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Original article

Who would benefit most from postprandial lipid screening?

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SUMMARY

Background & aims: Individuals with fasting triglycerides (TG) <150 mg/dL can experience a deleterious postprandial TG response ≥220 mg/dL to a high-fat meal (HFM). The purpose of this study was to identify individuals based on fasting TG that would benefit most from additional postprandial screening.
Methods: We conducted a secondary analysis of 7 studies from our laboratories featuring 156 disease-free participants (64 M, 92 F; age 18–70 years; BMI 18.5–30 kg/m^2). Participants observed a 10–12 h overnight fast, after which they consumed an HFM (10–13 kcal/kg body mass; 61–64% kcal from fat). Two methods were used to identify lower and upper fasting TG cut points. Method 1 identified the lower limit as the TG concentration at which ≥90% of individuals presented peak postprandial TG (PPTG) <220 mg/dL and the upper limit as the concentration which ≥90% of individuals presented PPTG ≥220 mg/dL. Method 2 utilized receiver operating characteristic (ROC) curves and identified the lower limit as the fasting TG concentration where sensitivity was ≈95% and the upper limit as the concentration at which specificity was ≈95%.
Results: In Method 1, 90% of individuals with fasting TG >130 mg/dL (>1.50 mmol/L) exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L), while 100% of individuals with fasting TG <66 mg/dL (0.75 mmol/L) had PPTG that did not exceed 220 mg/dL (2.50 mmol/L). In Method 2, when sensitivity was ≈95%, the corresponding fasting TG concentration was 70 mg/dL (0.79 mmol/L). When specificity was ≈95%, the corresponding fasting TG concentration was 114 mg/dL (1.29 mmol/L). Based on methods 1 and 2, there was a moderate positive association ($r = 0.37$, $p < 0.004$) between fasting and PPTG for individuals with fasting TG between 70 and 130 mg/dL (0.79–1.50 mmol/L), in which 24% exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L) while 76% did not.
Conclusions: Postprandial TG testing is likely most useful for individuals with fasting TG concentrations between 70 and 130 mg/dL (0.79–1.50 mmol/L). Outside of this range, postprandial TG responses are largely predictable. Establishing a specific patient group for which postprandial TG testing is most useful may lead to earlier risk detection in these individuals.

1. Introduction

Fasting triglycerides (TG) have long been used in research and clinical practice to assess cardiovascular disease (CVD) risk, although non-fasting/postprandial TG have been identified as a stronger predictor of CVD risk when compared to fasting concentrations [1,2]. Postprandial TG may not only be associated with, but may play a causal role in, the development of atherosclerosis –

Abbreviations: TG, triglycerides; PPTG, postprandial triglycerides; CVD, cardiovascular disease; TRL, triglyceride-rich lipoproteins; HFM, high-fat meal; OFTT, oral fat tolerance test; NAFL, non-alcoholic fatty liver; CM, chylomicrons; LPL, lipoprotein lipase; CM-R, chylomicron remnants.

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promoting the penetration and retention of lipoproteins and their lipid cargo in the sub-endothelial space as a result of reduced clearance or increased hepatic export of TG-rich lipoproteins (TRL) [3,4]. While a fasting TG sample is easier to obtain, and thus more widely used in clinical settings, from a physiological standpoint, it has been recognized that fasting TG are an incomplete assessment of risk [1,2]. This is largely because individuals spend the majority of their day in a non-fasted, postprandial state; thus, postprandial TG are more closely representative of a person's typical metabolic state. Lastly, it is possible for individuals to exhibit healthy fasting TG with concomitant unhealthy postprandial TG. Thus, the utility of risk assessment via fasting TG alone is limited and is likely less sensitive than measurement of postprandial TG [5].

Although postprandial TG testing is likely more sensitive and robust than traditionally used fasting TG, in its current form postprandial TG assessment is not clinically practical. Traditional postprandial TG testing is resource- and time-intensive, lasting up to 6 h and consisting of intrusive phlebotomy techniques. Thus, identifying specific groups that would benefit most from postprandial TG testing would be beneficial. Moreover, some individuals exhibit very low fasting TG, while some exhibit very high fasting TG. These individuals represent a group of people who likely have a predictable postprandial TG response and thus need not be recommended for postprandial TG testing. However, there is likely a range of fasting TG that may be considered "healthy" based on current guidelines (<150 mg/dL; <1.70 mmol/L), but that leads to a deleterious postprandial TG response. More specifically, some individuals may present with fasting TG below the recommended threshold (<150 mg/dL, <1.70 mmol/L), but experience a sharp rise in postprandial TG that would be otherwise undetected with fasting TG measurements. The concentration of ≥220 mg/dL (≥2.50 mmol/L) has been recommended by an expert panel as the postprandial TG concentration that is indicative of increased CVD risk and thus is representative of a deleterious postprandial TG response [5–7].

Considering the pro-atherogenic nature of postprandial TG and the strong relationship between postprandial TG and CVD risk, the ability to predict postprandial TG from fasting TG would lead to a robust clinical risk assessment tool. Standardizing a fasting TG range, in which postprandial TG are largely unpredictable, would capture a portion of the population that would benefit most from postprandial TG testing. Identifying this population could lead to a standard clinical CVD risk assessment tool that will advance and improve clinical recommendations, leading to potentially earlier detection and intervention and the avoidance of unnecessary medical testing for some individuals.

Therefore, the purpose of this analysis was to determine fasting TG cut points in which: 1) nearly all individuals with fasting TG below a certain concentration do not exceed postprandial TG ≥ 220 mg/dL (≥2.50 mmol/L), 2) nearly all individuals with fasting TG above a certain concentration exceed postprandial TG ≥ 220 mg/dL (≥2.50 mmol/L), and 3) the postprandial TG response is variable and thus individuals in this range would benefit from postprandial TG testing. Therefore, we aimed to identify individuals based on fasting TG for whom advanced postprandial TG screening would be most useful and aid in early detection of risk.

2. Methods

2.1. Overview

We conducted a secondary analysis of 7 studies from our laboratories featuring 156 disease-free adults. The study protocols were approved by the institutional review boards of Oklahoma State University, Kansas State University, and James Madison University. All participants provided written informed consent prior to beginning each respective study.

All participants engaged in an initial assessment and a meal assessment. For the initial assessments, baseline demographics, anthropometrics (i.e. height and weight) and blood pressure were collected. Participants completed a medical history questionnaire and received instruction on various lifestyle controls. Meal assessments began approximately 1 week after the initial assessment. Participants reported to the laboratory after observing a 10–12 h overnight fast, after which they consumed a high-fat meal (HFM) (10–13 kcal/kg body mass; 61–64% kcal from fat). Blood draws were taken fasted and serially every 1 or 2 h for 4–6 h post-meal to assess the postprandial TG response. Each meal trial began between 0600 and 1000 h.

2.2. Study participants and lifestyle controls

The study sample consisted of 156 disease-free adults (64 M, 92 F; age 18–70 years; BMI 18.5–30 kg/m^2). Inclusion and exclusion criteria were similar across studies. Detailed inclusion and exclusion criteria and participant and meal characteristics are presented in Tables 1 and 2, respectively, and discussed in detail elsewhere [8–13]. All studies included adults free of on-going chronic cardiovascular, pulmonary, or musculoskeletal disease and not taking lipid-lowering medications. Lifestyle instructions were assigned at the initial assessment, and all participants were instructed on specifics and compliance. Specifically, participants were instructed to record their dietary intake for the 3 days leading up to their meal assessment using a 3-day food record. Participants were instructed to avoid planned exercise 24–48 h prior to the meal assessment and alcohol and caffeine for 12 h prior to the meal assessment. Participants were given a ~200 kcal snack to consume the night before the meal assessment as the last thing they consumed that day. Participants were given a hard copy of these instructions and lifestyle controls.

