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Original Article

Determinant of postprandial triglyceride levels in healthy young adults

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ABSTRACT

Background: Fasting lipid profile does not necessarily illustrate the exact lipid dynamic in 24 h as human spends most of their time in postprandial state. Postprandial triglyceride (TG) has been reported to have advantages compared to fasting TG in terms of practicality and ability to predict cardiovascular events. This study aims to assess the determinant of postprandial TG in healthy young adults.
Methods: This is a quasy-experimental study that involved 200 healthy young adults. This study compared fasting with postprandial TG and analyzed the relationship between postprandial TG with various demographic and metabolic parameters after ingestion of standardized high fat liquid meal.
Result: There was an upward trend from fasting TG to 2 h postprandial TG and 4 h postprandial TG. There was strong correlation between fasting TG and 2 h postprandial TG with 4 h postprandial TG ($r = 0.731$; $p < 0.0001$ dan $r = 0.669$; $p < 0.0001$, respectively). Whereas body mass index (BMI) and age showed weak correlation with 4 h postprandial TG ($r = 0.141$; $p < 0.0001$ dan $r = 0.0747$; $p < 0.0001$), fasting TG was the strongest predictor of 4 h postprandial TG ($r = 0.669$, $B = 1.722$ (95% CI 1.552 to 1.892), $p < 0.0001$).
Conclusion: Fasting TG was the strongest determinant of 4 h postprandial TG in healthy young adults. We also observed strong correlation between 4 h postprandial TG and fasting TG. Hence, 4 h postprandial TG might potentially replaced fasting TG when measurement of fasting TG is not feasible.

1. Introduction

Dyslipidemia is a major modifiable risk factor for the atherosclerotic cardiovascular disease (ASCVD). Fasting lipid profile, including the measurement of total cholesterol, triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), has become a routine test for cardiovascular risk prediction. Because plasma triglyceride levels can increase substantially in a postprandial state, measuring fasting lipid levels might apparently avoid the variability associated with meals and provide a more stable estimate for risk assessment [1,2]. However, fasting lipid profile might not necessarily represent the real lipid profile in daily basis, as individuals spend the majority of their time in a postprandial state [1].

Postprandial lipemia (PPL) referred to a condition of elevated TG-rich cholesterol after ingestion of high-fat diet. In a healthy population, the peak of PPL can be measured at 4 h after ingestion

Abbreviations: TG, triglyceride; BMI, body mass index; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PPL, postprandial lipemia; WHO, world health organization; TC, total cholesterol; IQR, interquartile range; DM, diabetes mellitus.

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of high-fat diet [2]. Eventhough there is no significant difference between fasting and postprandial LDL-C and total cholesterol level, the difference between fasting and postprandial triglyceride varies from 10% to 20% [3]. Furthermore, the reliability of fasting TG in cardiovascular events prediction is relatively weak and highly influenced by the dietary pattern preceding the measurement. [4,5].

Postprandial TG has been shown to pose an important role in the pathogenesis of premature atherosclerosis. Elevation of postptrandial TG, whether higher peak concentrations or delayed clearance, represents an abnormal response to oral fat load which reflects insulin resistance. The disturbance of triglyceride-rich chylomicron remnants clearance from plasma would expose the vascular bed more rigorously to these atherogenic lipoproteins. Furthermore, macrophage will then uptake the lipoprotein and penetrate into the endothelial cell layer as foam cell, the hallmark of early atherosclerosis [3,5–8].

Taking into account the role of postprandial TG in atherosclerosis, several consensus have recommended postprandial TG measurement as a complementary measurement to fasting TG [1,9,10]. In clinical practice, the measurement of postprandial TG can complement fasting TG measurement and both have a good predictive ability. If anything, possibly postprandial TG measurement might be more practical as it does not require a 12–14 h of fasting. Hence, postprandial TG measurement is preferable in patients who are unable to fast.

However, not only that several factors have been inconsistently reported to be associated with postprandial TG such as gender, [11] age, [12] body composition, [13] physical activity [14,15] but also the association between fasting and postprandial TG has been rarely studied. To this end, our study aims to determine factors associated with postprandial TG after ingestion of high-fat diet in normoglycemic and normolipidemic healthy young Indonesian adults, especially its association with fasting TG.

