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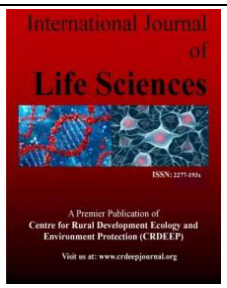

Full Length Research Paper

Comparison between Non Fasting and Fasting Lipogram Impact on Severity of Coronary Artery Disease

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ABSTRACT

***Background**: Coronary artery disease is the most common cause of death in cardiovascular disease. The rate of morbidity and mortality is high; the costs incurred for the treatment process are also very high, thus giving a bad impact on the welfare and quality of life both in patients, families, and health costs borne by the state. The proper management can reduce the number of losses, **Aim & Objectives:** the aim of the study **is** to compare impact of fasting and non-fasting lipid profile on severity of coronary artery disease by achieving two objectives were to correlate between fasting and non-fasting dyslipidemia and other traditional cardiovascular risk factors and to compare between fasting and non-fasting lipogram impact on atherosclerotic cardiovascular disease (severity of coronary artery disease). **Patient & methods**: this is prospective cohort study conducted on 400 Patients admitted in cardiac care unit in Zagazig university hospitals ,all patients were investigated and exposed to history taking and physical examination ,fasting and non-fasting lipid profile, ECG ,ECHO and comparative correlation were done among groups **results** :Comparative study between fasting and non-fasting measurements revealed; non-significant difference regarding fasting TC, TGs and HDL measurements ($p > 0.05$).Comparative study between fasting and non-fasting measurements revealed; highly significant increase in fasting LDL and TG/HDL ratio measurements; with highly significant difference ($p < 0.01$ respectively). **Conclusion**: There highly significant relationship between non-fasting and fasting lipogram and severity of coronary artery disease,*

Introduction

Most individuals consume several meals during the day and some consume snacks between meals; the postprandial state therefore predominates over a 24 h period. Nonetheless, in clinical practice, the lipid profile is conventionally measured in blood plasma or serum obtained after fasting for at least 8 h, and therefore may not reflect the daily average plasma lipid and lipoprotein concentrations and associated risk of cardiovascular disease (1,2).

Interestingly, evidence is lacking that fasting is superior tonon-fasting when evaluating the lipid profile for cardiovascular risk assessment. However, there are advantages to using non fasting samples rather than fasting samples for measuring the lipid profile (3,4,5), Since 2009, non-fasting lipid testing has become the clinical standard in Denmark, based on recommendations from the Danish Society for Clinical Biochemistry that all laboratories in Denmark use random non-fasting lipid profiles as the standard, while offering clinicians the option of re-measuring triglyceride concentrations in the fasting state if non-fasting values are>4 mmol/L (350 mg/dL) (6,7), Furthermore, the UK NICE guidelines have endorsed non-fasting lipid testing in the primary prevention setting since 2014 (8) . The most obvious advantage of non-fasting rather than fasting lipid measurements is that it simplifies blood sampling for patients, laboratories, general practitioners, and hospital clinicians and is also likely to improve patient compliance with lipid testing (9,4).). Indeed, patients are often inconvenienced by having to return on a separate visit for a fasting lipid profile and may default on essential testing.

Also, laboratories are burdened by a large volume of patients attending for tests in the morning. Finally, clinicians are burdened by having to review and make decisions on the findings in the lipid profile at a later date. This situation may also require an additional phone call, email, or even a follow-up clinic visit, placing extra workloads on busy clinical staff (10). Perceived limitations to adopting non-fasting lipid measurements include the following:

(i) Fasting before a lipid profile measurement is believed to provide more standardized measurements;
(ii) non-fasting lipid profiles are perceived as providing less accurate measurements and may make calculation of low-density lipoprotein (LDL)cholesterol via the Friedewald equation invalid; (iii) as fasting has been the clinical standard, it is unclear what values should be flagged as abnormal when using non-fasting rather than fasting plasma lipid profiles (10) .

The aim of the present joint consensus statement is to critically evaluate the use of non-fasting rather than fasting lipid profiles, and the clinical implications of this question with a view to providing appropriate guidance for laboratory and clinicians. Based on evidence from large-scale population studies and registries and on consensus of expert opinions, the European Atherosclerosis Society/European Federation of Clinical Chemistry and Laboratory Medicine (EAS/EFLM) joint consensus statement proposes recommendations on:
1. Situations when fasting is not required for a lipid profile
2. How laboratory reports should flag abnormal lipid profiles to improve compliance of patients and clinicians with concentration goals used in guidelines and consensus statements on cardiovascular disease prevention (11, 12).