2.3. Meal assessments and test meal

An oral fat tolerance test (OFTT) was conducted in each study. After a 10–12 h overnight fast, participants arrived in the laboratory on the morning of the assessment. To avoid the confounding effects of diurnal variations in metabolism, all assessments began between 0600 and 1000 h. For all studies, an indwelling catheter was inserted into a forearm vein and a slow infusion of 0.9% NaCl solution was initiated. Once the catheter was secure, a fasting blood draw was collected. Following the fasting blood draw, the test meal was consumed within 20 min. Participants were provided with water *ad libitum*. The 6-h time period initiated after the full consumption of the test meal. Serial blood draws were collected every 1 or 2 h in 6 mL ethylenediaminetetraacetic acid (EDTA)-coated tubes (BD, Franklin Lakes, NJ, USA). Triglycerides (coefficient of variation (CV) = 2–4%), total cholesterol (CV = 2–3%), low-density lipoprotein cholesterol (LDL-C) (CV = 4–6%), and high-density lipoprotein cholesterol (HDL-C) (CV = 3–6%) were measured in whole blood using a Cholestech LDX analyzer with Lipid + Glu cassettes.

For each study, the test meal consisted of an HFM and varied minimally across studies with regard to macronutrient content (60–64% fat). All test meals were scaled to body weight and averaged approximately 13 kcal/kg. Specific test meals used in the present studies were Marie Callender's Chocolate Satin Pie [9,12], high-fat pasta entrée [11], and Jimmy Dean's Meatlovers Breakfast Bowl [8,10]. The predominant fat source in all test meals was animal-based saturated fat.

Table 1
Design characteristics of included studies.

Study	Controls	Inclusion Criteria	Exclusion Criteria	Sample Included in Analysis
Kurti et al.* (randomized crossover)	3-day food record prior to meal trial, avoidance of planned exercise 48 h prior to meal trial, abstinence from caffeine and alcohol 12 h prior to meal trial	Age young (20–33 years) and old (62–77 years)	On-going chronic cardiovascular, metabolic, or renal disease; antioxidants, anti-inflammatory agents, anti-hypertensives or statins	Old (n = 12; 8M/4F) and young (n = 12; 5M/7F) adults (n = 24)
Emerson et al., 2018 [9] (cross-sectional)	3-day food record prior to meal trial, avoidance of planned exercise 48 h prior to meal trial, abstinence from caffeine and alcohol 12 h prior to meal trial, evening snack	Age young (18–35 years) and old (60+ years); Active: regularly meeting physical activity guidelines (≥150 min MVPA/week) Inactive: not regularly engaging in planned exercise (<30 min/week)	On-going chronic cardiovascular, pulmonary, or musculoskeletal disease; lipid-lowering medications	YA (n = 8; 4M/4F); OA (n = 8; 4M/4F); OI (n = 6; 3M/3F) adults (n = 22)
Teeman et al., 2015 [10] (randomized control trial)	Abstinence from caffeine, alcohol, and exercise 24 h prior to meal trial, evening snack	Age 18–40 years; <2 CVD risk factors; 1) meet physical activity guidelines (≥150 min MVPA/week) or 2) participate in <30 min MVPA/week	On-going chronic cardiovascular, pulmonary, or musculoskeletal disease; smokers; asthma, blood glucose, blood pressure, or weight controlling medications	Young adults (n = 20; 10M/10F) control, no exercise during postprandial period
Sciarrillo et al., 2019 [11] (randomized crossover)	3-day food record prior to meal trial, avoidance of planned exercise 48 h prior to meal trial, abstinence from caffeine and alcohol 12 h prior to meal trial, evening snack	Aged 18–40 years	On-going chronic cardiovascular, pulmonary, or musculoskeletal disease; pregnant; lipid-lowering or hypotensive medications; tobacco users; dietary intolerances precluding HFM consumption	Young adults (n = 10; 5M/5F)
Sciarrillo et al., 2019 [12] (randomized crossover)	3-day food record prior to meal trial, avoidance of planned exercise 48 h prior to meal trial, abstinence from caffeine and alcohol 12 h prior to meal trial, evening snack	Aged 18–40 years	On-going chronic cardiovascular, pulmonary, or musculoskeletal disease; pregnant; lipid-lowering medications; tobacco users	Young adults (n = 18; 8M/10F)
Koemel et al., 2020 [13] (cross-sectional)	3-day food record prior to meal trial, avoidance of planned exercise 48 h prior to meal trial, abstinence from caffeine and alcohol 12 h prior to meal trial, evening snack	Aged young (18–35 years) and old (60+ years); Active: regularly meeting physical activity guidelines (≥150 min MVPA/week or ≥75 min vigorous-intensity physical activity/week); Inactive: not regularly engaging in planned exercise (<30 min/week)	On-going chronic cardiovascular, pulmonary, or musculoskeletal disease; lipid-lowering or hypotensive medications; tobacco users; change in physical activity habits within past 5 years	YA (n = 9; 4M/4F); YI (n = 8; 5M/3F); OA (n = 8; 4M/4F); OI (n = 7; 3M/3F) adults (n = 32)
Jenkins et al.* (randomized control trial)	3-day food record prior to meal trial, avoidance of planned exercise 48 h prior to meal trial, abstinence from caffeine and alcohol 12 h prior to meal trial, evening snack	Post-menopausal women aged 45–65 years; BMI between 18.5 and 40.0; answer no to all questions on PAR-Q for people aged 15–69	On-going chronic cardiovascular, pulmonary, or musculoskeletal disease; lipid-lowering medications; currently meeting physical activity guidelines	Post-menopausal women (n = 30)

MVPA, moderate-to vigorous-intensity physical activity; HFM, high-fat meal; BL, baseline; YA, young active; YI, young inactive; OA, older active; OI, older inactive; PAR-Q, Physical Activity Readiness Questionnaire; CVD, cardiovascular disease.
*Unpublished data.

2.4. Statistical analyses

Fasting and peak postprandial TG (PPTG) were used in this analysis. One-way analysis of variance (ANOVA) was used to compare baseline characteristics between men and women. We used multivariate linear regression to model PPTG based on fasting TG while adjusting for the confounding effects of several covariates (age, sex, BMI, LDL-C, HDL-C, TG/HDL-C ratio, and study site). From the multivariate linear regression equation, we calculated the fasting TG concentration that corresponded to PPTG ≥220 mg/dL (≥2.50 mmol/L).

We computed the fasting TG cut points using two methods. In Method 1, we determined upper and lower fasting TG cut points by identifying fasting TG concentrations by which ≥90% of individuals exhibited PPTG <220 mg/dL (<2.50 mmol/L) and PPTG >220 mg/dL (>2.50 mmol/L), respectively. Using these identified lower and upper fasting TG cut points, we determined the fasting TG range in which individuals PPTG response could not be confidently predicted based on fasting TG, or the indeterminate category. In Method 2, we determined fasting TG cut points by evaluating the area under the receiver operating characteristic (ROC) curve (*c*-statistic) in linear regression models with fasting TG as the independent variable and PPTG as the dependent variable. We obtained the value of fasting TG that optimized the *c*-statistic and Youden index (sensitivity + specificity-1). The Youden index has an ideal balance of sensitivity and specificity [14]. A PPTG value of ≥220 mg/dL (≥2.50 mmol/L) was used as a positive test in ROC analysis. We defined the lower fasting TG cut point when sensitivity was ≈95% and the upper fasting TG cut point when specificity was ≈95%.

Using the identified fasting TG range based on Methods 1 and 2 described above, we employed multivariate linear regression analysis to validate the predictability of PPTG from fasting TG. We

Table 2
Meal and participant characteristics for included studies.

