Research Article

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Anna Skoczyńska*, Barbara Turczyn, Anna Wojakowska, Bogusława Kreczyńska, Marta Skoczyńska, Kamila Wojtas

Postprandial decrease in LDL-cholesterol in men with metabolic syndrome

Abstract: Background: In some epidemiological studies, blood lipids are determined at non-fasting state, which may impact cardiovascular risk estimation. The aim of this study was to evaluate postprandial LDL-C changes in men with newly diagnosed metabolic syndrome (MetSy). Methods: 36 male patients were examined: 12 men with and 24 men without MetSy. The fat tolerance test was performed before and after a three-month hypolipidemic treatment. Serum lipids were measured using routine methods, lipid peroxides (LPO) colorimetrically, apolipoproteins A-I, B, and hsCRP immunoturbidimetrically. Results: The postprandial increase in triglycerides was associated with a decrease in LDL-C and a small decrease in apo B. In men with MetSy, the mean change in LDL-C (-19.5 ± 2.3 mg/dl) was greater than in healthy men (-5.7 ± 3.8 mg/dl). All lipid changes (ΔTG, ΔLDL-C and ΔLPO) were linearly dependent on the postprandial non-LDL-cholesterol. After three months of hypolipidemic treatment, in all men with MetSy, the apoB/apoA-I ratio remained the same as before the therapy. Conclusion: In men diagnosed with MetSy, postprandial decreases in LDL-cholesterol may cause underestimation of cardiovascular risk. After three months of hypolipidemic treatment, there was only a partial reduction in this risk, as the apoB/apoA-I ratio remained the same.

Keywords: Postprandial LDL-cholesterol; metabolic syndrome; apoB/apoA ratio.

List of abbreviations

BMI – body mass index
LDL-C–low density lipoprotein cholesterol
MetSy–metabolic syndrome
LPO–lipid peroxides
hsCRP–high-sensitivity C-reactive protein
TG–triglycerides
apoB–apolipoprotein B
apo A-I–apolipoprotein A-I
HDL-C–high density lipoprotein cholesterol
HDL_3 (HDL_2) – C–high density lipoprotein $_3$ ($_2$) cholesterol
HTG–hypertriglyceridemia
FTT–fast tolerance test
TC–total cholesterol
R-C–remnant cholesterol
SE–standard error
LIPID study–Long-Term Intervention with Pravastatin in Ischaemic Disease study
AMORIS study–Apolipoprotein-Related Mortality Risk study
FINRISK study–Finland Cardiovascular Risk Study
NCEP–National Cholesterol Education Program
VLDLs–very low density lipoproteins
IDLs–intermediate density lipoprotein cholesterol

*Corresponding author: Anna Skoczyńska: Wroclaw Medical University, Department of Internal and Occupational Diseases, and Hypertension, Borowska 213, 50-556 Wrocław, Poland, tel.: 71-7364005, fax: 71-7364009, E-mail:annaskoc@ak.am.wroc.pl
Barbara Turczyn, Anna Wojakowska, Bogusława Kreczyńska, Marta Skoczyńska, Kamila Wojtas, Department of Internal Diseases and Hypertension, Wrocław Medical University, Wrocław, Poland

1 Introduction

Metabolic syndrome (MetSy) is defined as a cluster of cardiovascular risk factors, including: central obesity, insulin resistance, prediabetes or diabetes, atherogenic dyslipidemia and hypertension. However, the special treatment of

patients with MetSy is a subject of controversy. Gerald M. Reaven, recognized as the greatest authority in the field of research on MetSy, a few years ago stated that metabolic syndrome "is dead" [1]. The World Health Organisation has recently concluded that this syndrome has "limited practical utility as a diagnostic or management tool" [2]. On the other hand, it has been well documented that metabolic syndrome is associated with arterial stiffness [3], maladaptive vascular remodeling [4] and early development of atherosclerosis, especially in carotid arteries [5]. Furthemore, meta-analysis of prospective epidemiological studies confirmed that metabolic syndrome is an important risk factor for cardiovascular diseases' incidence and mortality [6-9].