2. Methods

Our study is a quasy-experimental study that involved 200 healthy young adults aged 17–45. The inclusion criteria were subject with fasting TGbetween 100–250 mg/dL and had mild to moderate physical activity. The exclusion criteria were type 2 diabetes mellitus, history of familial hypertriglyceridemia, total cholesterol >200 mg/dL and TG level >400 mg/dL, previous history of endocrine abnormalities, chronic kidney disease, chronic liver disease that had been confirmed by laboratory measurement, smoker, subjects under medications that may alter lipid metabolism and subjects with alcoholism. The study protocol has been approved by Ethical Committee of Universitas Indonesia (334/UN2.F1/ETIK/2016). All subjects have consented to be involved in this study.

Demographic data including age, smoking history and other medical conditions were retrieved by interview. Physical examination were conducted to obtain the hemodynamic profile and body mass index (BMI). BMI were categorized based on WHO criteria: $\leq$18.4 kg/m^2 as underweight", 18.5–22.9 kg/m^2 as normoweight, 23.0–24.9 kg/m^2 as overweight and $\geq$25.0 kg/m^2 as obese. Laboratorium variables such as lipid profiles (TG and total cholesterol), along with routine blood count, urea, creatinine, aspartate aminotransferase (ALT) and alanine aminotransferase (AST) level were measured after at least 12 h of fasting. Triglyceride (TG) and total cholesterol (TC) were measured at Prodia Clinical Laboratory with spectrophotometry method using Advia 1800 with reagent from Bayer.

Subjects were then given liquid meal which composed of 20 g of carbohydrates, 25 g of protein and 40 g of fat, with extra 140 kcal in a form of vanilla-flavored sweetened drink. The total calories ingested were 680 kcal. The study participants were required to finish the entire meal and beverage provided, then serum TG was measured at two and four hours after the meal ingestion.

2.1. Statistical analyses

Nominal data was presented in percentage. Normally distributed numerical data was presented as mean (standard deviation) while abnormally distributed data was reported in median (interquartile range/IQR). The comparison of fasting, 2 h post prandial and 4 h postprandial was analysed using Paired T test for normally distributed data and Wilcoxon test for skewed distributed data. The comparison of changes between 4 h postprandial TG and fasting TG was performed using Independent Sample T test for normally distributed data and Mann Whitney test for skewed distributed data. The comparison of TG across the BMI was performed using One-way Analysis of Variance for normally distributed data and Kruskal-Wallis test for skewed distributed data. The correlation between 2 variables were assessed using Pearson correlation for normally distributed data and Spearman correlation for skewed distributed data. Multiple linear regression analyses were performed using postprandial TG as a dependent factor. Several variables (age, gender, BMI, and fasting TG) were entered as independent factors. An alpha level of 0.05 was accepted as significant for all statistical procedures. Statistical analyses were performed using IBM Statistics SPPS 21 and GraphPad Prism 7.00.

3. Result

A total of 200 young adults were included in this study. Majority of the participants were women (59.5%), while the median of age was 23 (21–26) years old. Obesity and overweight were observed in 7 (3.5%) and 51 (25.5%) participants, respectively. The level of fasting TG and fasting blood glucose were in a normal range (Table 1).

Compared to fasting TG levels, post prandial TG levels increased progressively at 2 h [from 76.50 (57.00–97.50) to 118.50 (93.00–157.25), $p < 0.001$] and 4 h after the meal ingestion [from 76.50 (57.00–97.50) to 127.00 (98.25–172.5), $p < 0.001$]. Significant differences also found between 2 h and 4 h postprandial TG levels [118.50 (93.00–157.25) vs 127.00 (98.25–172.5), $p < 0.001$] (Fig. 1).

While at baseline we did not observed any significant differences in TG level between men and women, we observed a significant differences in 2 h postprandial TG levels [139.9 (62.2) mg/dL vs 120.3 (43.4) mg/dL, in men and women respectively, $p = 0.009$] as well as in 4 h postprandial TG levels [162.6 (86.3) mg/dL vs 137.6 (60.1) mg/dL, in men and women respectively, $p = 0.017$]. When we accounted the increase in TG levels at 2 h and 4 h, we did not found any significant difference between men and

Table 1
Baseline characteristics.

Parameter	Value
Women, n (%)	119 (59.5)
Age (year)	23 (21–26)
Systolic Blood Pressure (mmHg)	114.6 (10.3)
Body Mass Index(kg/m^2)\	21.3 (19.8–23)
Fasting Blood Glucose (mg/dL)	77 (73–80)
2 h Postprandial Blood Glucose (mg/dL)	76 (68–82)
Total Cholesterol (mg/dL)	179 (28.9)
Fasting TG (mg/dL)	76.5 (57–97)

Data was presented in percentage for categorical variable. Mean (SD) was used for normally distributed numerical variable and median (IQR) for abnormally distributed numerical variable. TG (triglyceride).