Study	Test Meal	Meal Composition	Oral Fat Tolerance Test Protocol	Age (years)	BMI (kg/m^2)
Kurti et al.*	Marie Callender's Chocolate Satin Pie	12 kcal/kg body mass; 61% fat (58% SF), 35% CHO, 4% protein	BL and serial blood draws for 6h post-HFM consumption	Young (23.4 ± 3.7); old (67.4 ± 4.9)	25.86 ± 4.0
Emerson et al., 2018 [9]	Marie Callender's Chocolate Satin Pie	12 kcal/kg body mass; 61% fat (58% SF), 35% CHO, 4% protein	BL and serial blood draws for 6h post-HFM consumption	YA (25 ± 5); OA (67 ± 5); OI (68 ± 7)	YA 23.6 ± 2.0; OA 26.6 ± 4.1, OI 27.9 ± 4.7
Teeman et al., 2015 [10]	Jimmy Dean's Meatlovers Breakfast Bowl	10 kcal/kg body mass; 64% fat (21% SF), 16% CHO, 20% protein	BL and 2h and 4h post-HFM consumption	24.5 ± 5.0	25.7 ± 4.8
Sciarrillo et al., 2019 [11]	Pasta sauce, whole-wheat noodles, French bread, yellow onion, green bell pepper, butter	13 kcal/kg body mass; 61% fat, 32% CHO, 7% protein	BL and serial blood draws for 6h post-HFM consumption	23.8 ± 1.3	25.5 ± 7.2
Sciarrillo et al., 2019 [12]	Marie Callender's Chocolate Satin Pie	12 kcal/kg body mass; 61% fat (58% SF), 35% CHO, 4% protein	BL and serial blood draws for 6h post-HFM consumption	21.2 ± 2.5	25.2 ± 6.1
Koemel et al., 2020 [13]	Marie Callender's Chocolate Satin Pie	12 kcal/kg body mass; 61% fat (58% SF), 35% CHO, 4% protein	BL and serial blood draws for 6h post-HFM consumption	YA 22.1 ± 1.4; YI 22.6 ± 3.7; OA 68.4 ± 7.7; OI 67.7 ± 7.2	YA 23.8 ± 2.7; YI 25.7 ± 3.7; OA 28.2 ± 3.4; OI 30.4 ± 4.9
Jenkins et al.*	Marie Callender's Chocolate Satin Pie	12 kcal/kg body mass; 61% fat (58% SF), 35% CHO, 4% protein	BL and serial blood draws for 6h post-HFM consumption	55.8 ± 4.8	26.3 ± 3.8

BMI, body mass index; CHO, carbohydrate; BL, baseline; YA, young active; YI, young inactive; OA, older active; OI, older inactive.
*Unpublished data.

then used multivariate linear regression analysis to evaluate the confounding effect of several covariates (age, sex, BMI, LDL-C, HDL-C, TG/HDL-C ratio) on predicting PPTG from fasting TG. A chi square test of independence was performed to determine the relation between sex and PPTG. All statistical analyses were performed using IBM SPSS Statistics (v. 25, IBM Corp, Armonk, NY).

3. Results

Participant characteristics are presented in Table 3. Across the seven studies, a total of 156 individuals are included in this analysis (64 M/92 F; age 41.1 ± 20.6 years; BMI: 25.9 ± 4.4 kg/m^2). One-way ANOVA revealed that women had higher fasting HDL-C compared to men (mean difference = 14.7 mg/dL (0.17 mmol/L); $p < 0.001$), although men and women did not differ with regard to fasting LDL-C ($p = 0.14$), age ($p = 0.19$), fasting TG ($p = 0.41$), PPTG ($p = 0.37$), or TG/HDL-C ratio ($p = 0.11$). Men had higher BMI when compared to women (mean difference = 1.81 kg/m^2; $p < 0.01$). Eleven (7%) of the participants reported with fasting TG > 150 mg/dL (1.69 mmol/L) (Fig. 1). One participant was underweight (BMI <18.5 kg/m^2), 71 participants were normal weight (BMI: 18.5–24.9 kg/m^2), 54 participants were overweight (BMI: 25–29.9 kg/m^2), and 30 participants were obese (BMI >30 kg/m^2).

There was a strong positive association between fasting and PPTG ($r = 0.80$, $p < 0.001$). When covariates were included in the regression (age, sex, BMI, LDL-C, HDL-C, TG/HDL-C ratio, and study site), the relationship between fasting and PPTG was stronger ($r = 0.848$, $p < 0.001$) (Table 4). Based on linear regression, starting at 24.8 mg/dL (i.e. the *y*-intercept), every 1.0 mg/dL increase in fasting TG was associated with a 1.84 mg/dL increase in PPTG. The

Table 3
Participant characteristics.

Covariate	Men	Women	*p*-value
Age (years)	38.5 ± 20.9	42.9 ± 20.1	0.19
BMI (kg/m^2)	26.9 ± 4.0	25.2 ± 4.5	0.01*
Fasting HDL-C (mg/dL)	44.9 ± 9.9	59.6 ± 15.7	<0.001*
Fasting LDL-C (mg/dL)	94.8 ± 26.2	103.7 ± 38.4	0.14
Fasting TG (mg/dL)	79.8 ± 38.4	85.3 ± 41.4	0.41
Peak Postprandial TG (mg/dL)	185.0 ± 83.0	171.2 ± 98.8	0.37
TG/HDL-C ratio	1.9 ± 1.2	1.6 ± 1.0	0.11

Data are presented as mean ± SD. BMI, body mass index; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.
*indicates statistical difference between groups ($p < 0.05$). HDL-C and LDL-C: multiply by 0.02586 to convert to mmol/L; TG: multiply by 0.01129 to convert to mmol/L.

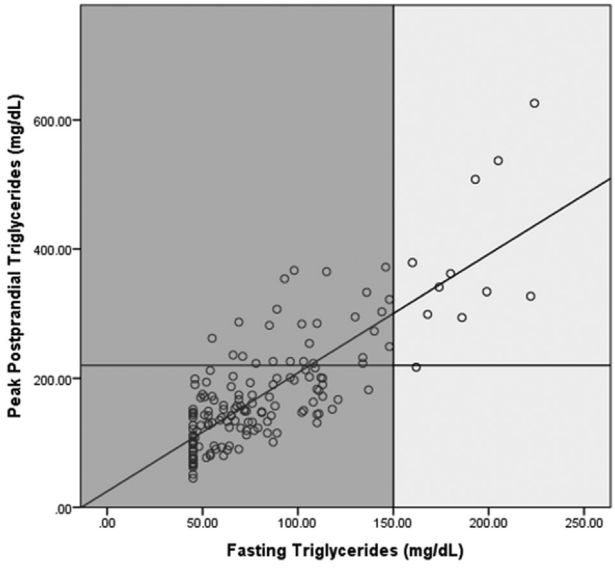

Fig. 1. Correlation between fasting and peak postprandial TG. Data points represent individuals. The light gray area represents 7% of individuals with fasting TG > 150 mg/dL (>1.69 mmol/L). All other participants presented with healthy fasting TG i.e. <150 mg/dL (<1.69 mmol/L). The solid line on the y axis represents peak postprandial TG of 220 mg/dL (2.50 mmol/L), the recommended cut point for adverse peak postprandial TG. Multiply by 0.01129 to convert to mmol/L.

Table 4
Regression of peak postprandial TG with covariates.

Covariate	β	*P*
Fasting TG (mg/dL)	0.79	<0.001
Sex	−0.16	<0.004
Age (years)	0.04	0.45
BMI (kg/m^2)	−0.04	0.48
Fasting HDL-C (mg/dL)	−0.06	0.53
Fasting LDL-C (mg/dL)	0.24	<0.001
TG/HDL-C ratio	−0.06	0.69
Study Site	−0.11	0.03

TG, triglycerides; BMI, body mass index; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein.

model predicted that fasting TG ≥ 106.3 mg/dL (≥1.21 mmol/L) are likely to yield PPTG ≥220 mg/dL (≥2.50 mmol/L).

3.1. Method 1

In our sample, 90% (18/20) of individuals with fasting TG > 130 mg/dL (>1.50 mmol/L) exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L), while 100% (67/67) of individuals with fasting TG < 66 mg/dL (<0.75 mmol/L) had PPTG that did not exceed ≥220 mg/dL (≥2.50 mmol/L) (Fig. 2). Therefore, based on this method, the fasting TG range in which PPTG are largely unpredictable is 66–130 mg/dL (0.75–1.50 mmol/L).

