We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS BOOK CITATION INDEX INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Postprandial Lipemia as Cardiovascular Disease Risk Factor

Neil Francis Amba and Leilani B. Mercado-Asis

Abstract

Postprandial lipemia (PPL) is characterized by prolonged and increased levels of lipids especially triglycerides (TG) and triglyceride-rich lipoprotein levels after a meal. There are an increasing number of evidence that postprandial lipemia is a significant risk factor for cardiovascular disease because of its causative role in atherosclerosis and endothelial dysfunction. This has serious implications because common dietary patterns are characterized by high fat content and meal consumption; hence, most will be in a postprandial state resulting to frequent and prolonged exposure to high lipid levels. The review will present the current evidences for the role of postprandial lipemia as a risk factor for cardiovascular disease and its association with other cardiovascular risk factors, namely, diabetes and obesity. We will also present recommendations on the diagnosis and management of postprandial lipemia.

Keywords: postprandial lipemia, postprandial dyslipidemia, endothelial dysfunction, hypertriglyceridemia

1. Lipoprotein metabolism

Lipoproteins are responsible for the distribution of cholesterol and triglyceride from the intestine and liver to peripheral cells. The process of lipoprotein distribution and metabolism is highly related to energy metabolism and the feed-fast cycle. Triglycerides (TG) are synthesized from dietary free fatty acids and glycerol in enterocytes. They are assembled together with phospholipids and cholesterol with apolipoproteins, mainly apoB-48 into chylomicron particles (apo A, C, E also present). These TG-rich particles enter the plasma via the intestinal lymph. Chylomicrons are then transported to peripheral cells where the enzyme lipoprotein lipase (LPL) hydrolyses their triglyceride content, releasing free fatty acids to be used by peripheral cells. The resulting chylomicron remnants are smaller and denser and are removed in the circulation by binding of the surface apo E to the LDL receptor or LDL receptor-related protein (LRP) [1]. Please also refer to the introductory chapter of this book for detailed and illustrated review of lipoprotein metabolism.

In the liver, synthesized TGs are released to the circulation by the very low-density lipoprotein (VLDL) particles. VLDL particles are TG-rich and, mainly, apo B-100-containing particles (apo A, C, E also present). VLDL synthesis takes place

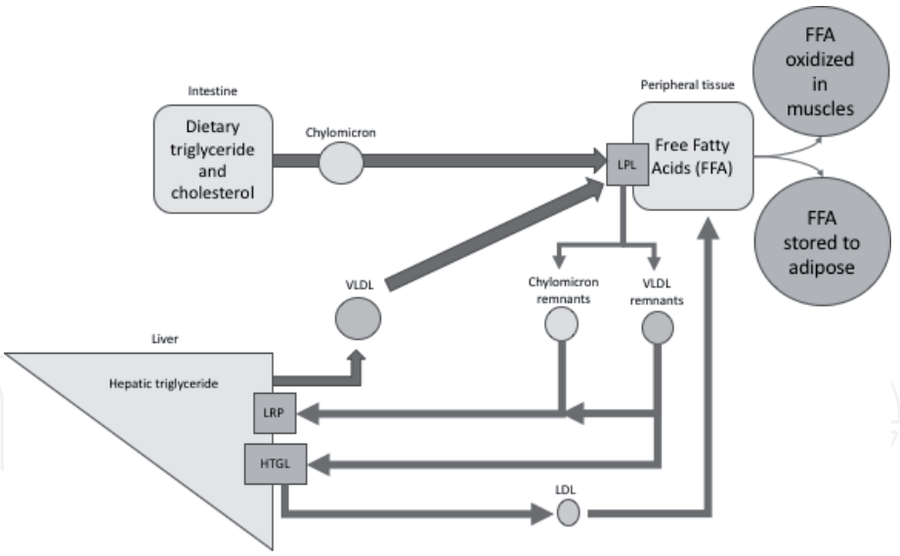

Figure 1.
Lipoprotein metabolism overview. Dietary TG transported via chylomicrons and hepatic TG transported via VLDL are delivered to peripheral tissue and acted upon by lipoprotein lipase to liberate fatty acids for energy fuel, cellular synthesis, or fat storage. Chylomicron and VLDL remnants are taken up by the liver. VLDL remnants can be further hydrolyzed by HTGL to form LDL particles.

during fasting and prandial state. Once delivered to peripheral tissues, the TG contents are hydrolyzed to free fatty acids by LPL, similar to that of chylomicrons. VLDL remnants, also called intermediate-density lipoproteins (IDL), are taken up by the liver via apo E binding to LDL receptor or converted to LDL by removal of TG content by the hepatic triglyceride lipase (HTGL) enzyme. The removal of TG renders the particles smaller allowing better vascular penetration, hence increasing atherogenicity [2].

