

REVIEW ARTICLE

Clinical significance and management of hypertriglyceridemia

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Summary

Despite significant advances in lowering LDL cholesterol, a substantial residual risk for atherosclerotic cardiovascular disease (ASCVD) persists, largely driven by triglyceride-rich lipoproteins (TRLs).

This narrative review emphasizes the importance of hypertriglyceridemia in the development of atherosclerotic cardiovascular disease and acute pancreatitis and clarifies the diagnostic dilemmas and current therapeutic options.

This narrative review explores the pathophysiology, diagnostic criteria, and epidemiological impact of hypertriglyceridemia. TRLs, including chylomicrons and VLDL, contribute to atherosclerosis through the accumulation of cholesterol-rich “remnant particles” and apolipoprotein B (Apo B) in the subendothelial space. Recent epidemiological data, including findings from the Copenhagen General Population Study and the SIMETAP-HTG study, confirm that mild-to-moderate hypertriglyceridemia (1.7–5.6 mmol/L) is prevalent in approximately 25% of the population and is strongly associated with increased risks of myocardial infarction, heart failure, and multiorgan diseases such as diabetes and MASLD. Conversely, severe hypertriglyceridemia (>10 mmol/L) significantly elevates the risk of acute pancreatitis. Current guidelines emphasize measuring fasting triglycerides, though non-fasting levels are increasingly recognized for screening. The paper concludes that secondary causes must be ruled out upon diagnosis and highlights non-HDL cholesterol as a critical secondary therapeutic target for comprehensive cardiovascular risk management. The final part of the review is focused on novel therapeutic options and emerging therapies for increased TRL.

Keywords: hypertriglyceridemia, triglyceride-rich lipoproteins, non-HDL cholesterol, atherosclerotic cardiovascular disease, residual cardiovascular risk, hypertriglyceridemic pancreatitis, therapy



INTRODUCTION

Since 1973, with the discovery of the LDL receptor and the finding that LDL receptor mutations are responsible for increased circulating LDL cholesterol (1), a new era in lipidology began. Subsequent studies have confirmed the importance of LDL particles in the development of atherosclerotic cardiovascular disease and cardiovascular events, and a tight association between genetic and lipid profiles in patients with familial hypercholesterolemia (2). Besides LDL particles, the focus has shifted to other possible risk factors such as hsCRP and PAI1 (3,4,5), but LDL particles are still considered the main causative factor. In contrast, other factors are considered contributors to the atherosclerotic process.

Over the past 20 years, it has been recognized that despite reductions in LDL cholesterol, a significant residual risk of atherosclerotic cardiovascular disease remains (6). The main lipid components of this residual cardiovascular risk are: an increase in triglyceride/triglyceride-rich lipoproteins and lipoprotein (a) (Lp(a)).

This narrative review aimed to summarize and discuss the existing evidence on the clinical significance of hypertriglyceridemia, with special emphasis on diagnosis and therapeutic options.

The literature search was conducted through a systematic, thorough search of relevant literature. The databases searched in this review included PubMed/MEDLINE, for publications between 1982 and 2025. We selected the period from 1 January 1982 to 30 November 2025.

Keywords for PubMed/MEDLINE: “hypertriglyceridemia”, “triglyceride-rich lipoproteins”, “non-HDL cholesterol”, “atherosclerotic cardiovascular disease”, “residual cardiovascular risk”, “hypertriglyceridemic pancreatitis”, “therapy” in various combinations using the Boolean operators AND and OR. The review included papers directly relevant to the topic, published in English, and available from 1982 to the end of November 2025. Papers relevant to the topic of the paper on the clinical significance and diagnosis of hypertriglyceridemia were included. Sources were selected based on their relevance, methodological quality, and contribution to understanding the topic. The findings were synthesized narratively and organized according to major thematic areas.

Why is hypertriglyceridemia so important, and how is it diagnosed?

Hypertriglyceridemia is a condition with increased triglycerides or triglyceride-rich lipoproteins (TRLs), and

Table 1. Triglyceride-rich lipoproteins and their apolipoproteins (7)

Apo B	Place of synthesis	Main lipoproteins	Apo function
Apo B 100	Liver	VLDL, IDL, LDL, Lp (a)	Binding to LDL receptor
Apo B 48	Intestine	Chylomicrons	Transport dietary lipids from the intestine (cholesterol and triglycerides)

Apo-apolipoprotein, VLDL-very low-density lipoprotein, IDL- intermediate density lipoprotein, LDL-low density lipoprotein

the reason why TRLs are so important is the fact that, in addition to triglycerides, they contain a significant number of phospholipids, apolipoproteins, cholesterol esters, and free cholesterol (Table1, Figure 1).

Triglyceride-rich lipoproteins, primarily chylomicrons and very low-density lipoproteins (VLDL), are spherical complexes responsible for transporting triglycerides (TGs) and cholesteryl esters (CE). As triglycerides are hydrolyzed by lipoprotein lipase (LPL), TRLs become “remnant particles” that are relatively enriched in cholesterol (Figure 1).

Both triglyceride-rich lipoproteins (TRLs) and LDL cholesterol belong to the class of lipoproteins that contain apolipoprotein B (Apo B). In addition to its structural function, Apo B acts as a ligand for binding to the LDL receptor. There are two major forms of Apo B: Apo B 100 and Apo B 48. The same gene located on the short arm of chromosome 2 encodes both forms of apolipoprotein B. Apo B 100, containing 4536 amino acids, is present in the liver and is the main apolipoprotein of LDL, VLDL, IDL, and Lp(a). In comparison, Apo B 48, containing 2512 amino acids, is present in the small intestine and is the main component of chylomicrons (7) (Table 1).

