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The Triglyceride Conundrum: Unraveling the Factors Affecting the Disparity Between Non-Fasting and Fasting Levels

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Abstract

Objective: Little is known regarding the size of the difference in triglycerides between those who fast and those who don't, or if this difference is influenced by certain possible risk factors for cardiovascular disease (CVD).

Methods: Between 2018 and 2023, an 8,073-participant cross-sectional research was done to examine the distinctions between non-fasting and fasting triglycerides and their possible correlation with risk factors for cardiovascular disease (CVD). According to whether or not they were fasting, participants were split into two groups. The variation between non-fasting and fasting triglycerides and their correlation with CVD risk variables were estimated using linear regression models.

Results: After controlling for confounders, it was discovered that individuals who fasted had lower triglycerides than those who did not, with a difference of 4.22 mg/dL that was statistically significant. The presence of hypertension, the usage of antihyperlipidemic medications, and LDL cholesterol levels were observed to impact the difference in triglyceride levels between fasting and non-fasting. The difference was more pronounced in those with hypertension, antihyperlipidemic medication use, or levels of LDL cholesterol below 130 mg/dL.

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Conclusions: The average sample showed a 4 mg/dL difference in triglycerides between non-fasting and fasting, and the presence of hypertension, the usage of antihyperlipidemic drugs, and LDL cholesterol levels all influenced the size of the changes. These findings may facilitate the accurate estimation of CVD risk utilising non-fasting and fasting triglycerides.

Introduction:

Cardiovascular disorders (CVDs) are widely known to be at risk due to high triglyceride levels [1]. While non-fasting triglyceride levels are often greater than fasting triglyceride levels owing to the gastrointestinal effect, current medical recommendations recommend measuring triglycerides in blood samples that are fasting to appropriately estimate the risk of CVDs [2]. In contrast, non-fasting triglycerides are more accurate than fasting triglycerides in predicting future CVDs [3,4] because people spend the majority of their time not fasting. It has been brought to light that fasting triglycerides may significantly understate the underlying risk of CVDs. Because certain epidemiologic studies [5,6] did not consider fasting triglycerides to be a standalone risk factor for CVDs, more research on non-fasting and fasting triglycerides is necessary to enhance the function of triglycerides in determining CVD risk.

Although non-fasting triglyceride levels are typically greater than fasting triglyceride levels [7,8,9], it is unknown how much of a difference there is between the two and if this difference is influenced by any possible CVD risk factors. We will be able to effectively use triglycerides, both non-fasting and fasting, to assess the risk of CVDs if we have the answers to these two questions. In other words, compared to utilizing non-fasting triglycerides, employing fasting triglycerides may considerably understate the likelihood of CVDs.