3.2. Method 2

For ROC analysis, we used a PPTG cut point of ≥220 mg/dL (≥2.50 mmol/L) as a positive test. The ROC curve for all values of fasting TG is shown in Fig. 3 (concordance (*c*)-statistic = 0.89; 95% confidence interval [CI]: 0.84, 0.95). The *c*-statistic is equivalent to the area under the ROC curve and is the probability that a randomly selected participant who experienced the outcome (PPTG ≥220 mg/dL; ≥2.50 mmol/L) has a higher risk score than a participant who did not experience the outcome (PPTG <220 md/dL; ≥2.50 mmol/L). A *c*-statistic >0.8 indicates a strong model [14]. The optimal threshold

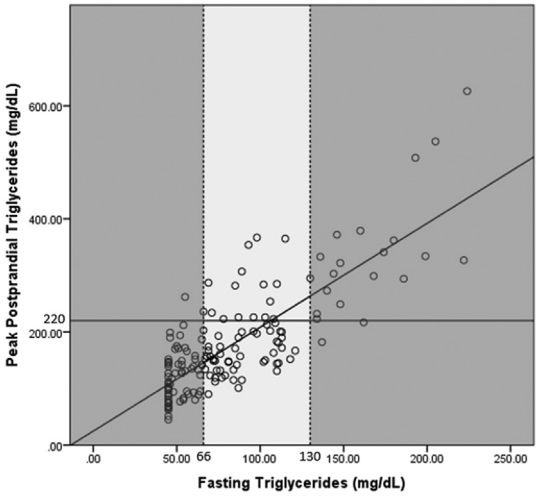

Fig. 2. Method 1 for identifying fasting TG cut points. We determined upper and lower fasting TG cut points by identifying fasting TG concentrations by which ≥90% of individuals exhibited PPTG <220 mg/dL (<2.50 mmol/L) and ≥90% of individuals exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L). Light gray area represents fasting TG between 66 and 130 mg/dL (0.75–1.50 mmol/L), or the fasting TG range in which the postprandial TG response is variable and thus individuals in this range would benefit from postprandial TG testing. The solid horizontal line on the y axis represents peak postprandial TG of 220 mg/dL (2.50 mmol/L), the recommended cut point for adverse PPTG. Multiply by 0.01129 to convert to mmol/L.

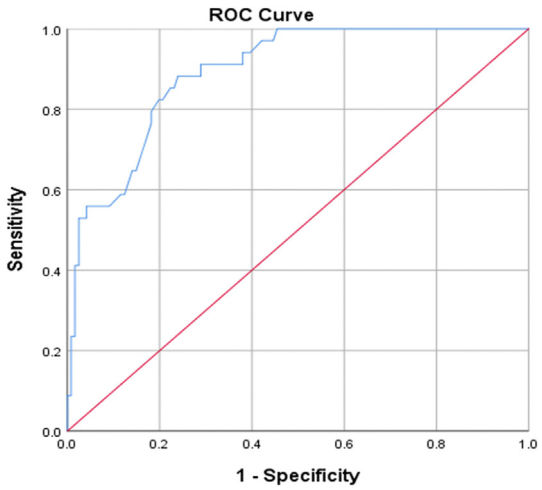

Fig. 3. ROC curve for the detection of adverse peak postprandial TG (≥220 mg/dL; ≥2.50 mmol/L) based on fasting TG.

of fasting TG for predicting PPTG was 84.5 mg/dL (0.95 mmol/L), corresponding to the maximum Youden index (0.64).

When sensitivity was ≈95%, the corresponding fasting TG concentration was 70 mg/dL (0.79 mmol/L). When specificity was ≈95%, the corresponding fasting TG concentration was 114 mg/dL (1.29 mmol/L). Based on this approach, the fasting TG range by which PPTG are not reliably predicted is 70–114 mg/dL (0.79–1.29 mmol/L) (Fig. 4).

3.3. Fasting TG range indicative of postprandial TG testing

There was considerable overlap regarding the fasting TG range indicative of postprandial TG testing between Method 1 and Method 2. Therefore, a conservative approach was utilized in order to define one fasting TG range indicative of postprandial TG testing, whereby the upper limit from Method 1 and the lower limit from Method 2 were combined. This inclusive range captures a sufficient percent of the population that is rightfully at risk for adverse

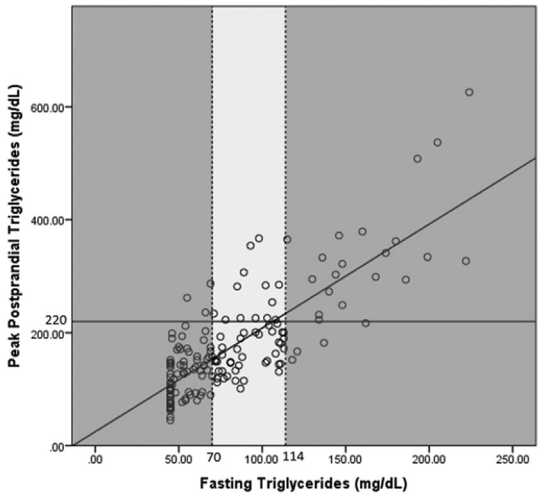

Fig. 4. Method 2 for identifying fasting TG cut points. We determined fasting TG cut points by evaluating the area under the ROC curve (*c*-statistic) in linear regression models and obtained the value of fasting TG that optimized the *c*-statistic and Youden index. Light gray area represents fasting TG between 70 and 114 mg/dL (0.79–1.29 mmol/L), or the fasting TG range in which the postprandial TG response is variable and thus individuals in this range would benefit from postprandial TG testing. The solid line on the y axis represents PPTG of 220 mg/dL (2.50 mmol/L), the recommended cut point for adverse PPTG. Multiply by 0.01129 to convert to mmol/L.

postprandial TG. Thus, based on Methods 1 and 2, the fasting TG range indicative of postprandial TG testing is 70–130 mg/dL (0.79–1.50 mmol/L). Within our sample, 49% (76/156), 38% (60/156), and 13% (20/156) of individuals had fasting TG < 70 mg/dL (<0.79 mmol/L), between 70 and 130 mg/dL (0.79–1.50 mmol/L), and (>130 mg/dL > 1.50 mmol/L), respectively. There was a moderate positive association ($r = 0.37$, $p < 0.004$) between fasting and PPTG for individuals with fasting TG between 70 and 130 mg/dL (0.79 and 1.50 mmol/L), in which 24% (14/59) exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L) while 76% (45/59) did not. When additional variables were included in the regression (age, sex, BMI, LDL-C, HDL-C, TG/HDL-C ratio), the relationship between fasting and PPTG was not significant for individuals with fasting TG between 70 and 130 mg/dL (0.79–1.50 mmol/L) ($r = 0.35$, $p = 0.08$) and sex was a significant predictor of PPTG ($r = -0.27$; $p = 0.02$) (Table 5). A chi-square test of independence revealed that men were less likely to experience PPTG <220 mg/dL (<2.50 mmol/L) when compared to women (X^2 (1, $N = 59$) = 5.23, $p = 0.02$) (Fig. 5). Within this sample (n = 59), 40 were women, of which 21 were post-menopausal, 19 were pre-menopausal, and 19 were men.

4. Discussion

To address our primary purpose, we determined the indeterminate fasting TG range as 70–130 mg/dL (0.79–1.50 mmol/L), where individuals within this range have an unpredictable PPTG response and should be recommended for postprandial TG testing. Individuals with fasting TG < 70 mg/dL (<0.79 mmol/L) and >130 mg/dL (>1.50 mmol/L) may not need to be recommended for postprandial TG testing because their postprandial TG response is largely predictable. According to NHANES data, approximately 26% (56.9 million) of U.S. adults ≥ 20 years have fasting TG ≥ 150 mg/dL and approximately 32% (70.5 million) of U.S. adults ≥20 years have fasting TG ≥ 135 mg/dL [15,16]. Considering this, our study helps to better classify some individuals that fall within the large percent of the population (~74% of U.S. adults) with fasting TG < 150 mg/dL but may justly be at risk for CVD. Additionally, considering that ~32% of U.S. adults exhibit fasting TG ≥ 135 mg/dL, by employing our fasting TG ranges, these individuals may avoid unnecessary medical testing in the form of postprandial lipid assessment.

Table 5
Regression of peak postprandial TG for the fasting TG range of 70–130 mg/dL (0.79–1.50 mmol/L) with covariates.