Apo B lipoproteins (VLDL/VLDL remnants, IDL, chylomicrons/chylomicron remnants, LDL, Lp(a)) are all recognized as major risk factors responsible for atherosclerotic cardiovascular disease. Accumulation of Apo-B lipoproteins in the subendothelial space initiates a cascade of events that lead to the activation of the inflammatory response and formation of the atherosclerotic plaque (8) (Figure 2). The most commonly used method for Apo B measurement is the immunonephelometric assay; however, current guidelines do not recommend routine Apo B measurement as a primary therapeutic target (7). Mutation of the Apo B gene, in addition to mutations in the LDL receptor and PCSK9 genes, may cause familial hypercholesterolemia, a well-known genetic disorder associated with higher cardiovascular risk.

Apolipoproteins stabilize the structure of lipoprotein particles and provide functional identity. Besides, Apo B 100 and Apo B 48 contain exchangeable apolipoproteins like ApoC-II (activates LPL for hydrolysis), ApoC-III (inhibits premature clearance), and ApoE (ligand for liver receptors). TRLs are highly dynamic; after releasing triglycerides to tissues, they become smaller, cholesterol-rich remnants known to promote atherosclerosis (Figure 2).

Blood triglyceride measurement is used to assess TRL levels clinically. An increase in TRL levels generally occurs as a result of increased synthesis and/or decreased clearance of these lipid particles. People with atherogenic

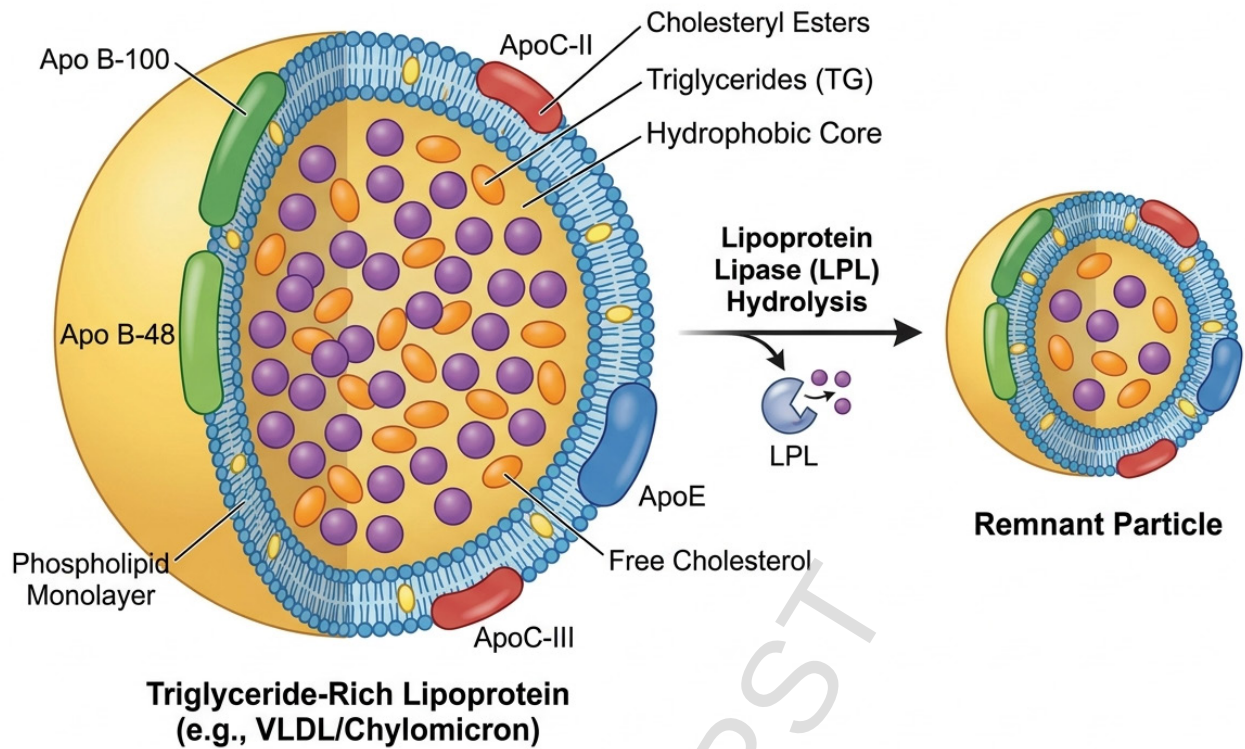
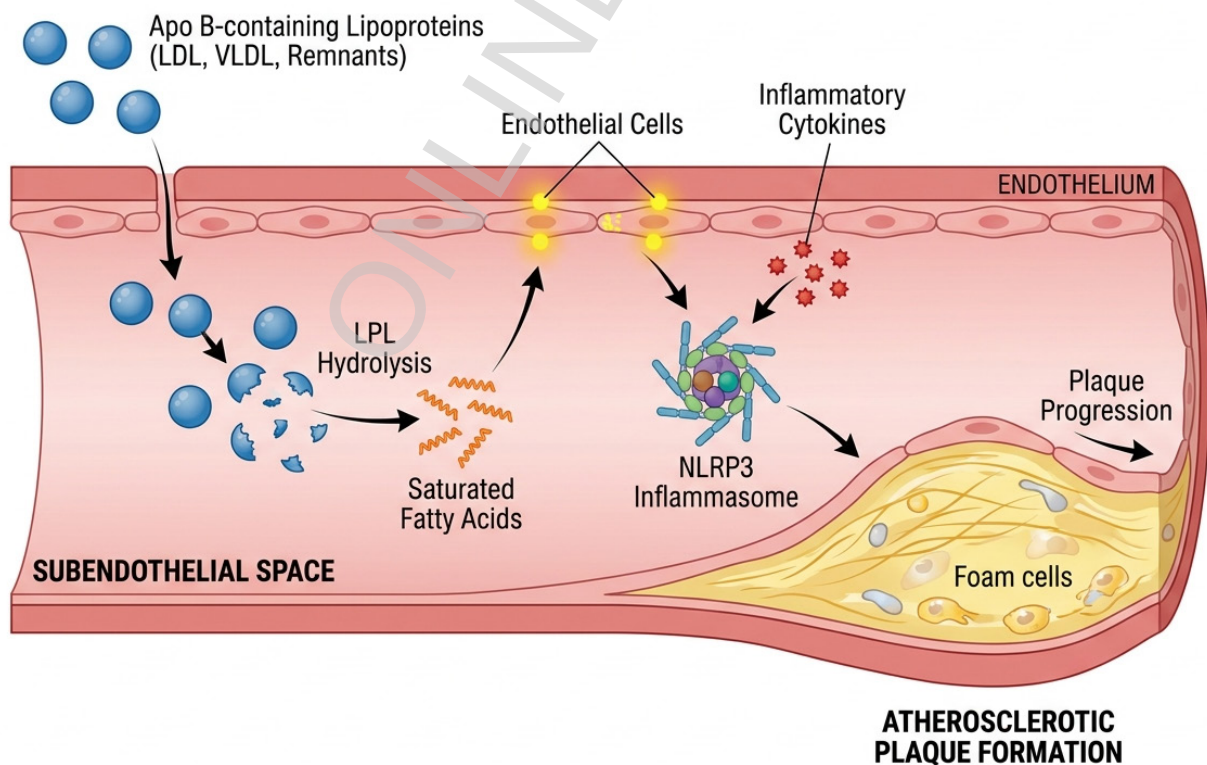