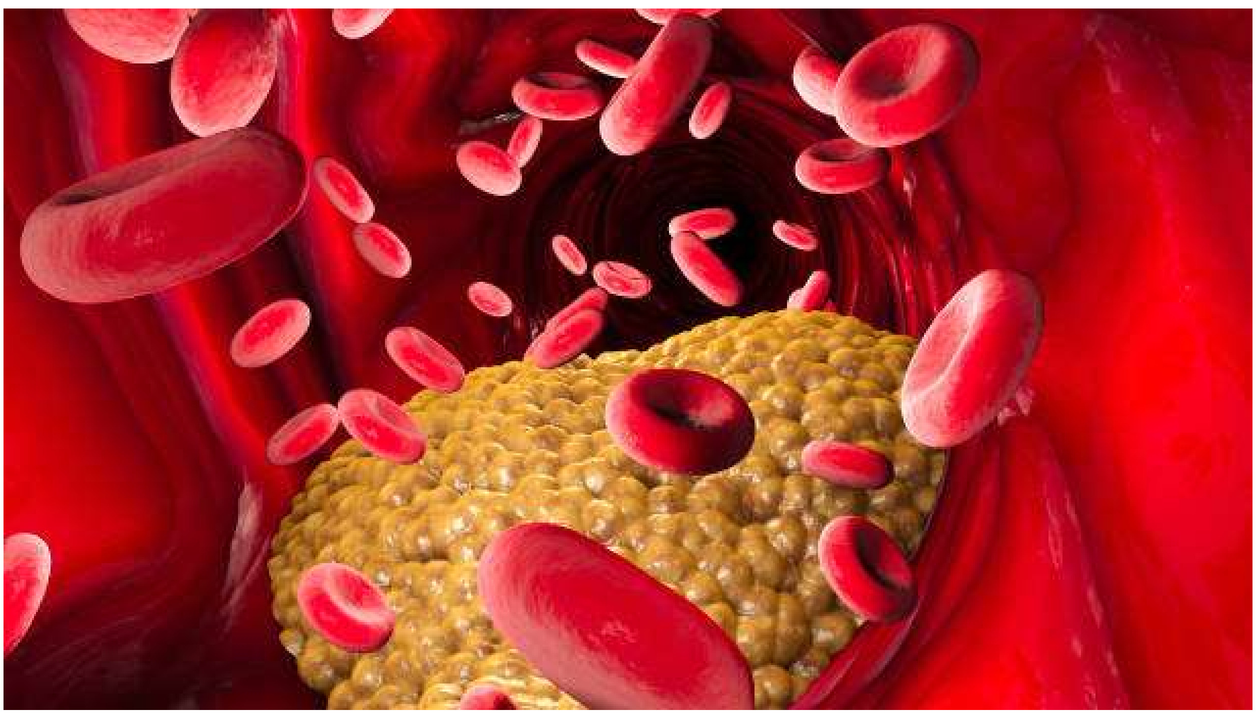

Figure 1: Triglycerides

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Additionally, it has been shown in previous studies that age, gender, and a few lipid metabolic variables that may affect fat metabolism may all have an impact on how much the distinction between non-fasting and fasting triglycerides differ from each other [10,11]. Few studies, however, have examined the possible impact of a profile of several CVD risk factors (such as demographic variables, diabetes, CVD biomarkers, hypertension, and the use of antihyperlipidemic agents) on the distinction between non-fasting and fasting triglycerides. To ascertain if various putative CVD risk variables influence the extent of the distinction between non-fasting and fasting triglycerides, our research set out to measure it.

Methods:

Study Design: From 2018 to 2023, this research was carried out at Mayo Medical Centre. 32,971 people in total were chosen for this research. After removing 19,219 people with triglyceride readings and 5,679 participants with unrecorded fasting hours, we ultimately included 8,073 participants in our study. Participants who were included and those who were omitted were both 30 years old, whereas those who were excluded were 31 years old. In people who were included, the BMI was 25.3 kg/m2, but in those who were omitted, it was 25.6.

Qualified surveyors used a standardized questionnaire to gather information on race, gender, age, level of physical activity, overall fat consumption, consumption of antihyperlipidemic medications, CVD history, and smoking habits. At the interview, the BMI was determined. Smokers were divided into three categories: current, former, and never smokers. Three categories were used to categorize the degrees of physical activity: active mild, and inactive lifestyle. Large increases in respiration or heart rate were considered to be part of a vigorous lifestyle if they lasted for a minimum of ten minutes consistently each week. Participants were considered to have a moderate lifestyle if they regularly engaged in activities such as walking vigorously or lifting little stuff for a minimum of ten minutes.

Participants who led inactive lifestyles made up the remainder of the group. From a 24-hour meal recall (which lasted from midnight to midnight) prior to the blood collection, the total amount of fat consumed was assessed. Prior to the interview date, the use of antihyperlipidemic medications was investigated. Only binary data on antihyperlipidemic drug usage (yes/no) was analyzed since the dosage of antihyperlipidemic agent utilization was not available. A questionnaire was used to determine the duration of the "food fast" at the time of the blood sample. Participants were classified as fasting subjects if they had been without food or liquids for at least eight hours prior to the blood sample. The remainder were classified as non-fasting subjects. We choose 8 hours as a threshold to distinguish between non-fasting and fasting states since monitoring triglycerides in patients is a frequent clinical practice. Eight hours of fasting samples of blood and the eight-hour mark in our study showed a higher difference between non-fasting and fasting triglycerides than earlier cut-points (such as six, ten, or twelve hours).

