

# Use of Lifestyle Modifications for Management of a Patient with Severely High Total Cholesterol (> 14 mmol/L) and Triglycerides (> 40 mmol/L)

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In this report, we describe a case of a 37-year old man who presented with a history of total cholesterol > 14 mmol/L and triglyceride levels > 40 mmol/L. The patient was initially thought to have familial hypercholesterolemia due to his elevated total cholesterol, by his family physician. He was prescribed evolucumab, a proprotein convertase subtilisin/kexin type 9 inhibitor drug which has shown efficacy for lowering low-density lipoprotein-cholesterol levels, to reduce his high total cholesterol. However, in this patient, the elevated total cholesterol was likely due to hypertriglyceridemia, rather than increased low-density lipoprotein-cholesterol levels. Through this case we provide an approach for the clinical management of patients with elevated total cholesterol with underlying triglycerides  $\geq 10$  mmol/L. The primary intervention for management of triglycerides  $\geq 10$  mmol/L involves lifestyle modifications including, changes in diet, exercise, reduction in body mass index, and abstinence from alcohol consumption. Secondary intervention involves management through pharmacotherapy with fibrates and statins. Creating a plan of action with the patient, incorporating lifestyle modifications alone, the patient was able to reduce the triglycerides from an average of 44.94 mmol/L to 3.28 mmol/L.

**Key Words:** Triglycerides, Patient care management, Lifestyle, Cholesterol

## INTRODUCTION

Elevated Triglyceride (TG) levels, especially TGs  $\geq 10$  mmol/L have been established as a marker of increased risk of acute pancreatitis, with estimated mortality in 5-6% of cases, in addition to residual cardiovascular risk [1,2].

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Although the prevalence of TGs  $\geq 10$  mmol/L is not well characterized in North America, its prevalence in Europe has been estimated to be as high as 1 in 1000 individuals [1]. It is crucial to recognize the underlying etiology of high total cholesterol to direct appropriate management. However, currently, there is a lack of comprehensive guidelines from National Societies for appropriate management of high total cholesterol due to elevated TGs (TGs  $\geq 10$  mmol/L). With cardiovascular disease being one of the most common modifiable diseases, using this case, we have tried to create a framework of management for patients with TGs  $\geq 10$  mmol/L.

## CASE REPORT

A 37-year old man with a history of dyslipidemia and severe triglyceridemia, was referred to our cardiology clinic for management of persistently high total cholesterol of 14.43 mmol/L and a TG level of 44.94 mmol/L. The low-density lipoprotein cholesterol and high-density lipoprotein cholesterol could not be estimated due to high TG levels. The patient was overweight with a BMI of 27.7 kg/m<sup>2</sup> and reported feeling well overall, except for mild, atypical chest pain. His stress test was normal with no indications of ischemia, and the echocardiogram showed a normal left ventricular systolic function with a preserved ejection fraction of 68%.

Despite being on Rosuvastatin 10 mg once daily and Proprotein convertase subtilisin/kexin type 9 inhibitor drug, Evolocumab, at 140 mg every 2 weeks, there was little change in his lipid values. His social history revealed alcohol consumption of 10 drinks or more per week and a diet that was high in carbohydrates and fat, primarily due to eating large portion sizes and late-night snacking. The patient lived a rather sedentary life, with no regular exercise. Based on the patient's lipid panel and unresponsiveness to pharmacotherapy, we diagnosed him with mixed hyperlipidemia.

## DISCUSSION

High total cholesterol is often attributed to increase in low-density lipoprotein levels as opposed to elevated TGs, thus the family physician initially misdiagnosed him with familial hypercholesterolemia. Additionally, a lack of understanding of appropriate management for TG  $\geq$  10 mmol/L subsequently led to the inappropriate prescription of Evolocumab, a drug which has shown efficacy for lowering low-density lipoprotein-cholesterol levels rather than high TGs. Therefore, it is important to recognize the etiology of elevated total cholesterol, and devise an approach to management of patients with TGs  $\geq$  10 mmol/L. Severe triglyceridemia is not an acute medical emergency, but a condition that can be managed well in a clinical setting primarily through lifestyle modifications and pharmacotherapy.