Figure 1. The triglyceride-rich lipoproteins. This figure was created with the assistance of the AI tool NotebookLM (<https://notebooklm.google/>) based solely on the concepts, data, and findings presented by the authors in this article.

THE LIFE CYCLE OF AN ATHEROSCLEROTIC PLAQUE



Gemini Notebook

Figure 2. The life cycle of a Plaque. This figure was created with the assistance of the AI tool NotebookLM (<https://notebooklm.google/>) based solely on the concepts, data, and findings presented by the authors in this article.

dyslipidemia, in addition to increased TRLs, usually have small, dense LDL particles with greater atherogenic potential along with small, dense HDL particles with reduced vasculoprotective function. Triglyceride levels are usually measured in fasting blood samples, although some studies indicate that postprandial TRL levels may be more relevant for assessing ASCVD risk. Mild and moderate hypertriglyceridemia occurs primarily as a consequence of increased synthesis, while severe hypertriglyceridemia results from reduced lipolysis and reduced clearance of triglycerides (9). Hypertriglyceridemia mostly accompanies obesity, metabolic syndrome, fatty liver and type 2 diabetes, and is rarely caused by genetic defects.

Current guidelines for the diagnosis and management of dyslipidemias recommend measuring triglyceride levels after an overnight fast. For initial screening in primary care, it is adequate to measure triglyceride levels in non-fasting conditions, except when non-fasting triglycerides are above 5 mmol/L, after hypertriglyceridemic pancreatitis, in previously diagnosed hypertriglyceridemia, or before starting therapy that might increase triglycerides (10). Non-fasting lipid profile is acceptable for initial screening. At the same time, fasting measurements are generally recommended when triglyceride concentrations are markedly elevated or when specific clinical circumstances require a more accurate assessment.

Since TRL contains a significant amount of cholesterol, it is recommended to calculate non-HDL cholesterol and/or, where available, to measure apo B lipoproteins. Non-HDL cholesterol and apo B more closely correlate with cardiovascular risk (11). In current European guidelines, non-HDL is recognized as a secondary target after LDL cholesterol for lipid-lowering therapies (12).

Epidemiological data

It is estimated that approximately 30% of people in the general population have hypertriglyceridemia; unfortunately, the exact prevalence is not precisely known, and it is mostly detected as an incidental finding. The situation is further complicated by the fact that triglyceride levels often vary seasonally and between individuals, depending on the diet, customs, and habits of a population in a given geographical region. Hypertriglyceridemia occurs relatively rarely as an isolated phenomenon, and it usually occurs concomitantly with other chronic diseases/conditions.