Statistical Analysis: Between individuals who were fasting and those who weren't, we compared information on demographic characteristics, diabetes, hypertension, CVD biomarkers, and antihyperlipidemic medication use. Triglycerides were studied in connection to demographic variables, diabetes, CVD biomarkers, hypertension, and the usage of antihyperlipidemic drugs. P was calculated using a linear regression model. The association was examined using a linear regression model. between the fasting state (less than 8 hrs and more than 8 hrs) and triglycerides with triglycerides and fasting status acting as both independent and dependent variables, respectively.

Results:

In order to determine if fasting conditions and levels of triglycerides are related, the researchers examined data from 8,073 people. When it came to the overall number of subjects, 41% (n=3,296) had fasted for a minimum of eight hours before blood was drawn. In comparison to non-fasting individuals, fasting participants were shown to be noticeably older, have higher BMIs, and total fat intakes, and be more probable to be current or former smokers. All other

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characteristics, however, showed no discernible difference between the two groups. (Table 1)

Table 1: Demographic information of the participants by fasting status

	Variables	Status		p
		Fasting	Non-fasting	
	Total	3296	4777	---
	Average Age	28	18	< 0.01
Gender	Male	49%	47.90%	0.34
	Use of Antihyperlipidemic agent	8.10%	8.30%	0.76
	CVD History	4.60%	3.50%	0.19
	Diabetes	6.50%	6.10%	0.61
	Hypertension	11%	10.10%	0.38
	Alcohol intake 4+ drinks per day	8.10%	6.60%	< 0.01
	Fat Use (mg per day)	71.8	68	< 0.01
	BMI	26.4	24.5	< 0.01
Physical activity	Inactive	48.50%	49.70%	0.14
	Mild	20.10%	18.30%	
	Active	31.50%	32%	
Cardiovascular Biomarkers	C-reactive protein (mg/dL)	0.16	0.16	0.7
	LDL cholesterol (mg/dL)	109	110	0.45
	HDL cholesterol (mg/dL)	54.1	54.2	0.82
Smoking	Past Smokers	14%	10.20%	< 0.01
	Current Smokers	13.30%	10.10%	

The research also discovered that larger proportions of patients who were fasting, smokers, and LDL cholesterol levels were linked to higher triglyceride levels. However, no additional factors were shown to be related to triglycerides. (Table 2)

Table 2: Demographic information of the participants by triglycerides quintiles

	Variables	Q5	Q4	Q3	Q2	Q1	p
	Total	1629	1643	1601	1608	1592	---
	Average Age	21	20	23	22	22	0.28
Gender	Male	47.70 %	45.90 %	49.50 %	50.10 %	48.90 %	0.14
	Use of Antihyperlipidemic agent	8%	8.70%	7%	9.20%	8.20%	0.71
	CVD History	3.90%	3.90%	3.80%	4.10%	4.20%	0.8
	Diabetes	6.30%	6.20%	5.90%	6.20%	6.90%	0.48

Amna Iqbal Butt
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	Hypertension	11.50 %	9.70%	10.30 %	9.70%	11.10 %	0.63
	Fasting Status more than 8 hrs	40.60 %	36.80 %	41%	42.90 %	43%	0.03
	Alcohol intake 4+ drinks per day	6.60%	6.60%	6.90%	8.50%	7.50%	0.41
	Fat Use (mg per day)	69.3	69.8	70.9	68.7	68.6	0.3
	BMI	25.3	25.6	25.4	25.3	25.1	0.37
Physical activity	Inactive	47.90 %	50.80 %	50%	47.80 %	49.60 %	0.63
	Mild	19.40 %	18.40 %	17.60 %	19.50 %	20.30 %	0.88
	Active	32.70 %	30.90 %	32.50 %	32.70 %	30.20 %	0.43
Cardiovascular Biomarkers	C-reactive protein (mg/dL)	0.38	0.16	0.15	0.16	0.17	0.32
	LDL cholesterol (mg/dL)	120	119	112	104	91	< 0.01
	HDL cholesterol (mg/dL)	54.5	53.5	53.5	54.8	54.4	0.79
Smoking	Past Smokers	11.80 %	11.60 %	12.60 %	10.80 %	11.90 %	0.05
	Current Smokers	11.40 %	11.70 %	11.90 %	11.50 %	10.40 %	0.04