Material and Methods
This was prospective cohort study conducted on 400 Patients admitted in cardiac care unit in Zagazig university hospitals.

Inclusion criteria were as follow: Patients admitted either for:
1. Elective coronary angiography.
2. Coronary angiography with acute coronary syndrome.
3. Available during the period of data collection.

Exclusion criteria for cases:
1. Seriously ill.
2. Suffering from mental disorders.
Patients admitted in cardiac care unit in Zagazig university hospitals

Sampling technique and sample size determination:
A) Sample size: 400 patients
B) Sampling technique: The participants were chosen by systematic random sampling from Patients admitted in cardiac care unit in Zagazig university hospitals

All patients included in the study were subjected to the following:
A . History taking: A sheet was performed for all patients included in this study, including:
1. Personal history: name, age and gender.
2. Complaint of present illness: onset, course, duration.
3. History of the present illness:

- Cardiovascular risk factors such as hypertension, diabetes mellitus, smoking, and prior myocardial infarction.

F) –

- History of addiction, symptoms suggestive of cardiac disease,

1. History of drug intake: current medications.
2. History of systemic disease.
3. Family history: of ischemic heart disease.

B . Full clinical examination:
1. General examination
2. Vital signs
3. Cardiac and chest examination examinations.

C-Electrocardiography (ECG): Twelve-lead surface electrocardiogram (ECG) was performed to all patients to confirm the diagnosis of acute coronary syndrome. ACS included acute myocardial ischemia and/or infarction due to an abrupt reduction in coronary blood flow which was associated with ST-segment elevation (ST elevation) or new left bundle-branch block on the electrocardiogram (ECG). The absence of persistent ST elevation was suggestive of NSTE-ACS (except in patients with true posterior myocardial infarction [MI]). Non ST-elevation acute coronary syndrome was subdivided on the basis of cardiac biomarkers of necrosis (e.g., cardiac troponin). If cardiac biomarkers were elevated and the clinical context is appropriate, the patient was considered to have NSTEMI; otherwise, the patient was deemed to have UA. ST depression, transient ST elevation, and/or prominent T-wave inversions may be present but were not required for a diagnosis of NSTEMI **(13)**.

D-Echocardiography: Standard resting transthoracic echocardiography (TTE) was performed to all patients using General Electric VIVID 7, Echo ultrasonograghy machine 2008, and M4S transducer, with a frequency of 1.5-4.3MHz.

E-Coronary angiography: Diagnostic coronary artery catheterization was done to patients, through a femoral artery access, to assess the severity and extent of CAD within hospital admission, those with significant occlusion performed coronary angioplasty with or without stenting. Evaluation of all coronary angiographies was made by at least two independent cardiologists.

F-Fasting and non-fasting lipid profile: This study assessed the blood samples of 400 Patients for lipid Profile. Blood samples were collected after 12 hr fast, 2 hr post-prandial samples were also collected and compare the results in fasting and fed states. The serum was separated and the assays were performed on the same day of sample collection. In addition, non-fasting and fasting concentrations vary similarly overtime and were comparable in the prediction of cardiovascular disease. To improve patient compliance with lipid testing, we therefore recommend the routine use of non-fasting lipid profiles, while fasting sampling may be considered when non-fasting triglycerides >5 mmol/L (440 mg/dL).

Administrative considerations:

- An Official permission was obtained from cardiac care unit in Zagazig University.

An official permission was obtained from the Institutional Research

- Approval from ethical committee in the faculty of medicine (Institutional Research Board IRB)

Ethical consideration:
Informed consent was obtained from all participants after being informed about the aims and process of the study as well as applicable objectives. The study procedures were free from any harmful effects on the participants as well as the service provided. The principal investigators have kept individual data as private information safely. There was no extra fee to be paid by the participants and the investigators covered all the costs in this regard.

Data management and Statistical Analysis

Data entry, processing and statistical analysis was carried out using MedCalc ver. 18.2.1 (MedCalc, Ostend, Belgium). Tests of significance (Kruskal-Wallis, Wilcoxon's, Chi square, logistic regression analysis, and Spearman's correlation) were used. Data were presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. P-values less than 0.05 (5%) was considered to be statistically significant.