Epidemiological data on hypertriglyceridemia published in 2024 in the JACC journal on the association of hypertriglyceridemia with multiorgan disease in the adult population unequivocally indicate that the prevalence of chronic and multiorgan diseases (diabetes, chronic kidney disease, MASLD, and ASCVD) is higher in people with moderate and severe hypertriglyceridemia (13). The SIMETAP-HTG study confirms the association between

increased triglycerides and increased body weight/obesity, disorders of glucose tolerance, and an increased risk of atherosclerotic cardiovascular disease (14). Data from the Copenhagen General Population Study estimate that 24-25% of people have mild to moderate hypertriglyceridemia (1.7 to 5.6 mmol/L), while 0.1% have severe hypertriglyceridemia (15). Data from this study, as well as the Copenhagen City Heart Study, showed that increased fasting triglycerides were associated with a higher risk of ischemic heart disease, ischemic stroke, and myocardial infarction (15). In comparison, non-fasting triglycerides were associated with a higher risk of ischemic heart disease and heart failure (16).

According to recommendations (17), normal triglyceride values are defined as up to 1.2 mmol/L, borderline increased between 1.2 and 1.7 mmol/L, and mild and moderately increased triglyceride values are those between 1.7 and 5.6 and between 5.7 and 11.3 mmol/L. A triglyceride level over 11.3 mmol/L is defined as severe hypertriglyceridemia (Table 2). From a clinical point of view, mild to moderate hypertriglyceridemia is significant in terms of an increased risk for atherosclerotic cardiovascular disease. At the same time, triglyceride values over 11.3 mmol/L are associated with an increased risk for acute hypertriglyceridemic pancreatitis. The general recommendation is that, for persons found to have elevated triglycerides during routine laboratory analyses, secondary causes of hypertriglyceridemia should be ruled out first. The second general recommendation is that, in addition to determining triglyceride levels, non-HDL cholesterol should be recalculated, bearing in mind that non-HDL is listed as a secondary therapeutic target.

Table 2. Triglyceride levels (17)

Normal (Healthy): Less than 150 mg/dL (1.7 mmol/L)
Borderline High (Mildly elevated): 150 to 199 mg/dL (1.7 to 2.25 mmol/L)
High (Moderately elevated): 200 to 499 mg/dL (2.3 to 5.64 mmol/L)
Very High (Severe): 500 mg/dL or higher (more than 5.64 mmol/L)
Extremely High: Greater than 1,000 mg/dL (11.3 mmol/L)

Mild and moderate hypertriglyceridemia

Mild to moderate hypertriglyceridemia mainly results from secondary causes such as abdominal obesity, diabetes, alcohol abuse, a diet with a high glycemic index, and certain drugs (Table 3), with polygenic inheritance.

Triglyceride values in the range of mild/moderate hypertriglyceridemia are primarily important considering their role in the development and progression of atherosclerosis. Genetic and epidemiological studies indicate a causal connection between TG, TRLs, and TRL residues and ASKVB (8), primarily because hypertriglyceridemia favors the formation of small dense LDL particles with greater atherogenic potential and small dense HDL

Table 3. Hipertriglyceridemia [26]

Primary	Secondary
<i>Relatively rare, genetically determined, characterized by chylomicronemia</i> LPL deficiency, apo C2 deficiency apo A5 deficiency GPIHBP1 deficiency <i>Relatively common, genetically determined</i> Familial hypertriglyceridemia (probably polygenic) Familial combined hyperlipidemia (due to polymorphism of molecules and enzymes involved in lipid metabolism)	<i>Diseases/conditions</i> Abdominal obesity Diabetes Hypothyreosis Renal diseases Systemic lupus erythematosus HIV infection Pregnancy (third trimester) <i>Drugs</i> Nonselective beta blockers, thiazide diuretics, corticosteroids, tamoxifen, raloxifene, oral estrogens, protease inhibitors, immunosuppressives, antipsychotics, retinoic acid, sirolimus, phenothiazine drugs, etc. <i>Habits</i> Alcohol abuse, food rich in saturated fats, and food with a high glycemic index.

LPL-lipoprotein lipase, GPIHBP1-Glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1

particles with defective vasculoprotective function. It has also been shown that a triglyceride value over 1.7 mmol/L is associated with a higher cardiovascular risk (although this value was previously considered optimal) (18) according to the results of two large epidemiological Atherosclerosis Risk in Communities Studies. It is clearly shown that reduction of LDL cholesterol to target levels contributes to cardiovascular risk reduction, but often not completely, which is why a residual risk has been defined: residual cardiovascular risk, which includes lipid and non-lipid parameters such as hypertriglyceridemia, decreased HDL cholesterol, increased Lp (a), inflammation, and endothelial dysfunction. The results of the NHANES Study have shown that one in three persons with type 2 diabetes who, despite the reduction of LDL cholesterol to target levels, had triglyceride levels above 1.7 mmol/L (19); similar data have been published for the Ontario cohort where 25.4% of people with cardiovascular disease treated with statins achieved LDL levels below 2.5 mmol/L and had triglyceride levels above 1.5 mmol/L (14). It is still unclear how TRLs contribute to the development of atherosclerosis. Still, it is assumed that free fatty acids formed during TRL lipolysis at the endothelium and in the subendothelial space, along with the consequent release of reactive oxygen species and inflammatory cytokines and activation of the NLRP3 inflammasome, may play a role in this process (20). The atherogenicity of TRLs due to their accumulation in the subendothelial space results from increased release of saturated fatty acids, as well as from the induction of endothelial dysfunction and inflammation (20,21). Genetic studies confirm the importance of TRLs in the development of ASCVD independently of other traditional risk factors, primarily due to structural and functional differences and the content of APOC3, APO5, Apo E, and ANGPTL3/4/5 (20).