Covariate	β	*p*-value
Fasting TG (mg/dL)	0.35	0.08
Sex	−0.27	0.02
Age (years)	0.14	0.26
BMI (kg/m^2)	0.17	0.19
Fasting HDL-C (mg/dL)	−0.26	0.36
Fasting LDL-C (mg/dL)	0.23	0.08
TG/HDL-C ratio	−0.19	0.56

B represents standardized *B* coefficients. TG, triglycerides; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

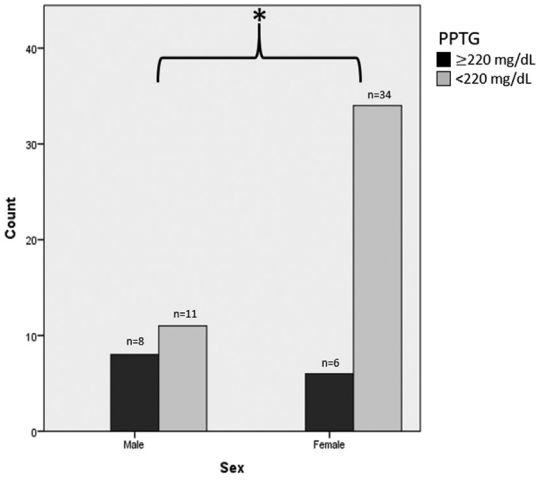

Fig. 5. Frequency of peak postprandial TG ≥ 220 mg/dL (≥2.50 mmol/L) by sex. Black columns represent peak postprandial TG ≥ 220 mg/dL (≥2.50 mmol/L) and gray columns represent peak postprandial TG < 220 mg/dL (<2.50 mmol/L). Men were more likely to experience peak postprandial TG ≥220 mg/dL (≥2.50 mmol/L) when compared to women ($X^2 = 5.23$, df = 1, $p = 0.02$). *indicates statistical difference between groups ($p < 0.05$). Multiply by 0.01129 to convert to mmol/L.

Evidence has revealed the role that postprandial TG play in atherogenesis [1,2,17] and elevated TG, despite the use of LDL-C lowering statin therapy, represents residual risk for atherogenesis [18]. The potentially causal role of elevated TG in CVD has not been fully elucidated; however, elevated levels of postprandial TG signify the presence of pro-atherogenic TRL (apolipoprotein-B containing lipoproteins), including very-low density lipoprotein (VLDL), chylomicrons (CM), and their remnants. Chylomicrons and VLDL can accumulate in the postprandial period and this phenomenon is largely explained by the fact that CM and VLDL compete for lipoprotein lipase (LPL) hydrolysis. Thus, in the context of a HFM, LPL can become saturated and may lead to VLDL accumulation and impaired clearance of TRL by the liver [6,19].

As the CM are hydrolyzed by LPL at peripheral tissues, they become chylomicron remnants (CM-R); both CM-R and VLDL can penetrate the vascular endothelium and contribute to foam cell development, a hallmark of atherogenesis [20]. For example, VLDL in particular can be taken up by macrophages directly without modification and contribute to foam cell development in the vasculature [21,22]. In addition, CM-R and VLDL may be preferentially retained in the endothelium due to their larger size, when compared to LDL [23,24]. Lastly, high levels of postprandial TG may serve as a proxy for insulin resistance, visceral adiposity, and non-alcoholic fatty liver (NAFL), all of which significantly increase risk for CVD [25–28].

In the present study, when covariates were included in the regression model, fasting TG for those in the indeterminate range (70–130 mg/dL; 0.79–1.50 mmol/L) were not predictive of PPTG, despite the fact that ~24% of individuals within this range exhibited an adverse PPTG response. This highlights the importance of the need for further postprandial TG testing within this range. To potentially better predict PPTG via the inclusion of risk indices, we investigated the association between covariates and PPTG. Sex, age, BMI, LDL-C, HDL-C, physical activity, and diet have been shown to influence or be associated with PPTG concentrations [9,29–32]. In our study, we did not find that age, BMI, fasting LDL-C, or fasting HDL-C were associated with PPTG for those within the 70–130 mg/dL (0.79–1.50 mmol/L) fasting TG range. However, we observed that sex was a predictor of PPTG. Specifically, the proportion of men that did not exhibit a deleterious postprandial TG response (<220 mg/dL; <2.50 mmol/L) was lower when compared to women. In agreement with our findings, the Copenhagen General Population Study (mean age: 62 years) observed that men exhibited a greater proportion (38%) of undesirable non-fasting TG (≥180 mg/dL; ≥2.03 mmol/L) when compared to women (20%) [5,33]. The finding that men are more likely to exhibit a deleterious PPTG response may be partly explained by the fact that higher estrogen levels in women tend to influence lipoprotein lipase activity (LPL) activity and may attenuate postprandial TG [29]. In our present study, ~68% of individuals in the 70–130 mg/dL (0.79–1.50 mmol/L) range (n = 59) were women (n = 40), of which

21 were post-menopausal and 19 were pre-menopausal. Estrogen production is diminished in post-menopausal women; as such, post-menopausal women tend to exhibit higher PPTG when compared to pre-menopausal women [34]. Thus, considering that the same proportion of pre-menopausal women to men were included in this sample, it may be likely that the observed decrement in PPTG between men and women may be partly explained by differences in estrogen concentrations. Lastly, for those individuals that fell within the 70–130 mg/dL fasting TG range, other conventional risk factors (i.e. BMI, LDL-C, HDL-C) were unremarkable, further highlighting the need for novel risk detection methods.

In more recent years, the influence of genetic variance on postprandial TG has been explored and relevant genotype–phenotype associations regarding TG metabolism may be one possible explanation for an unpredictable postprandial TG response [35]. For example, several single-nucleotide polymorphisms (SNPs) have been identified related to TG metabolism, including variants in genes encoding apolipoproteins, fatty acid binding protein 2, LPL, cholesterol ester transfer protein (CETP), hepatic lipase, microsomal transfer protein, and scavenger receptor B1 [36–38]. Specifically, SNPs in the apolipoprotein A-V (ApoAV) gene may be the most documented of the SNPs that affect TG. ApoAV is intimately involved in TG metabolism, where it is involved in hepatic VLDL production, TRL remnant clearance, and LPL activity. Historically, SNPs in the ApoAV gene have been associated with fasting TG. Recent findings from Olano-Martin et al. illuminated the fact that the ApoAV SNP (*rs662799*) is associated with postprandial TG in males and to a greater extent than the ApocIII SNP (*rs5128*) [37]. Moreover, a gender-based effect of the CETP SNP (*rs708272*) on postprandial TG has recently been documented [36]. In contrast to the ApoAV SNP (*rs662799*) and the CETP SNP (*rs708272*), carriers of the ApocIII SNP (*rs5128*) display lower fasting TG concentrations when compared to non-carriers, such that carriers also exhibit a reduced risk of CVD. Mechanistically, ApocIII is present on TRL and inhibits the lipolytic activity of LPL, leading to an increase in circulating TRL, such as VLDL and chylomicrons [38]. Investigating the additive effect of multiple SNPs in combination may be more physiologically meaningful with regard to postprandial TG, though, because single SNPs often explain <1% of the variance in postprandial TG [39]. Moreover, findings from the Personal Responses to Dietary Composition Trial (PREDICT) study highlighted that additive genetic factors explained 0% of the variance in postprandial TG, emphasizing further that genetics may explain little of the intra-individual variation in postprandial TG [40]. Despite the relatively small contribution of gene variants on postprandial TG, epigenetic variation may be partly responsible for the intra-individual variation in fasting and postprandial TG. For example, methylation sites in the carnitine palmitoyltransferase protein 1, ATP binding cassette subfamily G member 1 (ABCG1), and sterol regulatory element binding transcription factor (SREBF1) gene have been identified and are strongly associated with postprandial TG, contributing roughly 9.7%, 3.5%, and 3.2%, respectively, of variation in postprandial TG [41,42]. Interestingly, while genetic variation explains a small percent of the variance in fasting and postprandial TG, epigenetic variation accounts for considerably more phenotypic variation in postprandial TG.