The cholesterol ester transfer protein (CETP) facilitates the transfer of cholesteryl esters from high-density lipoproteins (HDL) particles to VLDL in exchange for TGs. Cholesteryl ester-enriched particles are better substrates for HTGL allowing greater decrease in size of the particle, creating small dense (sd) LDL. Small, dense LDL are more atherogenic due to their smaller size as they readily enter the subendothelial space [1].

Chylomicrons, VLDL, and their respective remnants (remnant lipoproteins (RLP)) are termed triacylglycerol-rich lipoproteins (TRL) (**Figure 1**).

2. Lipid profile in the postprandial state

The plasma lipid levels normally fluctuate during the day, in response to food intake. TG levels vary more considerably compared to LDL and HDL cholesterol levels. Nowadays, the common dietary habit is characterized by high fat contents and high frequency of meals; hence, most individuals will be in a nonfasting state. Because of the evidence of association of nonfasting lipid levels as a risk factor for CVD, it is important to analyze postprandial lipoprotein physiology and metabolism [2].

In a study by Stanhope et al., it has been found that TG levels are significantly elevated during the day in association to food intake. When fructose was administered, there was significant increase in TG compared with the regular meal. Plasma cholesterol levels did not significantly change during the day [3]. In our previous studies, we were able to demonstrate the pattern of postprandial lipid rise. We have found that there was significant increase in the levels for total cholesterol,

triglycerides, and HDL with peaking at the 4th–5th hour after a fatty meal [4]. The postprandial increase in TG is again demonstrated in another study by our group and has shown to be similar with VLDL postprandial increase beginning 4 hours after breakfast and sustained until 9–10 hours after [5]. In one of our trials, similar patterns of postprandial increase in TC, TG, and HDL were demonstrated with peaking at the 4th–5th hour and with noted decline at the 5th–6th hour [6]. None of our studies have demonstrated any pattern of postprandial rise for LDL.

The postprandial period is characterized by an increase in atherogenic lipoprotein particles. These are the TRLs including chylomicrons, VLDL, and their remnant particles. Their levels are affected by multiple individual and environmental factors, including sex, age, body mass index, physical activity, and smoking, and by the amount and type of dietary fat in a meal [7].

In the study by Cohn et al., they have shown that there may be more than one peak in postprandial TG concentration, that the magnitude of postprandial rise is dependent on age and gender, that postprandial plasma cholesterol concentration can increase or remain at baseline, and that postprandial cholesterolemia is inversely correlated with fasting HDL levels [8].

The postprandial lipid response has been shown to be modified by polymorphisms within the genes for apo A-I, E, B, C-I, C-III, A-IV, and A-V, LPL, hepatic lipase, fatty acid-binding protein-2, the fatty acid transport proteins, microsomal triglyceride transfer protein, and scavenger receptor class B Type I [9].

3. Postprandial lipemia in diabetes

Diabetes is associated with premature atherosclerosis and cardiovascular disease, and this may be contributed to diabetic dyslipidemia. Diabetes is characterized by multiple lipoprotein metabolism abnormalities that promote atherogenesis. The common lipid abnormality in diabetes includes hypertriglyceridemia, low HDL, and increase in small, dense LDL (sdLDL) levels. In a study by Shukla that investigated the postprandial response of type 2 DM patients after a standard fat challenge, it has been found that compared to normal controls, DM patients have significantly higher postprandial triglyceride levels despite having similar fasting levels. No significant difference in postprandial HDL levels was seen when adjusted to fasting levels [10].

The abnormalities in lipids among diabetics are secondary to multiple metabolic derangement that characterizes diabetes. For example, it has also been found that intestinal lipoprotein metabolism among diabetics is altered with increased lipoprotein production that prolongs postprandial lipemia [11].