Triglycerides can be elevated by a variety of different factors including high BMI, and alcohol intake, as that

guides appropriate management [3]. Secondary factors like uncontrolled diabetes mellitus, serum estrogen and thyroid stimulating hormone levels, retinoid consumption, and medications for human-immunodeficiency virus infections can also contribute to elevated TG levels and need to be monitored and managed for patients with TGs  $\geq$  10 mmol/L [4,5]. In addition to environmental factors, genetics also plays a role in influencing the lipid profile of individuals and families [2]. Although rare, one such condition, Family Chylomicronemia Syndrome has been reported to increase TGs in people with the disease [2]. Genetic testing can be used for diagnosis; however, it is not a readily available option for clinical management. Thus, genetic testing for the presence of Family Chylomicronemia Syndrome should be considered if TGs  $\geq$  10 mmol/L is not reduced despite rigorous lifestyle changes, adequate pharmacotherapy, and management of other secondary factors. It is crucial to understand the factors which increase TGs in an individual prior to initiating treatment. In our clinic's experience of managing over 200 patients with TGs  $\geq$  10, we have had 4 patients who have been unable to lower TG levels. Two of the patients were on anti-viral drugs for HIV and had uncontrolled diabetes, and we have had two patients lost to follow-up.

Building on the experience, through this case we wanted to share how lifestyle changes are the mainstay for our successful management of the patients. The management of TG levels varies depending on the serum TG levels and underlying pathophysiological factor. Mild to moderately elevated TGs (2-10 mmol/L) primarily consist of remnant very low-density lipoprotein particles, whereas severely high TGs consist of chylomicrons [6]. As such, regular monitoring of a patient's lipid profile is an important first step in management. There is strong evidence suggesting that little difference exists between fasting and non-fasting TG monitoring in risk prediction for cardiovascular disease and mortality [6]. However, these studies have excluded patients with TGs  $>$  4.5 mmol/L [7]. Additionally, measurements for low-density lipoprotein cholesterol levels at extremely high TG levels are not considered reliable and thus, the American Heart Association recommends doing a fasting test in people who have received a TGs  $>$  4.5 mmol/L on a previous non-fasting test [4]. This eliminates any effects of recent

meals on plasma TGs as TG levels are susceptible to increase with high glycemic index and fat food consumption. In this case, we conducted regular fasting TG tests every four months as the patient initially had TGs of 44.94 mmol/L.

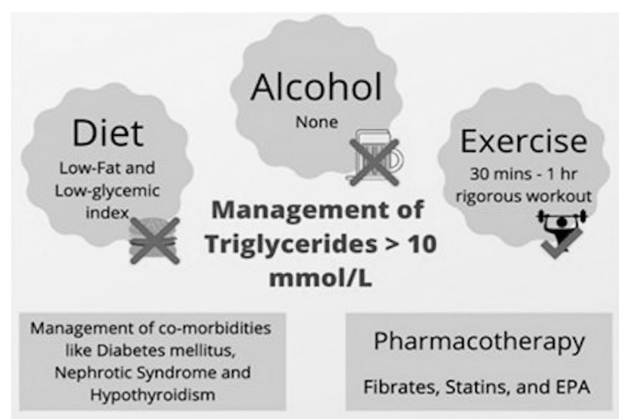
Individuals with elevated TG-rich remnant particles  $\geq$  10 mmol/L are more likely to have high BMI [6]. A combination of a diet control and exercise are required to reduce BMI, which was the cause of elevated TGs in our patient. A diet low in fat and glycemic index, including vegetables, whole grains, low-fat dairy and poultry as protein options should be promoted in addition to creation of personalized diet plans with patients as recommended by the European Society of Cardiology and European Atherosclerosis Society [3]. Additionally, the American Heart Association guidelines recommend following an active lifestyle, with at least 30 min of aerobic exercise of moderate/vigorous intensity daily in patients with elevated TGs [4]. We set goals for exercise and weight reduction with the patient, who agreed to work out by running 3-4 km for 4 days a week. The patient also restricted himself to a low fat and glycemic index diet with a focus on eating smaller portions and at consistent times.