Lifestyle factors that influence postprandial TG have been documented, including acute and habitual diet and exercise, and it is thought that these environmental factors may influence postprandial TG partly via epigenetic changes. Most notably, dietary fat, both with regard to type and amount, is the strongest modifier of postprandial TG. Typically, 30–50 g of dietary fat are needed to elicit a considerable postprandial TG response [43], however an expert panel recommends that a test meal containing 75 g of fat with 25 g of CHO and 10 g of protein should be the standard for fat tolerance testing in the clinical setting [44]. In our present study, we scaled each test meal to body weight, where approximately 61–64% kcal was derived from fat (10–13 kcal/kg body mass), largely due to the fact that fat tolerance testing in the research setting differs from the clinical setting. Specifically, scaling the test meal to body weight likely represents a fat bolus that is unique and appropriate to each participant's body size. Recently, the effect of different fatty acid compositions of a single test meal on postprandial TG has been investigated. In short, it is thought that meals rich in saturated fat, monounsaturated fat, or polyunsaturated fat do not differ in a clinically meaningful way with regard to postprandial TG [11]. One exception is the possibility that meals rich in the saturated fatty acid stearic acid may elicit a lower postprandial TG response when compared to meals rich in different saturated fatty acids, however these effects are inconsistent in the literature [45]. Although there is limited data published on the effect of habitual diet on postprandial TG, habitual diet has also been shown to influence postprandial TG, such that diets rich in PUFA have been shown to lead to a lower postprandial TG response [46]. Conversely, diets rich in refined carbohydrates, low in dietary fiber, and high in saturated fat have been associated with a greater postprandial TG response to a HFM [47]. The majority of the existing research on both acute and habitual diet and postprandial TG is limited by short blood sampling periods ($\leq$ 4 h). Longer blood sampling periods ($\geq$ 8 h) may differentiate the effects of various dietary patterns and acute dietary fatty acid intake. Lastly, both acute and chronic exercise influence postprandial TG. Acute exercise appears to reduce postprandial TG, attributed largely to intensity of exercise and energy deficit following exercise [48]. Physical activity within 24 h of and during fat tolerance testing also has been shown to ameliorate postprandial TG [49,50]. However, the effects of acute exercise in the present analysis were limited due to restriction on planned exercise within 24–48 h of the HFM in each study.

Historically, guidelines largely centered on fasting lipids and focused primarily on severe hypertriglyceridemia in the fasting state. Recently, non-fasting and postprandial hypertriglyceridemia has been increasingly considered. In fact, several societies and guidelines now support and emphasize the importance of non-fasting lipids for risk assessment [51–55]. This is largely because individuals spend majority of their day in a non-fasted, or fed, state; i.e. breaking their fast shortly upon waking and consuming additional meals throughout the day. Therefore, the importance of hypertriglyceridemia in the non-fasted state (i.e. collected within 8 h of consuming a meal) may have been overlooked in the past. As such, efforts have been made to define recommendations for non-fasting TG assessment. White et al. defined a diagnostic threshold for non-fasting hypertriglyceridemia as 175 mg/dL (1.98 mmol/L). This threshold was determined using ROC analysis, where the predictive capacity of non-fasting TG for incident cardiovascular events was calculated [56]. However, non-fasting TG differ from postprandial TG; TG are considered non-fasting when a meal was consumed within approximately 8 h of the blood draw [1]. Although non-fasting TG assessment is currently favored over postprandial TG assessment in the clinical setting due to greater logistical feasibility, non-fasting TG testing is subject to greater variance compared to postprandial TG assessment because clinicians cannot control for meal intake or physical activity prior to or during the postprandial period. Also, the random timing of the blood draw within the non-fasting period likely produces error and potential misclassification.

Conversely, TG are considered postprandial when an individual participates in an OFTT. OFTTs are standardized, controlled meal tests primarily used in the research setting wherein an HFM is administered and blood draws are conducted serially for several hours post-meal consumption to quantify postprandial TG. Thus,

OFTTs are a more sensitive and precise test of lipid tolerance. Due to the clinical impracticality of standard postprandial TG assessment, some previous research has sought to identify fasting and non-fasting TG ranges that are predictive of postprandial TG in disease-free populations. For example, Kolovou et al. recommended postprandial TG testing for individuals with non-fasting TG of 115–200 mg/dL (1.3–2.3 mmol/L) [5]. Further, the fasting TG range of 89–175 mg/dL (1–2 mmol/L) was useful in identifying postprandial hypertriglyceridemia in generally healthy U.S. adults and in Spanish patients with CHD [57,58]. Using ROC analysis, Kolovou et al. found that fasting TG $\geq$ 121 mg/dL ($\geq$1.37 mmol/L) were predictive of an abnormal postprandial TG response [59]. The authors defined an abnormal postprandial TG response as >219 mg/dL (>2.50 mmol/L), which was the postprandial TG concentration higher than the highest TG concentration in control subjects. Case subjects were those with low HDL-C (<40 mg/dL; <1.03 mmol/L). We similarly defined an adverse PPTG response as $\geq$220 mg/dL ($\geq$2.50 mmol/L), although we identified fasting TG of $\geq$85 mg/dL (0.96 mmol/L) as likely to exceed this threshold using ROC analysis. Additionally, their study included only men, a smaller sample (n = 52), and participants were separated into a low HDL-C group and controls (fasting TG < 150 mg/dL; HDL-C = 53 ± 19 mg/dL). Approximately half of the men in the low HDL-C group had coronary heart disease and a few had hypertension. On the other hand, our population was disease-free, which we view as ideal since patients with known cardiometabolic disease would not likely benefit from postprandial TG screening.

Further, in an expert panel statement, individuals with fasting TG of 89–175 mg/dL (1–2 mmol/L) were recommended for postprandial TG testing. This fasting TG range was later supported in a secondary analysis conducted by Perez-Martinez et al. including data from the Coronary Diet Intervention with Olive Oil and Cardiovascular Prevention Study (CARDIOPREV) and Genetic and Environmental Determinants of Triglycerides (GOLDN) studies [60]. There are a few differences and similarities between our approach and the approach used by Perez-Martinez et al. First, the CARDIOPREV study included participants with pre-existing CHD currently receiving treatment for CHD, which likely influences postprandial TG. Both the CARDIOPREV and GOLDN studies utilized a postprandial TG testing protocol different from the recommended standard postprandial TG testing protocol (i.e. fasting blood collection, meal consumption, and serial blood draws for 6–8 h post-meal consumption). Specifically, the CARDIOPREV cohort utilized a postprandial period of 5 h, such that blood was drown serially every hour for 4 h post-meal consumption. In the GOLDN cohort, the postprandial period was 6 h, however blood was drawn at 3.5- and 6-h post-meal consumption. Although practical, this protocol may not have captured the true peak postprandial TG. Further, Perez-Martinez et al. utilized pre-determined ranges that were based on expert opinion for fasting TG that were likely predictive of adverse postprandial TG. Taken collectively, the secondary analysis conducted by Perez-Martinez et al. that supported the expert panel recommendation of fasting TG of 89–175 mg/dL included robust study methods involving two strong cohorts from the CARDIOPREV and GOLDN studies and provides potential clinical advancement for the recommendation of postprandial TG testing for those with pre-existing CVD or undergoing treatment for CVD. However, the method used in our current secondary analysis included a cohort free of disease or treatment that would influence fasting or postprandial TG, a standard postprandial TG protocol capable of capturing the true peak postprandial TG, and analyses that included all data points such that the fasting TG range could be predicted from the entire cohort prior to predictions. Thus, our findings are similar to Perez-Martinez et al. but were developed in a dissimilar context and thus may have different implications for clinical recommendations.

The use of postprandial TG testing in clinical practice for CVD risk assessment has several advantages. Specifically, individuals spend the majority of their day in a postprandial state, therefore postprandial TG testing likely reveal more about a person's metabolic state than fasting TG. It is probable that most people consume several meals prior to returning to baseline TG concentrations in a given day. For those in the early stages of cardiometabolic disease, complete clearance of TG following meal consumption may be delayed for up to 12 h. Additionally, postprandial TG testing is a protocol that controls for factors that influence TG concentrations, including physical activity and exercise, dietary intake, degree of fasting, and HFM macronutrient and energy content. Lastly, postprandial TG are a more sensitive screening tool when compared to fasting TG, likely revealing cardiometabolic risk earlier than a fasting measurement. Although postprandial TG are a stronger predictor of CVD compared to fasting TG, traditional postprandial TG testing is resource and time intensive, requiring serial blood draws over many hours. Additionally, there is a lack of a standard clinical protocol for diagnosing postprandial TG and international guidelines are inconsistent, where some prioritize postprandial lipid assessment over fasting, and some recommend postprandial lipid assessment only when values reach or exceed certain cut points. Moreover, test meal preparation, meal macronutrient and ingredient content, and lack of established clinical protocol for time-point measurements of TG, limit the clinical application of postprandial TG testing in the clinical setting. Therefore, it is critical to adopt a simplified screening tool that will accurately capture PPTG while also being clinically feasible.