In our clinic-based retrospective study, we have found that HbA1c has strong positive correlation with postprandial TG, while the 2-hour plasma glucose has moderate positive correlation. These significant correlations of postprandial lipemia with glycemic control and postprandial glycemia suggest that despite optimal fasting lipid levels, poor glycemic control is still associated with elevation of postprandial lipids, specifically postprandial triglycerides [12]. Similarly, Nakamura et al. have demonstrated that insulin resistance is closely related to postprandial hyperlipidemia among type 2 DM patients with CAD. Specifically, they have found that the 6th hour postprandial TG and remnant-like particle cholesterol were significantly higher among type 2 DM subjects and that plasma insulin levels and insulin resistance index were correlated with serum TG and RLP-C levels [13]. In addition, it has been shown in an animal study that postprandial hypertriglyceridemia predicts the development of insulin resistance, glucose intolerance, and type 2 DM [14]. However, evidence is still lacking.

Although it has been shown that glycemia is correlated with postprandial dyslipidemia, there are evidences that even with good glycemic control, diabetes is still associated with postprandial dyslipidemia. Rivellese et al. have demonstrated that subjects with type 2 DM with good glucose control and optimal fasting triglyceride levels still presented with abnormal plasma lipid response after a standard mixed meal. In particular, large VLDL and chylomicron remnants were shown to be elevated postprandially [15].

4. Postprandial lipemia and obesity

Obesity is a global epidemic affecting both children and adults. It is commonly defined as a body mass index (BMI) of ≥30 kg/m^2, but other indexes such as waist circumference and waist to hip ratio have been used. It is an established risk factor for cardiovascular disease, and it has been associated with dyslipidemia and abnormalities in lipoprotein metabolism. However, it is not yet established how obesity affects postprandial lipid levels.

Obesity is associated with insulin resistance, favoring catabolism and lipolysis [16]. Hence, it may be expected that obesity is associated with postprandial lipemia. In our previous unpublished study, we have found that there was no significant difference in postprandial lipid response in obese subjects compared to normal-weight subjects. Interestingly, postprandial lipid levels were actually slightly lower in the obese group compared to the normal group. This study used BMI to classify obese subjects, and different results were seen in studies that focused on abdominal obesity. Abdominal obesity has been known to be a risk factor for cardiovascular disease [17], and it has been demonstrated that abdominal obesity is associated with prolonged and amplified postprandial lipid levels [18]. Interestingly, postprandial lipemia can be seen in abdominal obesity despite normal fasting levels of TG [18, 19].

5. Role of postprandial lipemia in endothelial inflammation and dysfunction

Postprandial lipemia is hypothesized to be a risk factor for cardiovascular disease by inducing endothelial dysfunction [20]. The vascular endothelial lining functions to maintain adequate blood flow and regulate coagulation and inflammation. Endothelial dysfunction signifies any disturbance to the vasodilatory response of the endothelium and impairment of its antithrombotic and antiproliferative function [21]. This eventually translates to atherosclerosis and CVD. Several studies have shown that intake of high-fat meals can induce an increase in postprandial TG levels and impair endothelial function [22, 23].

Postprandial lipemia promotes atherogenesis and endothelial dysfunction by contributing to the inflammatory state in the endothelial environment [24]. Postprandial lipemia has also been shown in in vitro and in vivo studies to activate leukocytes promoting adherence to endothelial walls and migration to the subendothelial space, therefore promoting atherosclerosis. VLDL, IDL, and chylomicron remnants have been shown to cause endothelial inflammation and promote increase in pro-inflammatory cells within the vascular walls. TG and TGRLs also induce pro-inflammatory cytokines that induce vascular cell adhesion molecule (VCAM)-1 expression in endothelial cells and monocyte adhesion. Lipolysis of TGRLs by the enzyme lipoprotein lipase (LPL) along with the endothelium produces by-products that are pro-inflammatory and pro-atherogenic. Lipolysis produces oxidized free

fatty acids that promote endothelial inflammation, vascular apoptosis, and reactive oxygen species (ROS). Inflammation in the endothelium increases permeability and uptake of VDL in the vascular wall [25].