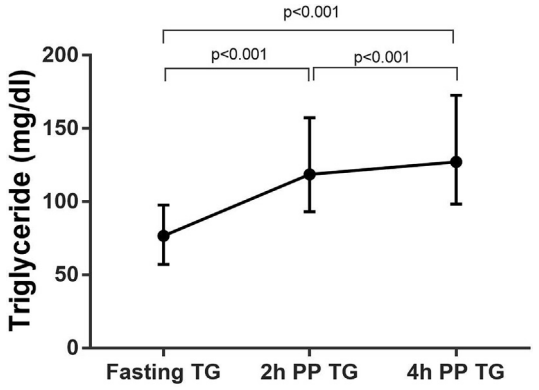

Fig. 1. Comparison of Fasting TG, 2 h post prandial TG and 4 h post prandial TG level. The comparison of TG level across examination timing was analyzed using Wilcoxon test. P value of <0.05 was considered statistically significant. 2 h PP TG (2 h post postprandial triglycerides), 4 h PP TG (4 h postprandial triglycerides). The data is displayed in median (interquartile range, IQR).

women. The amount of increased TG levels at 2 h were 43 (27.5–64.5) mg/dL in men and 37 (26–57) mg/dL in women [p = 0.235], similar to this the increase of TG levels at 4 h were 57 (37–98) in men and 49 (30–78) in women [p = 0.141].

When we stratified TG levels based on BMI, fasting TG were shown to escalate across the BMI status [(71 (55.00–110.70) vs 83 (67.00–135.00) vs 162 (98.00–168.00), in normoweight, overweight and obesity groups respectively; p < 0.001]. This trend was also seen in 2 h postprandial TG [108 (83.75–172.1) vs 146 (105.00–179.00) vs 213 (135.00–301.00), in normoweight, overweight and obesity groups respectively; p < 0.001] and 4 h postprandial TG [(121 (92.75–152.00) vs 156 (120.00–225.00) vs 214 (161.00–322.00), in normoweight, overweight and obesity groups, respectively; p < 0.001]. The increment of fasting TG to 4 h postprandial TG was parallel with the increase of BMI [(46 (30.75–72.00) vs 65 (43.00–105.00) vs 100.9 79 (46.00–159.00) in normoweight, overweight and obesity groups, respectively; p-value for trend = 0.007] (Fig. 2).

3.1. Determinants of postprandial TG

Both age (Fig. 3A and B) and BMI (Fig. 3C and D) were weakly correlated with 2 h and 4 h postprandial TG. However, fasting TG showed a strong correlation with either 2 h postprandial TG

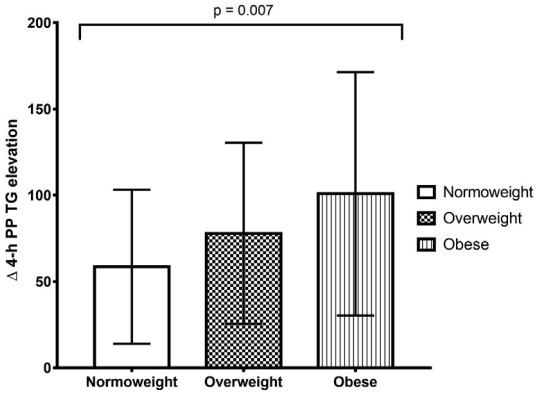

Fig. 2. The comparison of 4 h postprandial TG elevation from fasting TG across BMI status. The comparison of 4 h postprandial TG elevation from fasting TG for normoweight, overweight and obese subjects was analyzed using linear regression analysis, p value for trend = 0.007. Δ 4 h PP TG (4 h postprandial triglycerides elevation from fasting TG). The data is displayed in median (interquartile range, IQR).

(r = 0.731, Figure 3E) and 4 h postprandial TG (r = 0.669, Fig. 3F). The strong correlation between fasting TG and 4 h postprandial TG was confirmed in multivariate analysis which showed that fasting TG is the sole strong predictor of 4 h postprandial TG (p < 0.001) (Table 2).