Atherogenic dyslipidemia is an abnormal blood lipid pattern which includes: decreased high density cholesterol (HDL-C), hypertriglyceridemia (HTG) and a presence of small low density lipoproteins (LDL). The anti-atherogenic, multidirectional action of HDL is well documented [10-13]. Also, the atherogenic effect of hypertriglyceridemia, connected with their pro-inflammatory [14], pro-thrombotic [15] and pro-oxidative [16] action is well recognized. In subjects with HTG, all lipoproteins, including HDL, may be oxidatively modified, which leads to procoagulation state [17].

At present, the elevation of non-fasting triglycerides (TG) is recognized as an independent residual risk factor for cardiovascular diseases, although there is no consensus about appropriate target level [15,18]. A level of non-fasting TG ≥5 mmol/L vs <1 mmol/L determines a significantly increased risk of myocardial infarction, ischemic stroke and early death in the general population [19]. There is an agreement that after a meal, typically, there is an increase in chylomicrons, VLDL and lipid peroxides (LPO) levels [18-22].

As modern men most of the day remain in a state of postprandial lipemia, the lipid pattern should be determined not only at fasting, but also in postprandial state. Furthermore, some questions arise, regarding the significance of postprandial measurements, especially LDL cholesterol, in cardiovascular risk estimation. Data on how a meal impacts LDL-C is scarce [20]. This problem is especially relevant for patients diagnosed with MetSy, who generally display normal or slightly increased total- and LDL-cholesterol levels, as is presented in this study.

The aim of this study was to evaluate postprandial LDL cholesterol changes in men diagnosed with metabolic syndrome in comparison to men without MetSy, and to assess meal-induced changes in LDL cholesterol after a three-month hypolipemic treatment. Particular attention was paid not only to serum LDL-cholesterol fraction, but also to HDL_2- and HDL_3 subfractions, as well as to apoB- and apoA-lipoprotein concentrations, all measured at fasting state, and three hours after a standardized fat-rich breakfast.

2 Patients and methods

2.1 Patients

36 male volunteers were included in the study: 12 men newly diagnosed with MetSy and 24 men without metabolic syndrome. The sample was collected among hospital employees and their friends, interested in blood lipid measurements. In each of the examined subject, medical history and physical examination were performed, arterial blood pressure, height and weight were measured and body mass index (BMI) was calculated. The sample size was small. Nevertheless, it exceeded the value appointed automatically in power analysis by Statistica software (N = 32, the power of the analysis: 0,9044).

A diagnosis of the metabolic syndrome was established on the basis of a "harmonized" version of definition from the Adult Treatment Panel III and the International Diabetes Federation [2]. Exclusion criteria were: already diagnosed MetSy or diabetes and taking lipid-lowering or anti-diabetic drugs prior to the study. Among subjects, nobody had been diagnosed with diabetes, while all men newly diagnosed with metabolic syndrome had also newly diagnosed glucose intolerance (the fasting glucose concentration was 115 ± 10 mg/dl, and postprandial glucose did not reach value of 140 mg/dl (122 ± 9 mg/dl).

Arterial hypertension has been identified in the all groups. All hypertensive men were treated with an angiotensin-converting-enzyme inhibitor or a sartan, in some cases in combination with a diuretic or a beta blocker. Until the beginning of our study, no other drugs, including lipid-lowering drugs, anti-diabetic drugs or aspirin had been given.

The study took place in Department of Internal Diseases and Hypertension, Wroclaw Medical University in February–November 2011. The period of our investigation lasted three months. The written informed consent was obtained from all men taking part in the study. The study was approved by Local Ethical Committee in Wroclaw and followed the Declaration of Helsinki.

2.2 Fat tolerance test (FTT)

Regular diet prior to the study was defined by all subjects as rich in fat. After an 8-hour fast, all patients were given a single standardized fat-rich breakfast meal: 100g of fat, 25g of carbohydrates and 100g of protein (1500 kcal). Only drinking water was allowed postprandially. Venous blood samples were drawn before and 3h after meal consumption. After the analysis of fasting lipid serum values, men diagnosed with MetSy or mixed hyperlipemia started individualized therapy. The applied therapies were non-pharmacological and pharmacological; consisting of therapeutic diet and therapeutic lifestyle in all patients, fibrates in men with MetSy, statin or statin plus fibrate in men with mixed hyperlipemia. The kind and dose of fibrate or statin was dependent on the degree of lipid disturbances. The therapies were prescribed by a clinical physician and the same doctor followed all patients. After a three-month therapy, FTT was repeated. Not all participants were tested after 3 months, as healthy normolipidemic patients did not attend the second postprandial test. In the groups of men with MetSy or mixed hyperlipidemia, no one dropped out of the study.