There are several considerations to make when interpreting our data. We included seven independent studies with different inclusion and exclusion criteria. Although studies were similar with regard to OFTT protocol, differences remain. The percentage of kcals from fat across the meals was largely similar (61–64%). Individuals included in this secondary analysis also had various physical activity levels, which can potentially influence fasting and postprandial TG. Additionally, we did not have a measure of visceral adiposity for all studies. Visceral adiposity is a strong modifier of postprandial TG, thus future studies may investigate the confounding effect of visceral adiposity on postprandial TG. In addition, although adequately powered, our sample size for this study (n = 156) was moderate; thus, future studies may expand upon our findings in a larger cohort. Lastly, although the age range in our study was broad, the distribution did favor young adults, thus being cautious to apply these findings to the broader population is necessary.

5. Conclusions

We are the first to define fasting TG thresholds where 1) individuals with fasting TG < 70 mg/dL will likely not exceed postprandial TG $\geq$ 220 mg/dL, 2) individuals with fasting TG > 130 mg/dL will likely exceed postprandial TG $\geq$ 220 mg/dL, and 3) individuals with fasting TG between 70 and 130 mg/dL are categorized in an indeterminate category, whereby their postprandial TG response is heterogeneous and thus should be recommended for postprandial TG testing. These important cut points have the potential to inform clinical practice in order to better detect CVD risk in the clinical setting, simplify postprandial TG assessment, and avoid unnecessary medical testing. For primary prevention, it is increasingly important to define fasting TG ranges that are predictable of postprandial TG in disease-free

populations, in order to identify risk and begin targeted intervention early. Future research should identify these fasting TG cut points that are predictive of postprandial TG in individuals with CVD or cardiometabolic disease and validate our findings in a larger sample.

Statement of authorship

Christina M. Sciarrillo: conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, writing – review and editing, visualization; Nicholas A. Koemel: methodology, investigation, data curation, writing – review and editing, visualization; Bryant H. Keirns: methodology, writing – review and editing, visualization; Nile F. Banks: investigation, data curation, writing – review and editing, visualization; Emily M. Rogers: investigation, data curation, writing – review and editing, visualization; Sara K. Rosenkranz: conceptualization, methodology, investigation, data curation, writing – review and editing, visualization, funding acquisition; Stephanie P. Kurti: conceptualization, methodology, investigation, data curation, writing – review and editing, visualization, funding acquisition; Nathaniel D. M. Jenkins: conceptualization, methodology, investigation, data curation, writing – review and editing, visualization, funding acquisition; Sam R. Emerson: conceptualization, methodology, investigation, data curation, writing – review and editing, visualization, supervision, funding acquisition, project administration.

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Conflict of interest

Nathaniel D. M. Jenkins currently serves on the AHA Research Committee, as well as two AHA Research-related subcommittees. Nathaniel D. M. Jenkins is also currently supported by an AHA research grant (18AIREA33960528), as well as an NIH Clinical Research Loan Repayment Award. Within the last year, Nathaniel D. M. Jenkins has received compensation as a book reviewer, as well as a chapter author, for Human Kinetics. All other authors have nothing to disclose.

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References

[1] Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM, et al. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. Jama 2007;298(3):309–16.
[2] Stalenhoef AF, de Graaf J. Association of fasting and nonfasting serum triglycerides with cardiovascular disease and the role of remnant-like lipoproteins and small dense LDL. Curr Opin Lipidol 2008;19(4):355–61.
[3] Zheng C, Khoo C, Furtado J, Sacks FM. Apolipoprotein C-III and the metabolic basis for hypertriglyceridemia and the dense low-density lipoprotein phenotype. Circulation 2010;121(15):1722.
[4] Thomsen M, Varbo A, Tybjærg-Hansen A, Nordestgaard BG. Low nonfasting triglycerides and reduced all-cause mortality: a mendelian randomization study. Clin Chem 2014;60(5):737–46.
[5] D Kolovou GD, Mikhailidis D, Kovar J, Lairon D, G Nordestgaard B, Chye Ooi T, et al. Assessment and clinical relevance of non-fasting and postprandial triglycerides: an expert panel statement. Curr Vasc Pharmacol 2011;9(3):258–70.
[6] Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN, et al. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. Circulation 2011;123(20):2292–333.
[7] Kolovou GD, Watts GF, Mikhailidis DP, Pérez-Martínez P, Mora S, Bilianou H, et al. Postprandial hypertriglyceridaemia revisited in the era of non-fasting lipid profile testing: a 2019 expert panel statement, main text. Curr Vasc Pharmacol 2019;17(5):498–514.
[8] Emerson SR, Kurti SP, Teeman CS, Emerson EM, Cull BJ, Haub MD, et al. Realistic test-meal protocols lead to blunted postprandial lipemia but similar inflammatory responses compared with a standard high-fat meal. Current Dev Nutr 2017;1(4):e000232.
[9] Emerson SR, Kurti S, Emerson E, Cull B, Casey K, Haub M, et al. Postprandial metabolic responses differ by age group and physical activity level. J Nutr Health Aging 2018;22(1):145–53.
[10] Teeman CS, Kurti SP, Cull BJ, Emerson SR, Haub MD, Rosenkranz SK. The effect of moderate intensity exercise in the postprandial period on the inflammatory response to a high-fat meal: an experimental study. Nutr J 2015;15(1):24.
[11] Sciarrillo CM, Koemel NA, Tomko PM, Bode KB, Emerson SR. Postprandial lipemic responses to various sources of saturated and monounsaturated fat in adults. Nutrients 2019;11(5):1089.
[12] Sciarrillo CM, Koemel NA, Kurti SP, Emerson SR. Validity of an abbreviated, clinically feasible test for postprandial lipemia in healthy adults: a randomized cross-over study. Nutrients 2019;11(1):180.
[13] Koemel NA, Sciarrillo CM, Bode KB, Dixon MD, Lucas EA, Jenkins ND, et al. Postprandial metabolism and vascular function: impact of aging and physical activity level. Int J Sport Nutr Exerc Metabol 2020;1(aop):1–8.
[14] Unal I. Defining an optimal cut-point value in ROC analysis: an alternative approach. Computational Math Methods Med 2017;2017:3762651.
[15] Fan W, Philip S, Toth PP, Granowitz C, Wong ND. Prevalence of United States adults with triglycerides≥ 135 mg/dL: NHANES 2007–2014. Cardiol J 2019;26(5):604–6.
[16] Fan W, Philip S, Granowitz C, Toth PP, Wong ND. Prevalence of US Adults with Triglycerides≥ 150 mg/dl: NHANES 2007–2014. Cardiol therapy 2020:1–7.
[17] Freiberg JJ, Tybjærg-Hansen A, Jensen JS, Nordestgaard BG. Nonfasting triglycerides and risk of ischemic stroke in the general population. Jama 2008;300(18):2142–52.
[18] Miller M, Cannon CP, Murphy SA, Qin J, Ray KK, Braunwald E, et al. Impact of triglyceride levels beyond low-density lipoprotein cholesterol after acute coronary syndrome in the PROVE IT-TIMI 22 trial. J Am Coll Cardiol 2008;51(7):724–30.
[19] Bjorkegren J, Packard C, Hamsten A, Bedford D, Caslake M, Foster L, et al. Accumulation of large very low density lipoprotein in plasma during intravenous infusion of a chylomicron-like triglyceride emulsion reflects competition for a common lipolytic pathway. J Lipid Res 1996;37(1):76–86.
[20] Botham K, Moore E, Pascale CD, Bejta F. The induction of macrophage foam cell formation by chylomicron remnants. Biochem Soc Trans 2007;35(3):454–8.
[21] Goldberg IJ, Eckel RH, McPherson R. Triglycerides and heart disease: still a hypothesis? Arterioscler Thromb Vasc Biol 2011;31(8):1716–25.
[22] Mahley RW, Innerarity TL, Rall Jr SC, Weisgraber KH. Lipoproteins of special significance in atherosclerosis. Insights provided by studies of type III hyperlipoproteinemia. Ann N Y Acad Sci 1985;454:209.
[23] Nordestgaard BG, Benn M, Schnohr P, Tybjærg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. Jama 2007;298(3):299–308.
[24] Nordestgaard BG, Wootton R, Lewis B. Selective retention of VLDL, IDL, and LDL in the arterial intima of genetically hyperlipidemic rabbits in vivo: molecular size as a determinant of fractional loss from the intima–inner media. Arterioscler Thromb Vasc Biol 1995;15(4):534–42.
[25] Alcala-Diaz JF, Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Marin C, Quintana-Navarro GM, et al. Hypertriglyceridemia influences the degree of postprandial lipemic response in patients with metabolic syndrome and coronary artery disease: from the CORDIOPREV study. PloS One 2014;9(5):e96297.
[26] Diraison F, Moulin P, Beylot M. Contribution of hepatic de novo lipogenesis and reesterification of plasma non esterified fatty acids to plasma triglyceride synthesis during non-alcoholic fatty liver disease. Diabetes Metabol 2003;29(5):478–85.
[27] Lewis GF, Steiner G. Acute effects of insulin in the control of VLDL production in humans: implications for the insulin-resistant state. Diabetes Care 1996;19(4):390–3.
[28] Harbis A, Defoort C, Narbonne H, Juhel C, Senft M, Latgé C, et al. Acute hyperinsulinism modulates plasma apolipoprotein b-48 triglyceride—rich lipoproteins in healthy subjects during the postprandial period. Diabetes 2001;50(2):462–9.
[29] Weintraub M, Grosskopf I, Charach G, Eckstein N, Rubinstein A. Hormone replacement therapy enhances postprandial lipid metabolism in postmenopausal women. Metabolism 1999;48(9):1193–6.
[30] Gill JM, Hardman AE. Postprandial lipemia: effects of exercise and restriction of energy intake compared. Am J Clin Nutr 2000;71(2):465–71.
[31] Redard CL, Davis PA, Schneeman BO. Dietary fiber and gender: effect on postprandial lipemia. Am J Clin Nutr 1990;52(5):837–45.
[32] Emerson SR, Sciarrillo CM, Kurti SP, Emerson EM, Rosenkranz SK. High-fat meal–induced changes in markers of inflammation and angiogenesis in healthy adults who differ by age and physical activity level. Current Dev Nutr 2018;3(1):nzy098.
[33] Langsted A, Freiberg J, Nordestgaard B. Fasting versus NON-fasting lipid levels-influence of normal food intake on lipids, lipoproteins, and apolipoproteins. Atherosclerosis 2008;1(9):174.