According to the unadjusted model, those who fasted had triglyceride levels that were 3.65 mg/dL lower than those who weren't fasting. Even after accounting for possible confounding variables in the multivariate model, this difference continued to be statistically significant. (Table 3)

Table 3: Correlation between fasting status and triglycerides

Models	**Triglyceride levels**			**P value**
	Fasting	**Non-fasting**	**Diff**	
Adjusted	127	131	4.22	0.049
Unadjusted	115	119	3.65	0.01

The research also discovered that the relationship between triglyceride levels and fasting state varied depending on a number of variables. In contrast to other putative CVD risk factors, hypertension, the use of antihyperlipidemic drugs, and LDL cholesterol levels were observed to interact with fasting status. Individuals with and without hypertension, those on antihyperlipidemic medications, and those with high or low levels of LDL cholesterol were compared for their fasting and non-fasting triglyceride levels. The findings revealed that only those with hypertension, those on antihyperlipidemic medications, or those with LDL cholesterol levels under 130 mg/dL had substantially lower fasting triglyceride levels than those who weren't fasting. The data is shown in Table 4.

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Table 4: Correlation between fasting status and triglycerides distinguished by LDL cholesterol, use of antihyperlipidemic, and hypertension

Variables	Groups	Triglyceride levels			p
		Fasting	Non-fasting	Difference	
LDL cholesterol	More than 130	148	146	-1.49	0.73
	Less than 130	118	124	5.89	0.02
	More than 106	142	143	1.41	0.64
	Less than 106	107	114	6.46	0.03
Use of Antihyperlipidemic agent	No	123	125	2.41	0.3
	Yes	130	144	14.1	0.02
Hypertension	No	121	123	2.35	0.39
	Yes	117	131	14.24	0.03

In further investigation, non-fasting triglycerides remained greater than fasting triglycerides among people with LDL levels of cholesterol under 106 mg/dL, according to a revised cut-off point for LDL cholesterol levels (106 mg/dL).

Overall, the research offers evidence that lower triglyceride levels are associated with fasting status, especially in those with hypertension, who take antihyperlipidemic drugs, or who have LDL cholesterol levels below 130 mg/dL.

Discussions:

In the present cross-sectional investigation, we found that the values of fasting triglycerides in the whole population were 4 mg/dL less than those of non-fasting triglycerides. More significantly, the individuals' LDL cholesterol levels, usage of antihyperlipidemic drugs, and non-fasting and fasting triglyceride differences depended on their degrees of hypertension, use of these medications, and fasting triglyceride differences. Our understanding of the function of triglycerides in determining CVD risk will be improved by these results.

According to one theory, the quantity of fat consumed in the eight hours before blood sampling is the main factor influencing the distinction between non-fasting and fasting triglycerides [12]. The size of the distinction between non-fasting and fasting triglycerides wasn't substantially impacted by total fat consumption in our research, which contradicts this theory. Two arguments may be used to explain this: First, as stated in the Method section, the individuals' preceding diets were unknown at the time of blood collection, thus the total fat consumption in our study was determined using a 24-hour meal recall from midnight to midnight. As a result, one of the potential reasons for this discovery might be the untargeted fat consumption data. Second, defining the distinction between non-fasting and fasting triglycerides may depend more on other variables, such as lipid metabolic disorders, than on the quantity of fat consumed. Impairment of glucose or fat sensitivity may have a significant impact on non-fasting triglyceride levels, according to some research 13,14].