2.3 Biochemical measurements

Blood was centrifuged at 1000 g for 20 minutes at 4°C. Each serum sample was divided into three tubes and stored at -20°C. Serum lipids were measured using standard methods. Total cholesterol (TC), triglycerides (TG), and HDL cholesterol (HDL-C) were measured using enzymatic assay SPINREACT (SantEsteve De Bas, Girona, Spain). LDL-cholesterol (LDL-C) was estimated among patients with a TG concentration lower than 400 mg/dl by the Friedewald equation. To assess HDL_2 and HDL_3 cholesterol QUANTOLIP® HDL (Technoclone GmbH, Vienna, Austria) precipitation test was used. Remnant cholesterol (R-C) was calculated as postprandial total cholesterol minus low-density lipoprotein cholesterol minus high-density lipoprotein cholesterol [19].

Serum lipid peroxides (LPO) level was measured colorimetrically, using Satoh method. Glucose was also measured by a colorimetric method, using DADE Behringer test. Serum apolipoprotein A-I (apoA-I) and apolipoprotein B (apoB) were determined by the immunoturbidimetric method DADE Behringer Marburg GmbH (Marburg, Germany). The serum high-sensitivity C-reactive protein (hsCRP) was determined using the CardioPhasehs CRP Dade Behringer preparation with the molecular immunonephelometric method, accordingly to N Rheumatology Standard SL (BCR-CRM 470).

2.4 Statistical analysis

Statistical analysis was performed with the use of 'Statistica PL 10.0' computer program (Stat Soft, Poland). The distribution of the variables was checked with W-Shapiro-Wilk test. All variables and their changes showed an approximately normal distribution, and were reported as mean ± standard error (SE). Statistical analysis included t tests and analysis of variance. Statistically significant differences between the independent means were estimated with LSD post-hoc test. Values of $p<0.05$ were assumed as statistically significant. Correlations between parameters were assessed by Spearman's correlation coefficient.

3 Results

In all groups of men (with MetSy and without MetSy), physiological dependences between apoA and HDL-cholesterol ($r = 0.6734$; $p<0.05$ and $r = 0.4439$, $p<0.05$) and between apoB, and LDL-cholesterol level ($r = 0.8356$; $p<0.001$ and $r = 0.5201$, $p<0.01$, in men with and without MetSy, respectively) were shown. On the basis of Figure 1, showing the correlation between total- and LDL-cholesterol in the group of men without MetSy, two subgroups of men may be identified: with total cholesterol level lower or greater than 200 mg/dl. Therefore, the control group was divided into control I and control II, depending on the total cholesterol concentration. Whereas the control I subgroup included healthy men with normal lipid pattern, men from the control II group were newly diagnosed with mixed hyperlipemia.

There were many differences between the three groups at the beginning of the study, Table 1. In comparison to normolipemic men, men that we diagnosed with MetSy, according to our findings, displayed i.a. higher BMI, serum TG, total cholesterol, glucose and hsCRP, and lower HDL cholesterol concentration.

