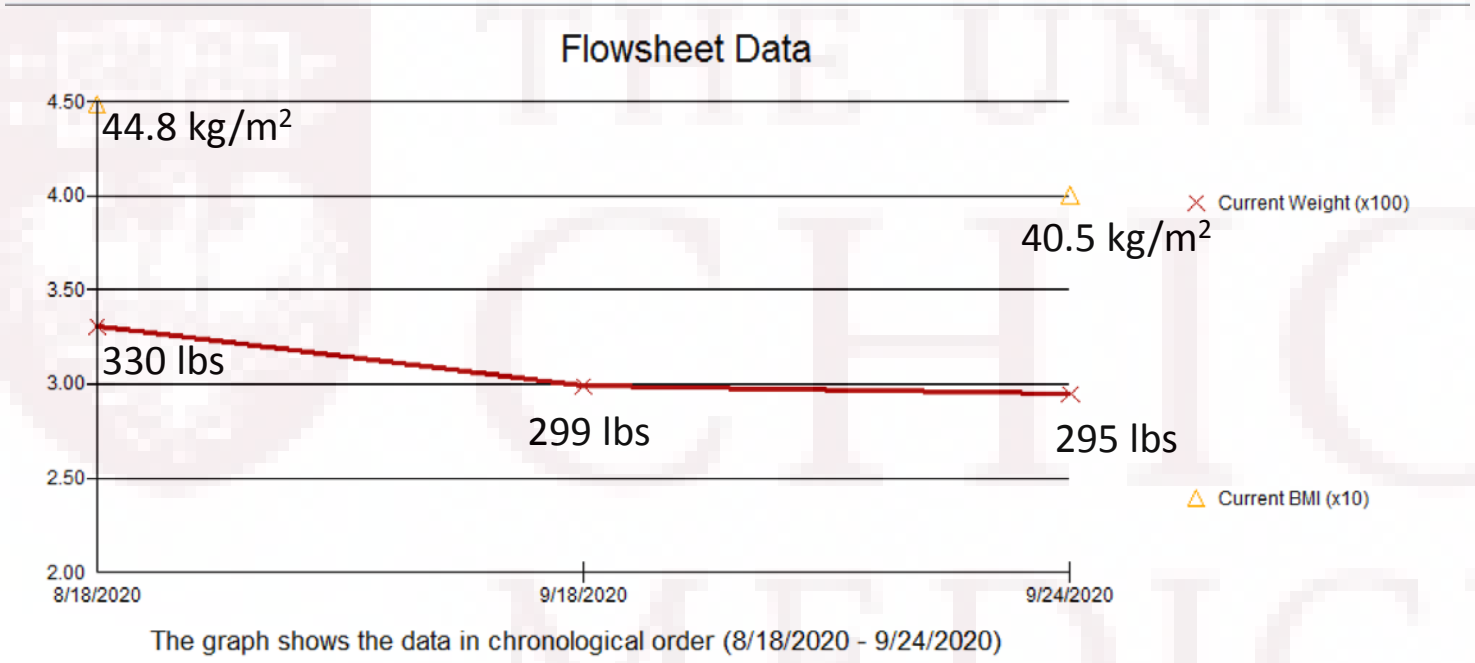
AACE - 2020 Algorithm on the Management of Dyslipidemia

Discharged

- Basal/bolus insulin
- Omega 3 (Lovaza) 2g BID
- Lipitor 80 mg daily
- Metformin 1g BID

- Low carb diet
- Exercise

Post-discharge



The graph shows the data in chronological order (8/18/2020 - 9/24/2020)

GLUCOSE STATISTICS AND TARGETS

October 8, 2020 - November 4, 2020	**28 Days**
% Time CGM is Active	**88%**

Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges Target Range 70-180 mg/dL	**Targets** % of Readings (Time/Day) Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)
Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.	

Average Glucose	**116** mg/dL
Glucose Management Indicator (GMI)	**6.1%**
Glucose Variability	**26.0%**

Defined as percent coefficient of variation (%CV); target ≤36%

Conclusions

- Acute pancreatitis due to hypertriglyceridemia typically occurs when TG levels are >1000 mg/dL
- No randomized trials evaluating insulin therapy or plasmapheresis, but should be considered in severe hypertriglyceridemia when complicated by pancreatitis.
- Addition of fibrates, niacin, or omega-3 fatty acids is recommended if elevated triglyceride levels persist despite the use of high-intensity statin therapy.
- Consider Vascepa in high risk patients with persistently elevated TGs despite statin therapy.