Maggi et al. have shown that postprandial levels of remnant lipoproteins (RLP) and TG contribute to endothelial dysfunction as measured by flow-mediated dilatation (FMD) of the brachial artery. They have demonstrated that the increase in postprandial RLP and TG levels was associated to the decrease in FMD. In addition, the peak level of RLP at 6 hours after meal coincided with the maximal endothelial dysfunction [26]. Their findings are supported by similar

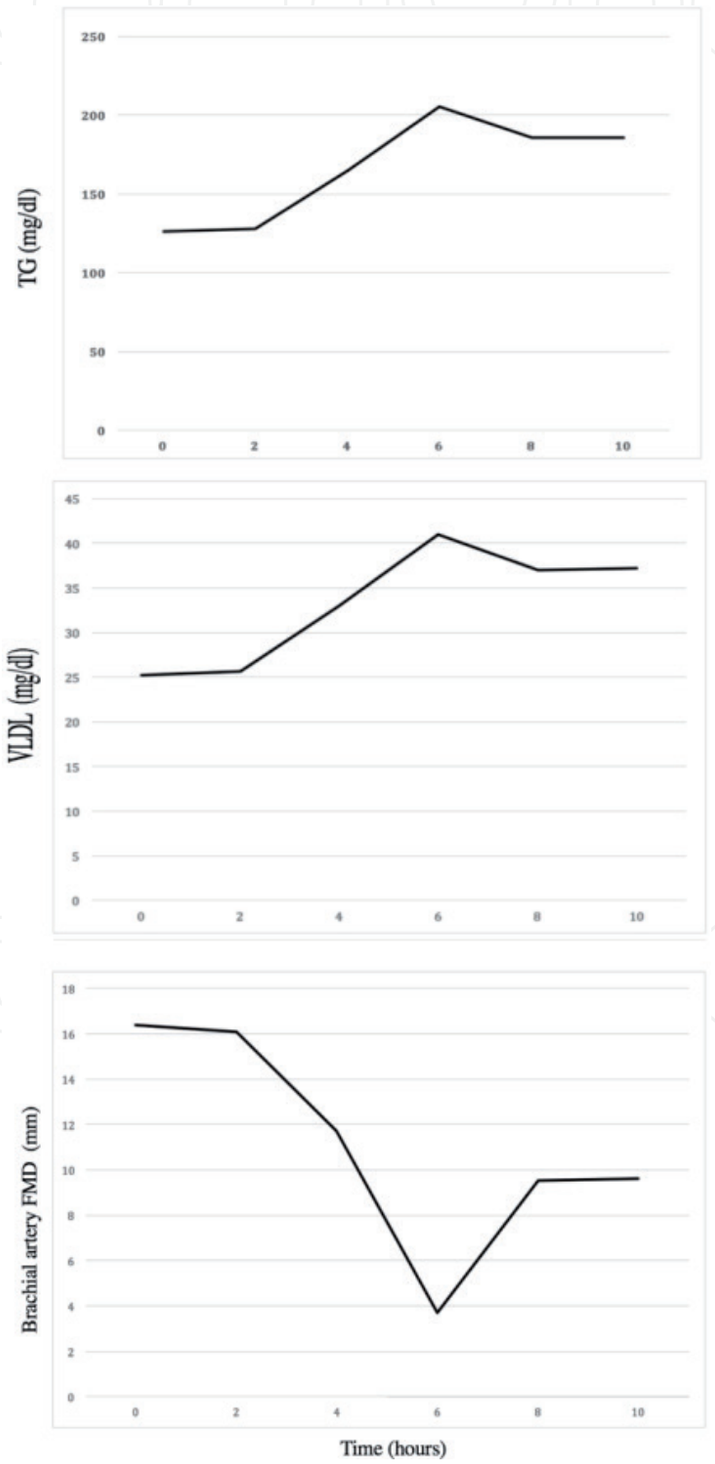

Figure 2.
The result from a study by Caringal et al. showing trends of lipid levels and brachial artery flow-mediated dilatation (FMD) after a standard diet.

results in a study by Caringal et al. that investigated the relationship between postprandial lipid levels and endothelial dysfunction using FMD as surrogate marker. Five high-risk subjects with normal fasting lipid levels were given a standard low-fat diet. Interestingly, it was observed that even though the fasting lipid levels were normal, the peaking of TG and VLDL 6 hours postprandially and the decrease in HDL postprandially appear to coincide with the decrease in brachial artery FMD [27] (**Figure 2**).

A study by Giannattasio et al. involving 16 asymptomatic hypertriglyceridemic and 7 normotriglyceridemic controls showed attenuation of arterial vasodilatory response following a high-fat meal among subjects with dyslipidemia. This reflects postprandial impairment of endothelial function after a high-fat meal [23].

6. Postprandial lipemia and CV events

Lipid-lowering therapy focusing on LDL-C reduction has been proven to reduce coronary events and stroke [28]. However, with the evidences of association of postprandial lipemia, specifically TG and RLP with endothelial dysfunction, it is important to assess their role in morbidity and mortality.