Results

This was a prospective cohort study conducted on 400 cardiac care unit (CCU) patients; to compare the impact of fasting and non-fasting lipid profile on severity of coronary artery disease.

Descriptive data

The demographic and clinical variables in 400 CCU patients who were included in the study are shown in the following tables& figures:

Clinical data

Table 1: Basic clinical data among 400 CCU patients:

Variables		Frequency (%)
Age (years)		55.53 ± 9.08*
Height (cm)		172.1 ± 4.3*
Weight (kg)		81.4 ± 4.8*
BMI		27.5 ± 1.9*
Gender	Female	119 (29.8%)
	Male	281 (70.2%)

Table 2: Cardiovascular risk factors among 400 CCU patients:

Variables	Frequency (%)
HTN	305 (76.2%)
DM	187 (43.7%)
IHD	159 (39.7%)
Smoking	188 (45.2%)

Clinical data:

Table 3: Comparison between the 3 groups as regards basic clinical and risk factor data using Kruskal-Wallis and Chi square tests:

Variable		Mild CAD group (199)	Moderate CAD group (174)	Severe CAD group (27)	Kruskal-Wallis test
		Median (IQR)	Median (IQR)	Median (IQR)	P value
Age (years)		56 (51 – 63)	55 (51 – 63)	57 (57 – 59)	= 0.224
Height (cm)		171 (170 – 173)	172 (170 – 175)	170 (170 – 170)	= 0.314
Weight (kg)		80 (78 – 84)	80 (78 – 84)	91 (89 – 91)	< 0.0001**
BMI		28 (27 – 29)	26 (26 – 28)	31 (31 – 31)	< 0.0001**
Variable		Mild CAD group (199)	Moderate CAD group (174)	Severe CAD group (27)	Chi square test
					P value
Gender	Female	92 (46.2%)	27 (15.5%)	0 (0%)	= 0.0028**
	Male	107 (53.8%)	147 (84.5%)	27 (100%)	
HTN	+ve	132 (66.3%)	148 (85.1%)	25 (92.5%)	= 0.224
DM	+ve	93 (46.7%)	67 (38.5%)	15 (55.5%)	= 0.445
IHD	+ve	92 (46.2%)	40 (23%)	27 (100%)	< 0.0001**
Smoking	+ve	80 (40.2%)	81 (46.6%)	20 (74%)	= 0.157

Radiological data:

Table 4: Comparison between the 3 groups as regards radiological data using Kruskal-Wallis and Chi square tests:

Variable		Mild CAD group (199)	Moderate CAD group (174)	SevereCAD group (27)	Kruskal-Wallis test
		Median (IQR)	Median (IQR)	Median (IQR)	P value
EF (%)		50 (54 – 64)	50 (45 – 57)	43 (43 – 45)	= 0.368
Variable		Mild CAD group (199)	Moderate CAD group (174)	Severe CAD group (27)	Chi square test P value
ECG data	**Old MI**	40 (20%)	81 (46.6%)	13 (48.1%)	< 0.0001**
	NSTEMI	53 (26.6%)	65 (37.4%)	10 (37%)	= 0.258
Echo data	**AS**	53 (26.6%)	39 (22.4%)	7 (25.9%)	= 0.759
	MAC	26 (13.1%)	27 (15.5%)	7 (25.9%)	= 0.337

Paired comparative studies regarding all 400 patients

We further analyzed and compared all 400 (paired) patients according to the serial measurements of (fasting and non-fasting lipograms); data are shown in the following tables and figures:

- Serial lipogram assessments:

Table 5: Comparison between all patients as regards serial lipogram assessments:

Variables	Fasting lipogram Median (IQR)	Non-fasting lipogram Median (IQR)	Wilcoxon's test P value
TC (mg/dl)	186 (149 – 215)	185 (152 – 219)	= 0.965
TGs (mg/dl)	165 (81 – 212)	177 (168 – 184)	= 0.152
HDL (mg/dl)	49 (31 – 63)	50 (45 – 54)	= 0.378
LDL (mg/dl)	113 (67 – 137)	109 (53 – 132)	< 0.0001**
TG/HDL	3 (1 – 7)	2 (2 – 5)	< 0.0001**