Severe hypertriglyceridemia

As mentioned before, circulating triglyceride levels depend on the balance between TRL synthesis/lipolysis in the liver and enterocytes and hepatic clearance, as well as on dietary intake and the body's needs for these lipids. An imbalance between the production and clearance of TRLs leads to the development of mild, moderate, and severe hypertriglyceridemia. As with other dyslipidemias, hypertriglyceridemia can be primary and secondary. Severe hypertriglyceridemia is mostly the result of genetic defects (Table 3). While mild/moderate hypertriglyceridemias are associated with increased cardiovascular risk, severe hypertriglyceridemia (with triglyceride values over 11.3 mmol/L), besides increased cardiovascular risk, is also associated with a higher risk of developing hypertriglyceridemic pancreatitis. Familial chylomicronemia syndrome is a rare condition that results from an autosomal recessive mutation of the LPL gene with subsequent LPL deficiency and, rarely, from mutations in other genes with subsequent deficiency in apo C2, apo A5, GPIHBP, and LMF1 (Table 3)

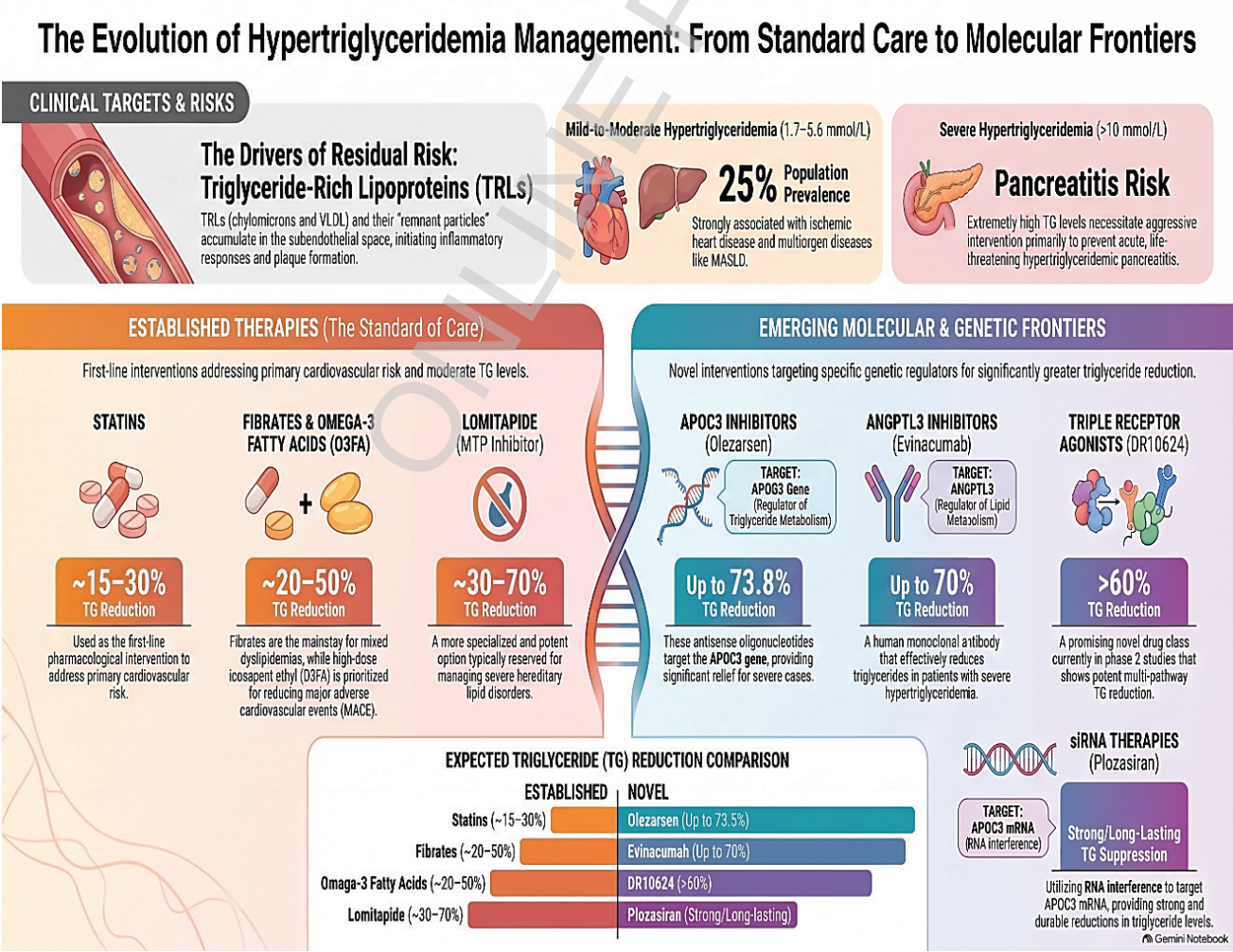
Therapeutic options

Therapeutic options for hypertriglyceridemia are primarily focused on reduction of residual cardiovascular risk and prevention of acute pancreatitis through lifestyle modifications (dietary changes, exercise and weight loss) and on pharmacological intervention when necessary. First-line treatment often involves lifestyle changes along with statins for mild hypertriglyceridemia, while for moderate-to-severe cases (TG > 5.6 mmol/L) more intensive therapy is required. Severe, familial, or persistent hypertriglyceridemia despite standard measures requires more aggressive therapy with newer medications (22). According to the 2019 ESC/EAS guidelines