The postprandial changes in triglycerides, LDL cholesterol and apolipoprotein B

The meal-induced postprandial changes in serum TG (ΔTG) were not dependent on fasting TG levels ($r = -0.0805$) but were linearly dependent on postprandial non-LDL cholesterol ($r = 0.5208$; $p<0.01$) and remnant cholesterol (R-C; $r = 0.500$, $p< 0.01$). These TG changes (mean ΔTG ± SE) in men diagnosed with MetSy (56.7 ± 10.1 mg/dl) were
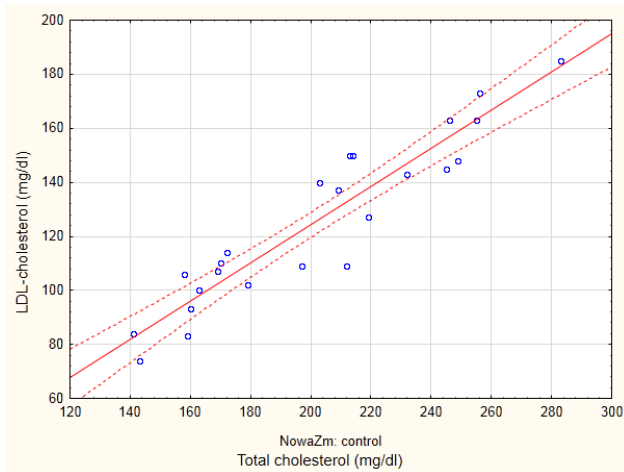
Figure 1: The dependence between total and low density lipoprotein (LDL) - cholesterol in the group of men without metabolic syndrome

Figure 2: Postprandial changes (mean ± standard error) in triglycerides (delta TG) in men diagnosed with metabolic syndrome (MS) in comparison to healthy men (control I group) and men diagnosed with mixed hyperlipemia (control II group) before- (delta TG) and after (delta TG-3) a three month hypolipidemic treatment

* p<0.05 in comparison to delta TG in fat tolerance test performed before the treatment

slightly lower in comparison to healthy men (88.4 ± 21.6 mg/dl) or men diagnosed with mixed hyperlipemia (115.1 ± 41.1 mg/dl), Figure 2. In MetSy group, the postprandial increase in TG was associated with a significant decrease in LDL cholesterol (p < 0.01), Table 2. This decrease (mean ∆LDL-C ± SE) in MetSy group (-19.5 ± 2.3 mg/dl) was greater (p = 0.0125), in comparison to healthy men (-5.7 ± 3.8 mg/dl), Figure 3. A linear correlation between postprandial non-LDL cholesterol and ∆LDL-C (r = -0.4605; p<0.01) was shown. Also, the dependence between postprandial remnant cholesterol and ∆LDL-C (r = -0.4201; p<0.05) was observed. In all studied groups, the postprandial decrease in LDL-C was associated with a small decrease in apo-B concentration, Table 2.

3.1 The postprandial changes in lipid peroxides

Men with MetSy displayed postprandial reduction in LPO concentration, whereas in healthy men (control I group) and men with mixed hyperlipemia (control II group), LPO level measured after the meal was higher than the one measured at fasting state, Figure 4. Similarly to postprandial changes in TG or LDL-C, meal-induced LPO changes were dependent on the postprandial non-LDL-C (r = -0.4469; p<0.05) and R-C (r = -0.4059; p<0.05). The mean fasting and postprandial remnant cholesterol concentrations were significantly greater in MetSy men in comparison to healthy subjects (p<0.001), Table 2.
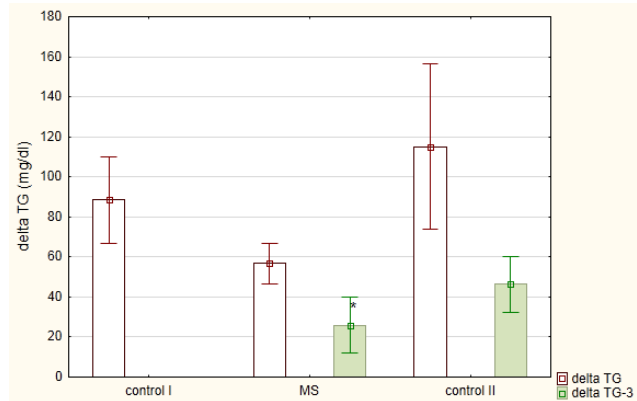

Figure 3: Postprandial changes (mean ± standard error)in low density lipoprotein (LDL)-cholesterol in men diagnosed with metabolic syndrome (MS) in comparison to healthy men (control I) and men with mixed hyperlipemia (control II) before- (delta LDL) and after (delta LDL-3) a three month hypolipidemic treatment

* p<0.05 in comparison to delta LDL in the control I group

3.2 The postprandial changes in HDL cholesterol, apolipoprotein A and hsCRP

The meal-induced HDL-C changes in studied groups were presented in the Figure 5. They were linearly dependent on fasting HDL_2-C (r = -0.6268; p<0.01). Meal induced changes in apolipoproteins A-I and hsCRP were statistically insignificant, Table 2.