Correlation studies

Table 6: Spearman's correlation analysis between Syntax score and baseline clinical data:

Associated Factor	Syntax score	
	Rho	P
Age (years)	0.146	=0.313
Height (cm)	0.0925	=0.0645
Weight (kg)	0.201	<0.0001**
BMI	0.102	=0.042*

Table 7: Spearman's correlation analysis between Syntax score and non-fasting laboratory data:

Associated Factor	Syntax score	
	Rho	P
TC (mg/dl)	-0.0232	=0.6443
TGs (mg/dl)	-0.0337	=0.5014
HDL (mg/dl)	0.0365	=0.4663
LDL (mg/dl)	0.453	<0.0001**
TG/HDL	0.380	<0.0001**
Direct LDL (mg/dl)	0.590	<0.0001**

Discussion

This was a prospective cohort study conducted on 400 cardiac care unit (CCU) patients; to compare the impact of fasting and non-fasting lipid profile on severity of coronary artery disease .

The main results of the study were as following:

From womb to tomb" it matters, argues the 2001 Institute of Medicine report; biological sex should be a fundamental consideration in human health and disease. Indeed, a number of human diseases manifest profound sex-based differences in prevalence, incidence, severity, and response to treatment. Yet, sex as a biological variable has long been ignored experimentally in the biomedical sciences and clinically in the application of evidence-based medicine (11) Such a sex bias is well entrenched in our understanding, It is slightly more common in men, there are generally at greater risk of coronary artery disease); family history; and race.(14) .Our study shows that out of the 400 patients, the majority (70.2%) of patients were males; while (29.8%) were females .The mean age of all patients was (55.53 ± 9.08) years, and the average height, weight and BMI were (172.1 ± 4.3) cm, (81.4 ± 4.8) kg, and (27.5 ± 1.9) respectively.

This coped with the study of(19)who studied Fasting and non-fasting lipid levels: influence of normal food intake on lipids, lipoproteins, Apo lipoproteins, and cardiovascular risk prediction in which out of 1930 patients with the age of the patients ranged from 19–90 years old with a mean age of 54 years, 77.6% of the patients were males, 543.

Also this agreement with study conducted by (16) who studied V Fasting Compared With Non-fasting Triglycerides and Risk of Cardiovascular Events in Women in which Of the 500 questionnaires distributed, a total of 468 participants responded. Male participants comprised 41.2% of the recruited participants (n=193) (20.73 ± 3.32) years and (23.80 ± 7.37) year. In the present study cardiovascular risk factors, (76.2%) of patients had HTN, (43.7%) had DM, (39.7%) had IHD, while (45.2%) of patients were smokers.

SYNTAX integration is the standard in the application of cardiovascular disease in recent years, and the related studies suggest that, which has acertain value for the prognosis of patients with cardiovascular disease, SYNTAX score .The SYNTAX score characterizes the anatomical extent of CAD in terms of the number of lesions, functional importance, and complexity .The obtained results showed that ECG data, (33.5%) of patients had old MI, and (32%) had NSTEMI. Also echocardiographic data, the average EF was (54.57 ± 9.1) %, and (24.7%) had AS, while (15%) had MAC. there was highly significant increase in old MI in moderate and severe CAD groups; compared to mild CAD group; with highly significant statistical difference ($p < 0.01$).

Also we found that, weight and BMI had a highly significant positive correlation with Syntax score; with highly significant statistical difference ($p < 0.05$ respectively). This coped with study conducted by reported that explored and analyzed SYNTAX score Ⅱ integral in acute myocardial infarction patients with emergency application of primary PCI, mainly compared the evaluation results of SYNTAX score Ⅱ points <21 points, 21 to 31 points and >31 .A standard lipid profile includes measurements of plasma or serum concentrations of total cholesterol, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (1) .In the present study, there was highly significant increase in fasting LDL and TG/HDL ratio, in severe CAD group; compared to other groups; with highly significant statistical difference ($p < 0.01$ respectively .Also there was highly significant increase in non-fasting LDL in moderate and severe CAD groups; compared to

mild CAD group; with highly significant statistical difference ($p < 0.01$) .There was non-significant difference as regards non-fasting TC, TGs and HDL ($p > 0.05$). This coped with the study of (15) who reported that Mean values (mg/dl) for LDL-C, HDL-C, TC and triglycerides (TG) were 140.6, 41.5, 217, and 160.9, respectively. Low HDL-C (<40 mg/dl) was present in 49.2% of CAD patients, increased LDL-C (>160 mg/dl) in 30.2%, increased triglycerides (>150 mg/dl) were present in 45% of patients. The pattern of lipid abnormalities differed according to gender and type of CAD. In males, the most frequent abnormality was a low HDL-C (55.4%). In females, the commonest abnormality was increased LDL-C (41.1%) .