and the 2025 Focused Update, management includes statins as initial therapy (20) (Figure 3). For high- or very high-risk patients with persistently elevated triglycerides despite statin treatment, specific therapies like high-dose icosapent ethyl may be considered to reduce cardiovascular events. In severe cases, such as those with Familial Chylomicronemia Syndrome, newer medications like Volanesorsen can be considered to lower triglyceride levels and mitigate pancreatitis risk. The guidelines advise against using dietary supplements or vitamins that lack proven LDL-C-lowering efficacy for reducing CV risk. The updated guidelines also recognize triglycerides and remnant cholesterol as factors in residual CV risk. Discussions at the 93rd EAS Congress highlighted emerging therapies, including Plozasiran, which showed potential in lowering triglycerides. Additionally, the 2025 update recommends measuring Lipoprotein(a) in all adults, noting levels above 50 mg/dL as a CV risk enhancer (23). Purified eicosapentaenoic acid is important for reducing major adverse cardiovascular events (MACE) (24), while fibrates are primarily used for mixed dyslipidemias and to lower pancreatitis risk. The main target in high/very-high-risk patients remains LDL reduction, with TG-lowering agents used as adjuncts. In contrast, for patients

with severe hypertriglyceridemia, particularly those at risk of pancreatitis, intensive triglyceride-lowering treatment is necessary.

In recent years, hypertriglyceridemia (HTG) therapy has been shifting toward targeted therapies for severe cases, alongside established statin/fibrate regimens (25) (Table 4, Figure 3). Novel treatments for severe hypertriglyceridemia (sHTG) focus on targeting genetic and molecular pathways, with key innovations including: ANGPTL3 Inhibitors (Evinacumab): a human monoclonal antibody that reduces triglycerides by up to 70% in patients with severe HTG; APOC3 Inhibitors (Volanesorsen, Olezarsen): these antisense oligonucleotides reduce apolipoprotein C-III, a key regulator of triglyceride metabolism, with Olezarsen showing potential to significantly lower triglyceride levels (up to 73.8% in trials); siRNA Therapies (Plozasiran/ARO-APOC3): a next-generation siRNA that targets APOC3 mRNA, providing a strong, long-lasting reduction of triglycerides; Triple Receptor Agonist (DR10624): A promising novel drug that reduced triglyceride levels by over 60% is in a phase 2 study. Volanesorsen is authorized in the EU for selected patients with genetically confirmed familial chylomicronaemia syndrome (FCS). At the same time,



olezarsen has also recently received EU marketing authorization for adult patients with genetically confirmed FCS. In contrast, evinacumab is authorized for homozygous familial hypercholesterolemia rather than severe hypertriglyceridemia, although its triglyceride-lowering effects have been investigated. In addition to these new therapeutic options, new and specialized approaches include gene therapy (Alipogene tiparvovec) for specific patients with familial lipoprotein lipase deficiency and Microsomal Triglyceride Transfer Protein (MTP) Inhibitors (Lomitapide) for managing severe hereditary lipid disorders. These novel therapies offer significant hope for reducing the risk of acute pancreatitis in patients with severe hypertriglyceridemia, where traditional therapies may be inadequate.

Table 4. Lipid-lowering drugs and expected triglyceride reduction (25)

Lipid-lowering drug	Expected % Tg reduction
Statins	~15-30%
Bempedoic acid	~0-5%
Fibrates	~20-50%
Ezetimibe	~5-10%
O3FA	~20-50%
PCSK9i	~10-20%
Lomitapide	~30-70%

TG-triglycerides, O3FA-omega-3-fatty acids

In conclusion, LDL cholesterol remains a crucial causal factor and therapeutic target. Still, in recent years, triglyceride-rich lipoproteins have been recognized as significant contributors to atherogenesis and, when extremely high, to hypertriglyceridemic pancreatitis. New recommendations for the treatment of dyslipidemia state that TRLs are a secondary target for cardiovascular risk reduction and must be treated promptly after achieving target LDL cholesterol levels.

This narrative review has few shortcomings, related primarily to a need for more detailed insight into the results of studies that analyze effects of triglyceride reduction on residual cardiovascular and acute pancreatitis risk reduction; however, the topic of this review was

primarily focused on the clinical significance of hypertriglyceridemia *per se*, how to diagnose and treat it. Studies confirm the positive effect of triglyceride-level reduction on cardiovascular risk (27) and the benefit of novel therapies for acute hypertriglyceridemic pancreatitis (28), but further studies are needed to clarify how these new therapeutic options affect residual cardiovascular risk and to inform future therapeutic recommendations.