Table 1: Basal characteristics of group of men diagnosed with MetS, healthy normolipemic men (control I) and group of men diagnosed with mixed hyperlipidemia (control II) in a fasting state

			Group		
			MetS (12 men)	Control I (14 men) total cholesterol < 200 mg/dl	Control II (10 men) total cholesterol > 200 mg/dl
Age	years		51.91 ± 2.34*	40.75 ± 2.73	48.30 ± 4.13
BMI	kg/m²		33.83 ± 1.52***	26.78 ± 0.94	25.30 ± 0.65
Smokers	number/all		9/12	4/14	4/10
	%		75%	29%	40%
Hard drinkers	number/all		0/12	0/14	0/10
	%		0%	0%	0%
Hypertension	number/all		9/12*	5/24	5/10
	%		75%	21%	50%
T-C	mg/dl	mmol/l	219.91 ± 8.67***	174.35 ± 6.38	240.60 ± 7.24***
			5.68 ± 0.22	5.19 ± 0.21	6.22 ± 0.18
TG	mg/dl	mmol/l	275.41 ± 21.93***	100.00 ± 6.85	188.70 ± 24.23**
			3.11 ± 0.25	1.55 ± 0.16	2.12 ± 0.27
HDL-C	mg/dl	mmol/l	39.38 ± 1.84*	46.64 ± 1.9	53.50 ± 3.28*
			1.01 ± 0.05	1.29 ± 0.05	1.37 ± 0.09
Glucose	mg/dl	mmol/l	114.83 ± 10.23*	92.14 ± 3.29	89.70 ± 1.82
			6.39 ± 0.57	5.11 ± 0.18	5.0 ± 0.10
LPO	nmol/ml		3.75 ± 0.46	2.76 ± 0.37	2.10 ± 0.34
hsCRP	mg/l		2.36 ± 0.51*	1.05 ± 0.27	1.71 ± 0.54
Apo A-I	g/l		1.43 ± 0.10	1.49 ± 0.04	1.56 ± 0.08
Apo B	g/l		1.11 ± 0.12	1.06 ± 0.04	1.28 ± 0.06

Results are presented as mean ± standard error (SE). T-C: total cholesterol; TG: triglycerides; HDL-C: HDL cholesterol; LPO: lipid peroxides; hsCRP: high sensitivity C-reactive protein; apo A-I: apolipoprotein A-I; apo B: apolipoprotein B
*,**,*** differences statistically significant in comparison to group of normolipemic men (control I): * $p<0.05$; ** $p<0.01$; *** $p<0.001$

3.3 The postprandial changes in lipids, apolipoproteins and other parameters in men with MetSy or mixed hyperlipidemia after a three-month hypolipidemic therapy

The parameters measured before and after three month hypolipidemic treatment, were compared using paired Student t test and checked by paired Wilcoxon test and sign test. It was shown that after a three-month treatment, men diagnosed with MetSy and mixed hyperlipemia displayed significantly lower, in comparison to initial concentrations, serum total cholesterol, TG, non-LDL, non-HDL and postprandial remnant cholesterol levels, Table 3.