In a prospective cohort by Nordertgaard et al., involving a large number of white women and men of Danish descent, they have found that elevated levels of nonfasting triglyceride were associated with increased risk for CV events. They have specifically demonstrated that increasing levels of nonfasting TG were associated with progressively increasing hazard ratio for myocardial infarction (MI), ischemic heart disease (IHD), and death. In addition, they have also demonstrated that remnant lipoprotein cholesterol increases as nonfasting TG increase [29]. A study by Bansal et al. further supports the role of TG in predicting CV events. They have demonstrated that both fasting and nonfasting TG are risks for CV events. However, because HDL-C level is a confounding variable, after adjusting to HDL-C, they have seen that compared to fasting TG, nonfasting TG has a stronger independent relationship with cardiovascular events. Interestingly, they also demonstrated in secondary analyses that TG levels 2–4 hours postprandially had the strongest association with CV events [30]. This can be explained by the possibility that peaking of endothelial dysfunction coincides with peaking of postprandial lipemia [26]. Also, most studies mentioned have noted that peaking of postprandial TG and RLPs occurred 4 hours after a meal [5, 6, 26, 27]. On the contrary, in a study by Kats et al. involving 559 participants who underwent oral fat challenge, they have found that none of the measures of postprandial change were associated with incident CVD events. However, the study is inadequately powered [31]. Hence, there is a need for more robust prospective studies to clearly demonstrate the role and extent of postprandial lipemia effect on CV events. At present, the evidences should be enough to effect change in the way me manage dyslipidemia.

7. Treatment

Optimal treatment goals for postprandial lipid levels that will result to risk reduction have not been determined. At present, most guidelines are focused on LDL-C reduction and use fasting lipid profile. LDL-C target goals also depend on risk stratification, with extremely high-risk patients recommended to decrease LDL-C to as low as 55 mg/dl and low-risk patients to <130 mg/dl [32].

Normal TG levels have been set to be <150 mg/dl during the fasting state [32]. In a study by White et al. that aimed to determine optimal nonfasting TG levels

involving middle-aged and older apparently healthy women, the diagnostic threshold for nonfasting hypertriglyceridemia is seen to be at 175 mg/dL [33].

8. Diet

The importance of lifestyle modification cannot be overemphasized. Patients with dyslipidemia are advised to have reduced-calorie diet. Saturated and trans fats should also be minimized [32]. In addition, it has been found that a minimum of 10 hours is needed for postprandial lipids to return to fasting or baseline levels [5]. Hence, to avoid prolonged exposure to elevated levels of postprandial lipids, fatty meals should be avoided or should at least be spaced 12 hours accordingly.

9. Statins

Statins are considered one of the first-line treatments for dyslipidemia. It has been established that statins are efficacious in lowering fasting lipids and that statin treatment has resulted to significant reductions in cardiovascular morbidity and mortality. Some studies also have proven that statins can be used to lower postprandial lipid levels. However, in our study, we found that even on low fat diet, statin treatment, and normal fasting lipids, triglyceride and VLDL peaking and plateauing were still observed in patients with cardiovascular disease [34]. Furthermore, Schaefer et al. did a comparative study among statins and their efficacy in lowering postprandial levels. They have found that atorvastatin was significantly more effective in lowering LDL cholesterol and non-high-density lipoprotein cholesterol than all other statins and significantly more effective than all statins, except for simvastatin, in lowering triglyceride and remnant lipoprotein cholesterol. At 40 mg/day, atorvastatin was significantly more effective than all statins, except for lovastatin and simvastatin, in lowering cholesterol levels in small LDL, and was significantly more effective than all statins, except for simvastatin, in increasing cholesterol in large HDL and in lowering LDL particle numbers [35].

10. Fibrates

In a study by Cavallero et al., it has been found that fenofibrate normalized the abnormal postprandial response and improved the fasting lipoprotein abnormalities in patients with type 2 diabetes [36]. This is supported by the study of Ooi et al., which showed that fibrate treatment resulted to a significant decrease in remnant lipoprotein levels postprandially [37].