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REFERENCES

- Goldstein J.L., Brown M.S. The LDL receptor defect in familial hypercholesterolemia: Implications for pathogenesis and therapy. *Med. Clin. N. Am.* 1982; 66:335–362. doi: 10.1016/s0025-7125(16)31424-9.
- Singh LS, Gašić V, Komazec J, Grubiša I, Popović L, et al. Biochemical characterisation of familial hypercholesterolemia: Associations between genetic and lipid profiles. *J Med Biochem.* 2026;44(9):2026-2034. doi:10.5937/jomb0-62224.
- Lalić K, Jotić A, Rajković N, Singh S, Stosic L, Popovic L, et al. Altered Daytime Fluctuation Pattern of Plasminogen Activator Inhibitor 1 in Type 2 Diabetes Patients with Coronary Artery Disease: A Strong Association with Persistently Elevated Plasma Insulin, Increased Insulin Resistance, and Abdominal Obesity. *Int J Endocrinol.* 2015;2015:390185. doi: 10.1155/2015/390185.
- Popović L, Lalić K, et al. C-reactive protein predicts progression of peripheral arterial disease in patients with type 2 diabetes: a 5-year follow-up study = C-reaktivni protein predviđa progresiju bolesti perifernih arterija kod pacijenata sa dijabetesom tipa 2. *Journal of Medical Biochemistry.* 2014;33(4): 347–355. doi: 10.2478/jomb-2014-0042.
- Lalić K, Nedeljković M, Jotić A, Babić R, Rajković N, Popović L, et al. Endothelial dysfunction of coronary arteries in subjects without diabetes: An association with both insulin resistance and impaired insulin secretion response. *Diabetes Research and Clinical Practice.* 2018; 139, 179-187. doi: 10.1016/j.diabres.2018.03.005.
- Hoogeveen RC, Ballantyne CM. Residual Cardiovascular Risk at Low LDL: Remnants, Lipoprotein(a), and Inflammation. *Clin Chem.* 2021 Jan 8;67(1):143-153. doi: 10.1093/clinchem/hvaa252.
- Contois JH, McConnell JP, Sethi AA, Csako G, Devaraj S, Hoefner DM, Warnick GR., AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Apolipoprotein B and cardiovascular disease risk: position statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on

- Best Practices. Clin Chem. 2009 Mar;55(3):407-19. doi: 10.1373/clinchem.2008.118356.
8. Borén, J., Packard, C.J. & Binder, C.J. Apolipoprotein B-containing lipoproteins in atherogenesis. Nat Rev Cardiol 2025, 22, 399–413. doi: 10.1038/s41569-024-01111-0.
9. Baratta F, Cocomello N, Coronati M, Ferro D, Pastori D, Angelico F, Ben MD. Cholesterol Remnants, Triglyceride-Rich Lipoproteins and Cardiovascular Risk. International Journal of Molecular Sciences. 2023; 24(5):4268. doi.org/10.3390/ijms24054268.
10. Nordestgaard BG, Langsted A, Mora S, et al. Fasting is not routinely required for determination of a lipid profile: clinical and laboratory implications including flagging at desirable concentration cut-points-a joint consensus statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine. Eur Heart J. 2016; 37:1944–1958. doi: 10.1093/eurheartj/ehw152.
11. Varbo A, Benn M, Tybjaerg-Hansen A, et al. Remnant cholesterol as a causal risk factor for ischemic heart disease. J Am Coll Cardiol. 2013;6:427–436. doi: 10.1016/j.jacc.2012.08.1026.
12. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020; 41(1):111-188. doi: 10.1093/eurheartj/ehz455.
13. Gurevitz, C, Chen, L, Muntner, P. et al. Hypertriglyceridemia and Multiorgan Disease Among U.S. Adults. Research letter, JACC Adv. 2024, May, 3 (5). doi.org/10.1016/j.jacadv.2024.100932.
14. Ruiz-García A, Arranz-Martínez E, López-Urriarte B, et al.; en representación del Grupo de Investigación del Estudio SIMETAP. Prevalence of hypertriglyceridemia in adults and related cardiometabolic factors. SIMETAP-HTG study. Clin Invest Arterioscler. 2020 Nov-Dec;32(6):242-255. doi: 10.1016/j.arteri.2020.04.001
15. Nordestgaard BG. Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease: New Insights From Epidemiology, Genetics, and Biology. Circ Res. 2016 Feb 19;118(4):547-63. doi: 10.1161/CIRCRESAHA.115.306249
16. Varbo A, Nordestgaard BG. Nonfasting Triglycerides, Low-Density Lipoprotein Cholesterol, and Heart Failure Risk: Two Cohort Studies of 113 554 Individuals. Arterioscler Thromb Vasc Biol. 2018; 38(2):464-472. doi: 10.1161/ATVBAHA.117.310269
17. Ginsberg HN, Packard CJ, Chapman MJ, Borén J, Aguilar-Salinas CA, Averna M, Ference BA, Gaudet D, Hegele RA, Kersten S, Lewis GF, Lichtenstein AH, Moulin P, Nordestgaard BG, Remaley AT, Staels B, Stroes ESG, Taskinen MR, Tokgözoğlu LS, Tybjaerg-Hansen A, Stock JK, Catapano AL. Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies-a consensus statement from the European Atherosclerosis Society. Eur Heart J. 2021 Dec 14;42(47):4791-4806. doi: 10.1093/eurheartj/ehab551.
18. Abera T, Peterson ED, Pagidipati NJ, et al. The association between triglycerides and incident cardiovascular disease: What is “optimal”? Journal of Clinical Lipidology. 2020 Jul - Aug;14(4):438-447. doi: 10.1016/j.jacl.2020.04.009.
19. Fan W, Philip S, Granowitz C, Toth PP, Wong ND. Prevalence of US Adults with Triglycerides ≥ 150 mg/dl: NHANES 2007-2014. Cardiol Ther. 2020 Jun;9(1):207-213. doi: 10.1007/s40119-020-00170-x.
20. Lawler PR, Kotrri G, Koh M, Goodman SG, Farkouh ME, Lee DS, Austin PC, Udell JA, Ko DT. Real-world risk of cardiovascular outcomes associated with hypertriglyceridaemia among individuals with atherosclerotic cardiovascular disease and potential eligibility for emerging therapies. Eur Heart J. 2020 Jan 1;41(1):86-94. doi: 10.1093/eurheartj/ehz767
21. Chapman MJ, Packard CJ, Björnson E, Ginsberg HN, Borén J. Triglyceride-rich lipoproteins, remnants and atherosclerotic cardiovascular disease: What we know and what we need to know. Atherosclerosis. 2025 Nov;410:120529. doi: 10.1016/j.atherosclerosis.2025.120529.
22. Lalić K, Rajković N, Popović L, Singh Lukač S, Rasulić I, Petakov A, et al. Terapijski pristup u lečenju dislipidemija - novine i izazovi. Gale-nika Medical Journal. 2024;3(9):31-9. doi: 10.5937/Galmed2409031L
23. François Mach, Konstantinos C Koskinas, Jeanine E Roeters van Lennep, Lale Tokgözoğlu, Lina Badimon, Colin Baigent, Marianne Benn, Christoph J Binder, Alberico L Catapano, Guy G De Backer, Victoria Delgado, Natalia Fabin, Brian A Ference, Ian M Graham, Ulf Landmesser, Ulrich Laufs, Borislava Mihaylova, Børge Grønne Nordestgaard, Dimitrios J Richter, Marc S Sabatine, ESC/EAS Scientific Document Group, 2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias: Developed by the task force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS), European Heart Journal, 2025; 46 (42) 4359–4378. doi: 10.1093/eurheartj/ehaf190.
24. Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med. 2019;380(1):11-22. doi: 10.1056/NEJMoa1812792.
25. Zimodro JM, Rizzo M, Gouni-Berthold I. Current and Emerging Treatment Options for Hypertriglyceridemia: State-of-the-Art Review. Pharmaceuticals. 2025;18(2):147. doi:10.3390/ph18020147.
26. Cruz-Bautista I. Approach to hypertriglyceridemia syndromes: the importance of distinguishing between primary and secondary etiologies. Cardiovasc Metab Sci . 2021;32(Suppl: 3):s236-241. doi:10.35366/100804.
27. Marston NA, Giugliano RP, Im K, et al. Association Between Triglyceride Lowering and Reduction of Cardiovascular Risk Across Multiple Lipid-Lowering Therapeutic Classes: A Systematic Review and Meta-Regression Analysis of Randomized Controlled Trials. Circulation. 2019; 140 (16): 1308-1317. doi: 10.1161/CIRCULATIONAHA.119.041998
28. Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al. Olezarsen, Acute Pancreatitis, and Familial Chylomicronemia Syndrome. N Engl J Med. 2024; 390 (19): 1781-1792. doi: 10.1056/NEJMoa2400201