4. Discussion

Our study showed that fasting TG was the strongest predictor of 4 h postprandial TG, which confirmed results from previous studies [15,16]. Study by Syvanne M et al. in 49 men post coronary bypass surgery patients with low HDL-C levels reported that fasting TG was the sole determinant of postprandial TG (R^2 = 51.2%) [16]. This finding was also supported by Sharett et al. in 602 atherosclerotic patients based on the carotid intima-media thickness test (CIMT) measurement, including diabetic patients, showed that fasting TG as a strong predictor of postprandial TG aside from smoking history, dietary pattern, creatinine and alcohol consumption [15].

It is important to note that our study was the first study conducted in young adult with normolipid and normoglycemic profile, which resemble the major healthy population, without potential confounding bias from atherosclerotic condition. Previous studies by Lee et al. and Park et al. among 639 dysglycemic Korean subjects (impaired fasting glucose and type 2 DM) without other comorbidities also reported that fasting TG was a good predictor of postprandial TG (r = 0.973, r = 0.937, P < 0.001) [17,18]. These studies, however, used Korean low fat diet as the standard challenge meal. The differences in the challenge meal is of an importance since the level of postprandial TG is mainly influenced by fat content in a meal. Our challenge meal was a standardized fat liquid meal that reflects the common Indonesian single meal consumption, containing 40 g of fat with a total of 680 kcal [19].

Postprandial TG has risen up into attention since its good capability in predicting cardiovascular events [3,5,7]. Although fasting TG is considered to be a gold standard in TG testing to predict cardiovascular risk, there were several limitations. First, the examination process is inconvenient for both patient and laboratory analyst since it requires 12–14 h of fasting. Hence, the result of fasting TG examination may not be trully reliable, depending on the patient's cooperation during fasting procedure. Secondly, fasting TG might not reflect the actual whole day TG profile because the majority (15–18 h) of the individuals are on a postprandial state. Therefore, postprandial TG began to be perceived as better cardiovascular predictors in some consensus [9,10].

In accordance to previous study, our study also showed higher TG value in men. These differences may be attributed to higher visceral adipose tissue and waist circumference in men which may contribute to an exaggerated postprandial triglyceride-rich lipoprotein response [11,20]. Even though there is differences between men and women at baseline, when we compare the increase of 4 h postprandial-TG from fasting TG, there was no significant differences. These findings indicate that the dissimilarity of lipid metabolism between healthy young men and women might not affect postprandial TG test [8]. Our study also observed a weak correlation between BMI and age with postprandial TG. This has also been reported in previous study by Nogaroto et al. [21] Subjects in our study were relatively young with a narrow age range, which might also explain the weak correlation between age and postprandial TG.

To the best of our knowledge, our study was the first research conducted among normoglycemic normolipidemic young adults in Indonesia to determine the factors affecting postprandial TG. However, confounding factors such as physical activity and insulin resistance were unfortunately not measured.

In summary, fasting TG was the strongest determinant of 4 h postprandial TG in healthy young adults. We also observed strong