Fat tolerance test performed in men diagnosed with MetSy after a three month treatment showed significantly lower changes in TG ($p<0.05$) in comparison to changes induced by meal before the treatment, Figure 2. LDL-C level, which before treatment decreased postprandially, after the treatment was similar before and after a meal; a similar pattern was observed for LPO. On the contrary, HDL-C, and especially HDL$_2$-C, before the treatment remained on a similar level before and after a meal, and after the treatment decreased postprandially. Level of R-C before the treatment increased after a meal; after the treatment did not fluctuate between fasting and non-fasting levels, Tables 2 and 4.
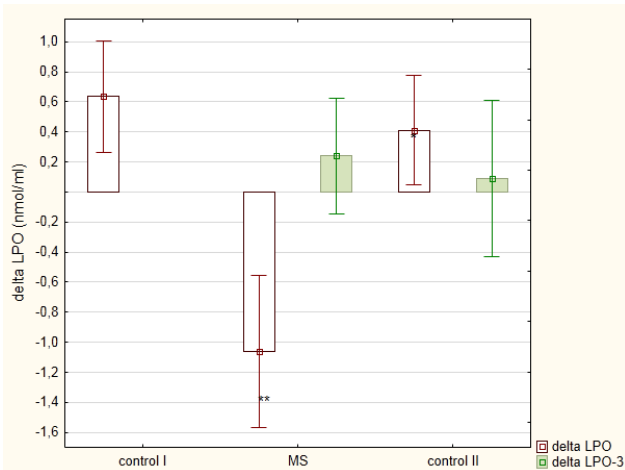
Figure 4: Postprandial changes (mean ± standard error) in lipid peroxides (LPO) in men diagnosed with metabolic syndrome (MS) in comparison to healthy men (control I) and men with mixed hyperlipemia (control II) before- (delta LPO) and after (delta LPO-3) a three month hypolipidemic treatment

* p<0.05 in comparison to delta LPO in the control I group

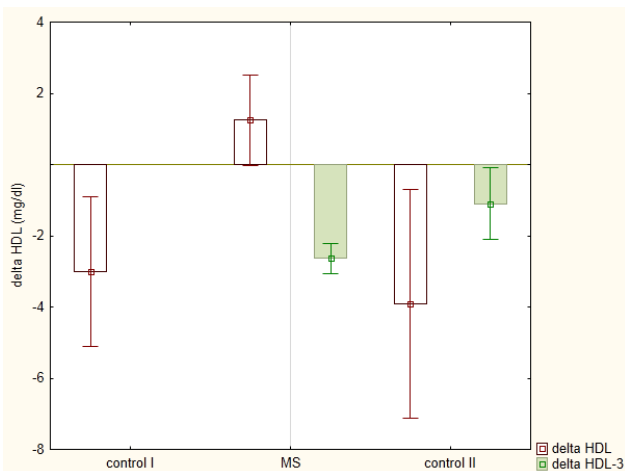** p<0.01 in comparison to delta LPO in the control I group

Figure 5: Postprandial changes (mean ± standard error) in high density lipoprotein (HDL) - cholesterol in men diagnosed with metabolic syndrome (MS) in comparison to healthy men (control I) and men with mixed hyperlipemia (control II) before- (delta HDL) and after (delta HDL-3) a three month hypolipidemic treatment

Additionally, in men with mixed hyperlipemia, hypolipidemic treatment led to decrease in LDL cholesterol, apo B lipoprotein, and, at fasting state, also apoB/apoA-I ratio. On the contrary, in men with MetSy, there were no significant changes in LDL cholesterol, apo B and apo B/apo A-I ratio during the three month observation, Table 3.

4 Discussion

A fasting TG level ≤ 150 mg/dl [21], a non-fasting TG level (measured at any time within up to 8 hour after any normal meal) ≤ 180 mg/dl, as well as a postprandial TG level (measured at a fixed time within up to 8 hour of a standardized fat tolerance test; FTT) ≤ 220 mg/dl [18], should be considered as desirable serum TG concentrations. In the context of these recommendations, only in the group of healthy, normolipemic men, a fasting TG level and postprandial response were physiological (Table 2). However, in men diagnosed with mixed hyperlipidemia, after a three-month hypolipidemic treatment, fasting and postprandial TG levels decreased to normal levels. Simultaneously, the three-month treatment decreased fasting and postprandial TG concentrations to levels close to normal also in men diagnosed with MetSy. The decrease in TG concentrations after a hypolipidemic therapy is usually observed as a result of the action of peroxisome proliferator-activated receptors alpha (PPAR-alpha) agonists [22]. Not fully satisfactory effect of hypolipidemic treatment in patients diagnosed with MetSy has been observed also in other studies [23,24].