KLINIČKI ZNAČAJ I TERAPIJA HIPERTRIGLICERIDEMIJE

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Sažetak

Uprkos značajnom napretku u snižavanju LDL holesterola, i dalje preostaje značajan rezidualni rizik za ateroskleroznu kardiovaskularnu bolest (ASKVB), uglavnom uzrokovan trigliceridima bogatim lipoproteinima (engl. TG-rich lipoproteins-TRLs).

Cilj ovog revijalnog narativa je da se naglasi značaj hipertrigliceridemije u nastanku aterosklerozne kardiovaskularne bolesti i akutnog pankreatitisa i da se razjasne dijagnostičke dileme i aktuelne terapijske opcije.

Ovaj narativni revijalni rad istražuje patofiziologiju, dijagnostičke kriterijume i epidemiološki značaj hipertrigliceridemije. TRL, uključujući hilomikrone i VLDL, doprinose razvoju ateroskleroze nakupljanjem "preostalih čestica" bogatih holesterolom kao i apolipoproteina B (Apo B) u subendotelijalnom prostoru. Skorašnji epidemiološki podaci, uključujući nalaze iz Opšte populacione studije u Kopenhagenu i studije SIMETAP-HTG, potvrđu-

ju da je blaga do umerena hipertrigliceridemija (1,7–5,6 mmol/L) prevladavajuća u približno 25% populacije kao i da je snažno je povezana sa povećanim rizikom od infarkta miokarda, srčanim popuštanjem i multiorganskim bolestima poput dijabetesa i MASLD-a. Suprotno tome, teška hipertrigliceridemija (>11.3 mmol/L) značajno povećava rizik od akutnog pankreatitisa. Trenutne preporuke naglašavaju značaj merenja triglicerida natašte, iako i nivo triglicerida ne natašte ima značaja za skrining. Rad zaključuje da se sekundarni uzroci moraju isključiti prilikom postavljanja dijagnoze hipertrigliceridemije a ističe se i značaj non-HDL holesterola kao sekundarnog cilja za sveobuhvatno kontrolisanje kardiovaskularnog rizika. Završni deo rada usmeren je na nove terapijske opcije i terapije u nastajanju za korigovanje povećanih nivoa TRL.

Glavne reči: hipertrigliceridemija, trigliceridima bogati lipoproteini, non-HDL holesterol, aterosklerozna kardiovaskularna bolest, rezidualni kardiovaskularni rizik, hipertrigliceridemijski pankreatitis, terapija

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