Patients with MI had a lower level of HDL-C (HDL- C< 40 mg/dl) than AP patients (62.2% versus 40%, respectively). Females with MI have the highest prevalence rate of increased LDL-C present in 51.7%. Male patients with MI have the highest rates of increased TG (49.4%). When cutoff points for low HDL-C were based upon the National Cholesterol Education Program (<40 mg/dl for men and <50 mg/dl for women) 55.4% of male patients and 65.6% of female patients had abnormal low HDL-C. Among patients with CAD, a completely normal blood lipid profile was present in 20.2% of male patients and 29.9% of females. Low HDL-C (<40 mg/dl) as the only lipid abnormality was present in 21.4% of males and 7.6% of females .Perceived limitations to adopting non-fasting lipid measurements include the following: (i) fasting before a lipid profile measurement is believed to provide more standardized measurements; (ii) non-fasting lipid profiles are perceived as providing less accurate measurements and may make calculation of low-density lipoprotein (LDL) cholesterol via the Friedewald equation invalid; (iii) as fasting has been the clinical standard, it is unclear what values should be flagged as abnormal when using non-fasting rather than fasting plasma lipid profiles(16).

In this study, regarding Comparative between fasting and non-fasting measurements revealed; highly significant increase in fasting LDL and TG/HDL ratio measurements; with highly significant difference ($p < 0.01$ respectively). Also fasting LDL and TG/HDL ratio had a highly significant positive correlation with Syntax score; with highly significant statistical difference ($p < 0.01$ respectively). Among all studies comparing non-fasting with fasting lipid profiles, minor increase in plasma triglycerides and minor decreases in total and LDL cholesterol concentrations were observed, with no change in HDL cholesterol concentrations. These minor and transient changes in lipid concentrations appear to be clinically insignificant; however, (16) observed a transient drop in LDL cholesterol concentration of 0.6 mmol/L (23 mg/ dL) at 1 – 3 h after a meal in diabetic patients, which could be of clinical significance (17). The reduction in total and LDL cholesterol at 1 – 3 h after the last meal observed in individuals with and without diabetes became statistically insignificant after adjusting for plasma albumin concentration as a marker of fluid intake; 3,9 therefore, such a drop in total and LDL cholesterol is unrelated to food intake, noting that a similar drop may even be observed in a fasting lipid profile, since water intake is allowed ad libitum before a fasting blood test(10). The relationship between BMI, other cardiovascular risk factors, and the prevalence and risk of CAD are complex. Obesity and/or an increased BMI are independently associated with greater risk of insulin resistance, metabolic syndrome, diabetes, hypertension and dyslipidaemia and data suggest that the presence of these comorbidities may be more important markers of CAD than obesity alone. Further, there is increasing evidence of a relationship between obesity and systemic inflammation, including an increased production of inflammatory factors such as leptin, tumor necrosis factor-a, interleukin-6, and resistin, as well as decreased production of adiponectin (18).

The present study showed that the increase in BMI, and IHD; had an independent effect on increasing the probability of (moderate-severe CAD) occurrence; with significant statistical difference ($p < 0.05$ respectively) .In this study, we recommended that each country, state, and/or province in individual countries should adopt strategies for implementing routine use of non-fasting rather than fasting lipid profiles as well as flagging of abnormal values based on desirable concentration cut-points rather than using traditional reference intervals. Ideally, there should be one standard for reporting lipid profiles in each country as also accreditation bodies should be aware of the present consensus statement.

Conclusion

- There is a highly significant correlation between non-fasting and fasting lipogram and severity of coronary artery disease.
- There is a highly significant positive correlation between fasting LDL and TG/HDL ratio and severity of coronary artery disease (syntax score).
- There is a highly significant positive correlation between non-fasting LDL , TG/HDL and direct LDL and severity of coronary artery disease (syntax score).

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