11. Orlistat

A study by Turker et al. involving normolipidemic, obese women with normal glucose tolerance suggests that 12 weeks of treatment with orlistat 120 mg/d plus low-calorie diet was associated with a 4.1-fold change from baseline in PPL [38]. Abejuela et al. have shown that orlistat abolishes the peaking of TC, TG, and HDL after a 50% OFCT [6]. In a study by Gabriel et al. which compared the effects of orlistat on the postprandial lipid levels after sequential high-fat meals in healthy individuals with normal fasting lipid levels, they have seen that administration of orlistat abolished the significantly sustained postprandial rise of TG and VLDL levels

in healthy individuals who were fed sequential 50% fat meals. Specifically, they have seen that in the control group, there is a significant postprandial rise in the levels of TG and VLDL beginning at 4 hours after breakfast that was sustained until 9 hours for TG and up to 10 hours for VLDL postprandially. In contrast, only one significant rise in both TG and VLDL levels was noted in the group given orlistat [5].

12. Ezetimibe

Ezetimibe is usually given to statin-intolerant patients or used in combination with statin to lower cholesterol, primarily LDL. There are evidences that it can also improve postprandial lipemia. In a study by Bozetto et al., they have shown that ezetimibe when given with simvastatin produces greater decrease in LDL cholesterol compared to simvastatin alone and produces a significant decrease in chylomicron lipid content both at fasting and postprandially, a significant decrease in chylomicron postprandial apoB-48, and significant fasting and postprandial decreases in the cholesterol content of VLDL, IDL, and LDL [39]. Yunoki et al. have demonstrated that a 4-week treatment with ezetimibe suppressed the postprandial peaking of TG, remnant lipoprotein, and apoB-48. Furthermore, they have shown that FMD reduction, which signifies endothelial dysfunction, also decreased with treatment [40].

13. Conclusion

We recognize that postprandial dyslipidemia is an undertreated disorder. Although robust prospective clinical trials are lacking, there is still increasing evidence of the clinical significance of postprandial dyslipidemia as a risk factor for CV disease. Clearly, postprandial elevations of lipids, specifically TG and TRLs, result to endothelial dysfunction and atherosclerosis. These result to increase in morbidity and possible mortality due to cardiovascular diseases. This should translate to a paradigm shift in the diagnosis and treatment of dyslipidemia. Presently, statins, fibrates, ezetimibe, and orlistat in sequential or combination regimen or as needed (orlistat) are possible treatment options for postprandial dyslipidemia in addition to proper diet and exercise. However, studies that focus on treatment of postprandial lipemia with measurement of solid clinical outcomes such as cardiovascular events and mortality should be undertaken. **Table 1** summarizes our recommendation.

	Recommendations
Diagnosis	• In addition to fasting lipid profile, postprandial lipid profile should also be determined, especially for patients at risk for cardiovascular disease • In high-risk individuals such as those with diabetes mellitus and those with diagnosed cardiovascular disease, postprandial lipid profile should routinely be evaluated • Postprandial lipid profile should include total cholesterol, TG, and HDL
Target	• Postprandial values must approximate normal fasting levels
Treatment	• Fibrates are the first-line drug of choice for postprandial lipemia with hypertriglyceridemia • Elevated postprandial total cholesterol should be treated with high-intensity statin • Ezetimibe can be considered if inadequately controlled by fibrates and statins • Orlistat as needed may be taken prior to a fatty meal

Table 1.
Summary of recommendations on the diagnosis and management of postprandial lipemia.

Conflict of interests

The authors have no conflicts of interests.

Author details

Neil Francis Amba and Leilani B. Mercado-Asis*
Section of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine and Surgery, University of Santo Tomas, Manila, Philippines

*Address all correspondence to: lmasis@ust.edu.ph

References

[1] Dominiczak MH. Lipoprotein Metabolism and Atherogenesis. Medical Biochemistry Fouth ed. Saunders; 2014. pp. 214-234

[2] Katsuyuki N, Takamitsu N, Yoshiharu T, Takeaki N, et al. Post-prandial lipoprotein metabolism: VLDL vs chylomicrons. Clinica Chimica Acta. 2011;**412**:1306-1318

[3] Stanhope KL, Schwarz JM, Keim NL, et al. Consuming fructose-sweetened, not glucose sweetened, beverages increase visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. The Journal of Clinical Investigation. 2009;**119**:1322-1334

[4] So T, Mercado-Asis LB, Zacarias MB, et al. A comparison of dose response postprandial lipid profile of healthy filipino subjects after an oral fat challenge test of varying fat contents. Philippine Journal of Internal Medicine. 2004;**42**:1-7

[5] Gabriel FS, Samson C, Abejuela Z, Sicat-Gabriel PR, Sumpio JP, Zacarias MB, et al. Post prandial effect of orlistat on the peaking of lipid level after sequential high fat meals. International Journal of Endocrinology and Metabolism. 2012;**10**(2):458-463