Triglycerides during a fast were substantially lower than those during a non-fast, which is in line with several human research [15,16,17]. Despite the fact that there was a 4 mg/dL average difference in triglycerides between fasting and non-fasting, not all subjects experienced this change. In this research, we discovered that people with hypertension, antihyperlipidemic drug usage, or lower levels of LDL cholesterol had non-fasting triglycerides that were significantly greater than fasting triglycerides. The main reason why fasting and non-fasting triglycerides differ in individuals with high blood pressure and antihyperlipidemic medication use is because both antihyperlipidemic and hypertension

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drug use are linked to risk factors that can raise triglycerides or cause lipid disorders. Insulin resistance, which results in a glucose problem [18] and higher triglyceride levels [19], has been reported to be positively connected to hypertension. Similar to those people, persons using antihyperlipidemic medicines were mostly experiencing lipid disorders while taking the antihyperlipidemic medication owing to the effectiveness of this class of drugs. We still don't fully understand the precise causes of the correlation between triglycerides and LDL cholesterol in the fasting state. However, a prior study [20] found that among individuals with reduced LDL cholesterol levels, the relationship between triglycerides and cardiovascular disease became independent. This conclusion is somewhat compatible with that study, nevertheless. As a result, additional research into the process is necessary for the future. Our use of a large number of participants in the current research has substantially increased the dependability of the findings, which is its main benefit. Furthermore, the individuals in our research are broad population representatives.

Being cross-sectional research with uncontrolled food consumption before blood collection is the primary limitation of our study. In addition, as was already indicated, we did not record information on food consumption prior to blood sampling. This might skew our findings in a negative way. In general, youthful people made up the study's participants. As a consequence, the findings may not apply to persons who are more experienced. The interaction test is also a low-power test, as was already indicated. Even though the cutoff for significance was established at 0.10, we could still have missed certain possible CVD risk variables that affected the difference between non-fasting and fasting triglycerides. On parameters including smoking, total fat consumption, BMI, and age, those who are not fasting and those who are fasting are not matched. Table 1 reveals that individuals who gave fasting samples were considerably older, had higher BMIs and total fat intakes, and had a greater proportion of current smokers. Each of these variables has the potential to raise triglyceride levels, which would tend to skew the findings in favor of the null. As a result, we may be able to identify triglyceride differences of a bigger size in the two groups if these parameters were comparable. The fact that the actual difference between non-fasting and fasting triglycerides might be considerably greater than what was found in our research provides indirect support for the reliability of our findings. Additionally, as matching would drastically limit our research's sample size and power, it is not a good choice for the current investigation. This may be attributed to two main factors: the sample sizes for the two groups were equivalent, and the gap between the groups was considerable. Lastly, the LDL level was determined, which might have influenced our findings.

Conclusions:

In our research, we delved into the impact of fasting and non-fasting triglycerides on the prognosis of cardiovascular ailments. Our findings indicated a mere 4 mg/dL disparity between the two groups. However, a closer inspection divulged that individuals with hypertension, antihyperlipidemic medication, or low LDL cholesterol levels displayed a range of 6-14 mg/dL difference, which implies that non-fasting triglycerides may be more precise in predicting future CVDs under these circumstances.

It's crucial to note that despite the subtle average contrast between fasting and non-fasting triglycerides, this slight difference could still affect their ability to anticipate CVDs. This is because the typical divergence in triglyceride levels between patients with and without incident coronary heart disease was a mere 15 to 19 mg/dL, with numerous individuals having normal levels beforehand. As a result, predicting future CVDs in some people may be challenging since the difference between fasting and non-fasting triglycerides can be as significant as 14 mg/dL.

While our research was solely cross-sectional and observational, it provides a solid foundation for future investigation, particularly in emphasizing the potential benefits of non-fasting triglyceride measures in specific categories. We eagerly anticipate future research that explores the prognostic value of fasting and non-fasting triglycerides in patients with hypertension, antihyperlipidemic medication, or low LDL

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cholesterol levels, as these studies will undoubtedly be highly informative.

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