[34] Zaman GS, Rahman S, Rahman J. Postprandial lipemia in pre-and postmenopausal women. J Nat Sci Biol Med 2012;3(1):65.
[35] Parnell LD, Ordovas JM, Lai C-Q. Environmental and epigenetic regulation of postprandial lipemia. Curr Opin Lipidol 2018;29(1):30–5.
[36] Anagnostopoulou KK, Kolovou GD, Kostakou PM, Mihas C, Hatzigeorgiou G, Marvaki C, et al. Sex-associated effect of CETP and LPL polymorphisms on postprandial lipids in familial hypercholesterolaemia. Lipids Health Dis 2009;8(1):1–14.
[37] Olano-Martin E, Abraham EC, Gill-Garrison R, Valdes AM, Grimaldi K, Tang F, et al. Influence of apoA-V gene variants on postprandial triglyceride metabolism: impact of gender. JLR (J Lipid Res) 2008;49(5):945–53.
[38] Tg NH. HDL working group of the exome sequencing project, lung, and B. Institute, loss-of-function mutations in APOC3, triglycerides, and coronary disease. N Engl J Med 2014;371(1):22–31.
[39] Jackson KG, Poppitt SD, Minihane AM. Postprandial lipemia and cardiovascular disease risk: interrelationships between dietary, physiological and genetic determinants. Atherosclerosis 2012;220(1):22–33.
[40] Berry SE, Valdes AM, Drew DA, Asnicar F, Mazidi M, Wolf J, et al. Human postprandial responses to food and potential for precision nutrition. Nat Med 2020;26(6):964–73.
[41] Lai C-Q, Wojczynski MK, Parnell LD, Hidalgo BA, Irvin MR, Aslibekyan S, et al. Epigenome-wide association study of triglyceride postprandial responses to a high-fat dietary challenge. J Lipid Res 2016;57(12):2200–7.
[42] Sayols-Baixeras S, Subirana I, Lluis-Ganella C, Civeira F, Roquer J, Do A, et al. Identification and validation of seven new loci showing differential DNA methylation related to serum lipid profile: an epigenome-wide approach. the REGICOR study. Hum Mol Genet 2016;25(20):4556–65.
[43] Cohen JC, Noakes TD, Benade A. Serum triglyceride responses to fatty meals: effects of meal fat content. Am J Clin Nutr 1988;47(5):825–7.
[44] Kolovou GD, Watts GF, Mikhailidis DP, Pérez-Martínez P, Mora S, Bilianou H, et al. Postprandial hypertriglyceridaemia revisited in the era of non-fasting lipid profiles: executive summary of a 2019 expert panel statement. Curr Vasc Pharmacol 2019;17(5):538–40.
[45] Sanders TA, Oakley FR, Cooper JA, Miller GJ. Influence of a stearic acid–rich structured triacylglycerol on postprandial lipemia, factor VII concentrations, and fibrinolytic activity in healthy subjects. Am J Clin Nutr 2001;73(4):715–21.
[46] Williams CM, Moore F, Morgan L, Wright J. Effects of n-3 fatty acids on postprandial triacylglycerol and hormone concentrations in normal subjects. Br J Nutr 1992;68(3):655–66.
[47] Perez-Martinez P, Ordovas JM, Garcia-Rios A, Delgado-Lista J, Delgado-Casado N, Cruz-Teno C, et al. Consumption of diets with different type of fat influences triacylglycerols-rich lipoproteins particle number and size during the postprandial state. Nutr Metabol Cardiovasc Dis 2011;21(1):39–45.
[48] Emerson SR, Kurti SP, Snyder BS, Sitaraman K, Haub MD, Rosenkranz SK. Effects of thirty and sixty minutes of moderate-intensity aerobic exercise on postprandial lipemia and inflammation in overweight men: a randomized cross-over study. Sports Nutr Rev J 2016;13(1):1–12.
[49] Miyashita M, Edamoto K, Kidokoro T, Yanaoka T, Kashiwabara K, Takahashi M, et al. Interrupting sitting time with regular walks attenuates postprandial triglycerides. Int J Sports Med 2016;37(2):97–103.
[50] Freese EC, Gist NH, Cureton KJ. Effect of prior exercise on postprandial lipemia: an updated quantitative review. J Appl Physiol 2014;116(1):67–75.
[51] Detection, N.C.E.P.E.P.o. and T.o.H.B.C.i. Adults, Third report of the national cholesterol education program (NCEP) expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). The Program; 2002.
[52] Rabar S, Harker M, O'Flynn N, Wierzbicki AS. Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance. BMJ 2014:349.
[53] Anderson TJ, Grégoire J, Pearson GJ, Barry AR, Couture P, Dawes M, et al. 2016 Canadian Cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 2016;32(11):1263–82.
[54] Nordestgaard BG, Langsted A, Mora S, Kolovou G, Baum H, Bruckert E, 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(25):1944–58.
[55] Jellinger PS, Handelsman Y, Rosenblit PD, Bloomgarden ZT, Fonseca VA, Garber AJ, et al. American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract 2017;23:1–87.
[56] White KT, Moorthy M, Akinkuolie AO, Demler O, Ridker PM, Cook NR, et al. Identifying an optimal cutpoint for the diagnosis of hypertriglyceridemia in the nonfasting state. Clin Chem 2015;61(9):1156–63.
[57] Wojczynski MK, Parnell LD, Pollin TI, Lai CQ, Feitosa MF, O'Connell JR, et al. Genome-wide association study of triglyceride response to a high-fat meal among participants of the NHLBI Genetics of Lipid Lowering Drugs and Diet Network (GOLDN). Metabolism 2015;64(10):1359–71.
[58] Mihas C, Kolovou GP, Mikhailidis D, Kovar J, Lairon D, G Nordestgaard B, et al. Diagnostic value of postprandial triglyceride testing in healthy subjects: a meta-analysis. Curr Vasc Pharmacol 2011;9(3):271–80.
[59] Kolovou GD, Anagnostopoulou KK, Pilatis N, Kafaltis N, Sorodila K, Psarros E, et al. Low fasting low high-density lipoprotein and postprandial lipemia. Lipids Health Dis 2004;3(1):18.
[60] Perez-Martinez P, Alcala-Diaz JF, Kabagambe EK, Garcia-Rios A, Tsai MY, Delgado-Lista J, et al. Assessment of postprandial triglycerides in clinical practice: validation in a general population and coronary heart disease patients. J Clin Lipidol 2016;10(5):1163–71.