Alcohol is a risk factor for acute pancreatitis, especially in people with elevated TGs [1]. The European Society of Cardiology and European Atherosclerosis Society recommend abstaining from alcohol for people with TGs  $\geq$  10 mmol/L [3]. Therefore, when managing lipid profile, it is important to evaluate the patient's alcohol consumption and educate on abstinence of alcohol consumption if TGs  $\geq$  10 mmol/L. Studies show benefit in using specific questions to quantify alcohol consumption [8]. As such, questions like "how many drinks did you have last night" followed by "is that usually how much you drink daily," were useful in our case. After establishing the patient's baseline alcohol consumption at 8-10 drinks per week and educating the patient about the risk of alcohol consumption, we established a plan to abstain from alcohol use with the patient.

Pharmacotherapy can be initiated alongside lifestyle modifications or when adherence to lifestyle changes is low. Both the American Heart Association and European Society of Cardiology and European Atherosclerosis Society guidelines recommend initiating statins with fibrate therapy for patients with elevated TGs [3,4]. Use of niacin over 1-2 g per day can lower TGs but its use is limited due to increased

side effects at higher doses [3,4]. There is increased interest in using fish oils rich in omega-3 fatty acids, especially eicosapentaenoic acid in management of high TGs. A recent trial called REDUCE-IT showed that increasing serum eicosapentaenoic acid levels has several cardiovascular benefits, however the extent of TG lowering benefit by Vascepa, the drug used in REDUCE-IT [9], is uncertain. Additionally, the drug is priced at \$400 USD per month, rendering it difficult for many patients to afford the drug without a private insurance plan. Moreover, the trial's patient population did not include patients with TGs  $\geq$  10 mmol/L, thus the drug's efficacy in this patient population is still not well known [9]. For our patient, we discontinued the use of Proprotein convertase subtilisin/kexin type-9 inhibitor. The patient continued with 10 mg Rosuvastatin for low-density lipoprotein cholesterol lowering, and an emphasis was placed on lifestyle modifications to lower TGs without use of pharmacotherapy. Patient successfully decreased his BMI from 27.7 to 24 and achieved reduction in TG and cholesterol levels. Fig. 1 provides a summary of overall management of people with TGs  $\geq$  10 mmol/L.

Given that triglyceride levels are amenable to lifestyle modifications [3,4], management of patients with high cholesterol due to underlying high triglycerides should primarily be focused on a reduction in BMI, specifically through adherence to a low-fat diet, daily exercise routines and ab-



**Fig. 1.** Management of Triglycerides. Shown here are pearls of clinical management of patients with triglycerides  $\geq$  10 mmol/L. Lifestyle modifications involving diet, alcohol and exercise should be the first line therapy. Management of pharmacotherapy that reduce triglycerides should be considered secondary to or alongside lifestyle modifications. EPA: Eicosapentaenoic acid.

**Table 1.** Shown here is a comparison between in patient characteristics between presentation and after lifestyle interventions

Patient characteristics	Initial presentation	After lifestyle interventions
Weight	210 lbs	186 lbs
BMI	27.7 lbs/inches <sup>2</sup>	24 lbs/inches <sup>2</sup>
Triglycerides (fasting)	44.94 mmol/L	3.28 mmol/L
Total cholesterol	14.43 mmol/L	4.02 mmol/L
Low-density lipoprotein cholesterol	Results unavailable due to elevated triglycerides	1.56 mmol/L
High-density lipoprotein cholesterol	Results unavailable due to elevated triglycerides	0.92 mmol/L

stinence from alcohol. Although not initially considered, a plan was made to start pharmacotherapy in the case of a lack of TG reduction with lifestyle modifications or patient non-compliance. The patient was closely followed every four months for a year, with regular measurements of blood pressure, heart rate and BMI. Additionally, blood work was recorded every four months. By simply making lifestyle changes, the patient was able to reduce the average TG level to 3.28 mmol/L from the previous 44.94 mmol/L over the year. Table 1 provides a comparison between the patient's BMI and lipid profile before and after the management as described in the report. It is important to consider that successful patient outcomes, however, are dependent on patient motivation and adherence to lifestyle changes, and therefore this case may be limited in its generalizability to patients, who might be unable to adhere to lifestyle changes. Therefore, it is important to take a patient-centered approach, taking into account patient's choices in triglyceride management.

## CONFLICTS OF INTERESTS

The views expressed in this article are of the authors based on current literature review, and not an official position of the institution or funder. Additionally, there are no competing interests for the authors.

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