[6] Abejuela ZR, Macaballug AG, Sumpio JP, Zacarias MB, Mercado-Asis LB. Orlistat abolishes postprandial lipid peaking. International Journal of Endocrinology and Metabolism. 2009;**3**:179-186

[7] Rosenson RS, Helenowski IB, Tangney CC. Heterogeneous post prandial lipoprotein responses in the metabolic syndrome, and response to fenofibrate therapy. Cardiovascular Drugs and Therapy. 2010;**24**:439-447

[8] Cohn J, McNamara J, Cohn S, Ordovas J, Schaefer E. Postprandial plasma lipoprotein changes in human subjects of different ages. Journal of Lipid Research. 1988;**29**:469-479

[9] Lopez-Mirandal J, Williams C, Lairon D. Dietary, physiological, genetic and pathological influences on postprandial lipid metabolism. British Journal of Nutrition. 2007;**98**:458-473

[10] Shukla A. Postprandial lipid abnormalities in type 2 diabetes mellitus, a study at NGMC, Kohalpur. Journal of Nepalgunj Medical College. 2015;**13**:21-24

[11] Arca M. Alterations of intestinal lipoprotein metabolism in diabetes mellitus and metabolic syndrome. Atherosclerosis Supplements. 2015;**17**:12-16

[12] Castro-Caringal J, Mendoza E, Mercado-Asis LB. Correlation of postprandial lipemia with postprandial hyperglycemia and poor glycemic control among patients with type 2 diabetes mellitus. Philippine Journal of Internal Medicine. 2015;**53**(4):1-4

[13] Nakamura A, Monma Y, Kajitani S, Noda K, Nakajima S, Endo H, et al. Effect of glycemic state on postprandial hyperlipidemia and hyperinsulinemia with coronary artery disease. Heart and Vessels. 2016;**31**(9):1446-1455

[14] Asiam M, Aggarwal S, Sharnma KK, Galay V, Madhu SV. Postprandial hypertriglyceridemia predicts development of insulin resistance, glucose in tolerance and type 2 DM. PLoS One. 2016;**11**(1):e0145730

[15] Rivellese A, De Natale C, Di Lucrezia M, Lidia P, Ciro L, Sylvana C, et al. Exogenous and endogenous postprandial lipid

abnormalities in type 2 diabetic patients with optimal blood glucose control and optimal fasting triglyceride levels. The Journal of Clinical Endocrinology & Metabolism. 2004;**89**(5):2153-2159

[16] Singla P, Bardoloi A, Parkash A. Metabolic effects of obesity: A review. World Journal of Diabetes. 2010;**1**(3):76-88

[17] Frayn K. Insulin resistance, impaired postprandial lipid metabolism and abdominal obesity a deadely triad. Medical Principles and Practice. 2002;**11**(suppl 2):31-40

[18] Mekki N, Christofilis MA, Charbonnier M, Atlan-Gepner C, Defoort C, Juhel C, et al. Influence of obesity and body fat distribution on postprandial lipemia and triglyceride-rich lipoprotein in adult women. The Journal of Clinical Endocrinology and Metabolism. 1999;**84**:184-191

[19] Watts GF, Chan DCF, Barrett PHR, Martins IJ, Redgrave TG. Preliminary experience with a new stable isotope breath test for chylomicron remnant metabolism: A study in central obesity. Clinical Science. 2001;**101**:683-690

[20] Matsumoto S, Gotoh N, Hishinuma S, Abe Y, Shimizu Y, Katano Y, et al. The role of hypertriglyceridemia in the development of atherosclerosis and endotheliasl dysfunction. Nutrients. 2014;**6**:1236-1250

[21] Murray T, Yang E, Brunner G, Kumar A, Lakkis N, Misra A, et al. Post prandial effects on arterial stiffness parameters in healthy young adults. Vascular Medicine. 2015;**20**(6):501-508

[22] Blendea M, Bard M, Sowers J, Winer N. High-fat meal impairs vascular compliance in a subgroup of young healthy subjects. Metabolism Clinical and Experimental. 2005;**54**:1337-1344

[23] Giannattasio C, Zoppo A, Gentile G, Failla M, Capra A, Maggi M, et al. Acute effect of high-fat meal on endothelial dysfunction in moderately dislipidemic subjects. Arteriosclerosis, Thrombosis, and Vascular Biology. 2005;**25**:406-410