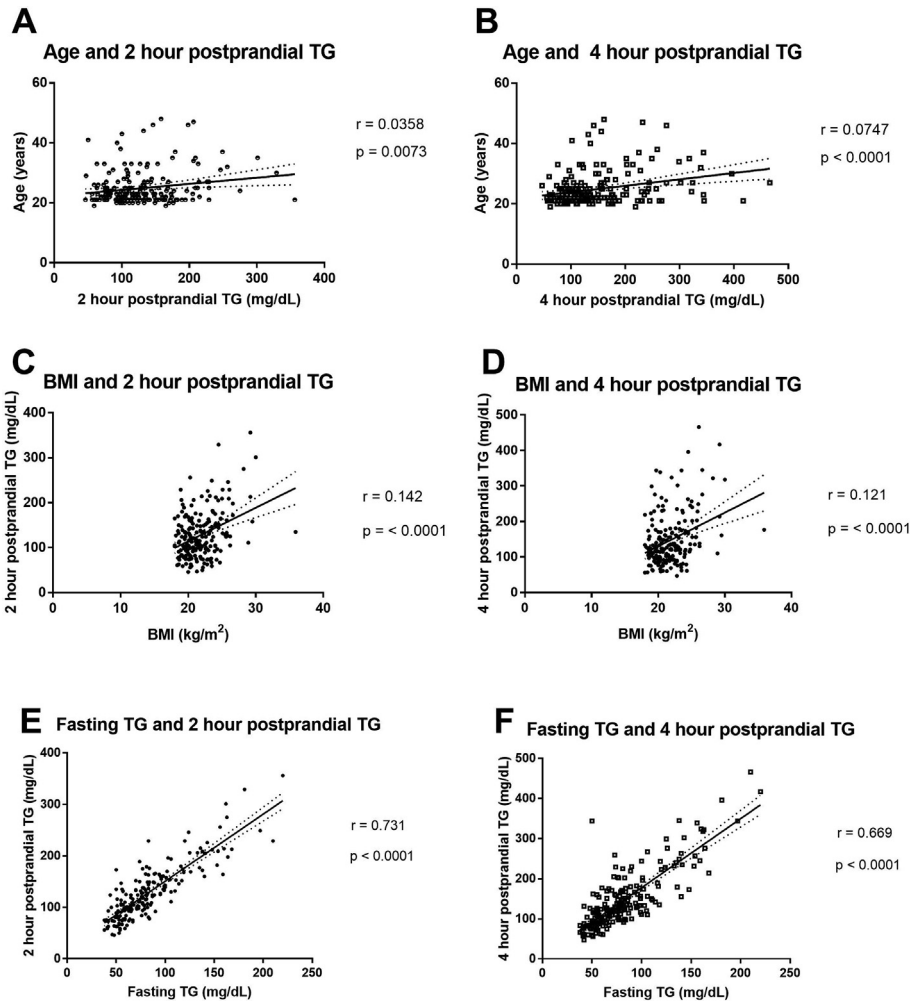

Fig. 3. Correlation between level of fasting TG, 2 h postprandial TG, 4 h post prandial TG, BMI and age. The correlation between each variable was analysed using linear regression analysis. (A) Age and 2 h postprandial TG, (B) Age and 4 h postprandial TG, (C) 2 h postprandial TG across BMI groups, (D) 4 h postprandial TG across BMI groups, (E) Fasting TG vs 2 h postprandial TG, (F) Fasting TG vs 4 h postprandial TG. P value < 0.05 was considered significant. BMI (body mass index), TG (triglycerides).

Table 2
Multivariate analysis of 4 h postprandial TG determinants.

Model		B	R square	P value	95% CI
Model 1	(constant)	- 9.815	0.675	0.631	−50.101–30.47
	Fasting TG	1.689		0.000	1.497–1.882
	BMI category	−2.131		0.733	- 14.43–10.169
	Age	1.033		0.062	- 0.053–2.118
	Gender	−1.859		0.764	- 14.049–10.331
Model 2	(constant)	−13.420	0.674	0.417	- 45.966–19.126
	Fasting TG	1.694		0.000	1.504–1.883
	BMI category	−1.954		0.753	−14.170–10.262
	Age	1.028		0.063	- 0.054–2.111
Model 3	(constant)	−16.202	0.674	0.246	- 43.650–11.247
	Fasting TG	1.682		0.000	1.507–1.856
	Age	0.997		0.066	- 0.065–2.059
Model 4	(constant)	5.292	0.669	0.494	- 9.928–20.513
	Fasting TG	1.722		0.000	1.552–1.892

Multivariate analysis of 4 h post prandial TG and its associated factors was analysed using multiple linear regression model. P value < 0.05 was considered significant. TG (triglyceride) and BMI (Body Mass Index).

correlation between 4 h postprandial TG and fasting TG in healthy young adults population in Indonesia. Thus, the measurement of postprandial TG might potentially replaced fasting TG when measurement of fasting TG is not feasible. However, further studies regarding the association of postprandial TG with long-term cardiovascular risk in Indonesian population are still needed.

Authors' contribution

Design of the original study: TJET, MA, IS; Design of this study:

TJEJ, DLT, AIK; Data analysis: AIK, DLT, SW, MJ; Interpretation of data analysis: TJEJ, DLT, AIK, SW; Manuscript writing: TJEJ, AIK, SW, MJ, DLT; Critically review the manuscript: TJEJ, AIK, SW, MJ, MA, IS, DLT.

Ethics approval and consent to participate

The study protocol has been approved by Ethical Committee of Universitas Indonesia (334/UN2.F1/ETIK/2016). Written informed consents were obtained from all the study participants.

Consent for publication

Not applicable.

Availability of data and material

All of the individual participant data collected during the trial, after deidentifcation, is available to researchers who provide a methodologically sound proposal. The study protocol is available upon request. The data are not publicly available due to containing information that could compromise research participant privacy.

Competing interests

The authors report no competing interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.027.

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