[24] Burdge G, Clader P. Plasma cytokine response during the postprandial period: A potential causal process in vascular disease? British Journal of Nutrition. 2005;**93**:3-9

[25] Lacroix S, Des RC, Tardif J, Nigam A. The role of oxidative stress in postprandial dysfunction. Nutrition Research Reviews. 2012;**25**:288-301

[26] Maggi FM, Raselli S, Grigore L, Redaelli L, Fantappiè S, Catapano AL. Lipoprotein remnants and endothelial dysfunction in the postprandial phase. The Journal of Clinical Endocrinology and Metabolism. 2004;**89**(6):2946-2950

[27] Castro-Caringal JA, Valera L, Llave K, Samson C, Ramirez M, Zacarias M, Mercado-Asis LB. Flow-mediated dilatation of brachial artery is inversely correlated with the postprandial peaking of triglyceride and very low-density lipoprotein. Unpubished

[28] Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: Prospective meta-analysis of date from 90,056 participants in 14 randomised trials of statins. Lancet. 2005;**366**(9493):1267-1278. Epub 2005 Sept 27

[29] Nordertgaard B, Benn M, Schnohr P, Tybjaerg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. JAMA. 2007;**298**(3):299-308

[30] Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting

compared with non-fasting triglycerides and risk of cardiovascular events in women. JAMA. 2007;**298**:309-316

[31] Kats D, Sharrett A, Ginsberg H, Nambi V, Ballantyne C, Hoogeveen R, et al. Postprandial lipemia and the risk of coronary heart disease and stroke: The Atherosclerosis Risk in Communities (ARIC) Study. BMJ Open Diabetes Research and Care. 2017;**5**:e000335

[32] Jellinger P, Handelsman Y, Rosenblit P, Bloomgarden Z, Fonseca V, Garber A, et al. American association of clinical endocrinologists and American college of endocrinologist guidelines for management of dyslipidemia and prevention of cardiovascular disease. CPG for managing dyslipidemia and prevention of CVD. Endocrine Practice. 2017;**23**(Suppl 2)

[33] White K, Moorthy M, Akinkuolie A, Demier O, Ridker P, Cook N, et al. Identifying an optimal cutpoint value for the diagnosis of hypertriglyceridemia in the nonfasting state. Clinical Chemistry. 2015;**61**(9):1156-1163

[34] Samson CE, Galia AL, Llave KI, Zacarias, MB, Mercado-Asis LB. Postprandial peaking and plateauing of triglycerides and VLDL in patients with underlying cardiovascular diseases despite treatment. International Journal of Endocrinology and Metabolism. 2012;**10**:587-593

[35] Schaefer EJ, McNamara JR, Tayler T, Daly JA, Gleason JL, Senman LJ, et al. Comparisons of effects of statins (atorvastatin, fluvastatin, lovastatin, pravastatin, and simvastatin) on fasting and postprandial lipoproteins in patients with coronary heart disease versus control subjects. The American Journal of Cardiology. 2004;**93**(1):31-39

[36] Cavallero E, Dachet C, Assadolahi F, Martin C, Navarro N, Ansquer JC, et al. Micronized fenofibrate normalizes the enhanced lipidemic response to a fat load in patients with Type 2 DM and optimal glucose control. Atherosclerosis. 2003;**166**:151

[37] Ooi TC, Cousins M, Ooi DS, Nakajima K, Edwards AL. Effect of fibrates on postprandial remnant-like particles in patients with combined hyperlipidemia. Atherosclerosis. 2004;**172**:375

[38] Turker I, Demirag NG, Tanaci N, Tutar N, Kirbas I. Effects of orlistat plus diet on postprandial lipemia and brachial artery reactivity in normolipidemic, obese women with normal glucose tolerance: A prospective, randomized, controlled study. Current Therapeutic Research, Clinical and Experimental. 2006;**67**(3):159-173

[39] Bozetto G, Annuzzi A, Della Corte G, Patti L, Cipriano B, Mangione A, et al. Ezetimibe beneficially influences fasting and postprandial triglyceride-rich lipoproteins in type 2 diabetes. Atherosclerosis. 2011;**217**(1):142-148

[40] Yunoki K, Nakamura N, Miyoshi T, Enko K, Kohno K, Morita H, et al. Ezetimibe improves postprandial hyperlipemia and its induced endothelial dysfunction. Atherosclerosis. 2011;**217**(2):486-491