The difference between men with MetSy and mixed hyperlipemia was the lack of hypolipidemic treatment effect on apo B and apo B/apo A-I ratio in men with MetSy (Table 3). Contrarily, in men with mixed hyperlipemia, significant decreases in apo B and apo B/apo A-I ratio at fasting state were observed. The value of the apo B/apoA-I ratio is a particularly effective parameter for risk assessment of atherosclerosis: the greater the value of the ratio, the greater the risk of cardiovascular disease [25]. Some studies, (i.e. Copenhagen City Heart Study, LIPID or AMORIS) showed that apo B has a stronger capacity as a predictor of cardiovascular risk than both LDL-C and non-HDL-C [26,27]. In AMORIS study, fatal myocardial infarction was related to increased values of apo B/apo A-I [28]. Simultaneously, apo B may be more closely associated with metabolic syndrome than either LDL-C, or non-HDL-C [29]. This study showed that in men with MetSy, a three-month hypolipidemic treatment was efficient with regard to lipid profile (reduced the TG, total and non-HDL cholesterol) but did not reduce cardiovascular risk determined by apo B/apo A-I ratio.

In some randomized multicenter studies on cardiovascular risk assessment, non-fasting lipid levels are determined. Correction of non-fasting serum TG to fasting values in Finnish population under the National FINRISK 2007 Study reduced miscalculation of high LDL-C in population from 5.1 to 1.6%, and the occurrence of metabolic syndrome from 4.2 to 2.1% [30]. This study showed

Table 2: Fasting and postprandial lipids and other parameters measured before beginning of the hypolipidemic treatment

		Group					
		MetSy 12 men		Control I: 14 normolipemic men		Control II: 10 men with mixed Hyperlipemia	
		mg/dl	mmol/l	mg/dl	mmol/l	mg/dl	mmol/l
T-C:	fasting	219.91 ± 8.67	5.67 ± 0.22	174.35 ± 6.38***	4.48 ± 0.16	240.60 ± 7.24	5.52 ± 0.19
	postprandial	218.50 ± 11.03	5.62 ± 0.28	178.00 ± 7.26**	4.59 ± 0.18	249.30 ± 6.69*	6.42 ± 0.17
TG:	fasting	275.41 ± 21.93	3.11 ± 0.25	100.00± 6.85***	1.13 ± 0.08	188.70 ± 24.23*	2.1 ± 0.27
	postprandial	350.83 ± 30.25	3.97 ± 0.34	182.85± 23.68***	2.06 ± 0.27	292.20 ± 49.35	3.3 ± 0.55
	f-p difference	*		**		**	
LDL-C:	fasting	134.10 ± 12.31	3.46 ± 0.32	108.83 ± 7.42*	2.79 ± 0.19	149.30 ± 7.11***	3.84 ± 0.18
	postprandial	108.60 ± 8.60	2.79 ± 0.22	102.42 ± 7.51	2.63 ± 0.19	141.50 ± 9.63*	3.64 ± 0.25
	f-p difference	**					
Non LDL-C:	fasting	94.33 ± 5.01	2,43 ± 0.13	66.64 ± 2.3***	1.73 ± 0.06	91.40 ± 3.10	2.35 ± 0.08
	postprandial	110.10 ± 6.22	2.84 ± 0.16	80.34 ± 4.3**	2.07 ± 0.11	107.80 ± 8.82	2.79 ± 0.23
	f-p difference	**		**		*	
HDL-C:	fasting	39.38 ± 1.84	1.00 ± 0.05	46.64 ± 1.99*	1.12 ± 0.05	53.50 ± 3.28***	1.37 ± 0.09
	postprandial	39.93 ± 2.55	1.03 ± 0.07	43.98 ± 2.27	1.13 ± 0.06	49.60 ± 2.70*	1.29 ± 0.07
HDL_2-C:	asting	7.35 ± 1.18	0.19 ± 0.03	9.00 ± 1.45	0.23 ± 0.04	12.52 ± 2.76	0.32 ± 0.07
	postprandial	7.26 ± 1.46	0.18 ± 0.04	10.65 ± 1.64	0.27 ± 0.04	8.51 ± 1.10	0.22 ± 0.03
HDL_3-C:	fasting	32.00 ± 1.75	0.82 ± 0.05	38.06 ± 1.84*	0.98 ± 0.05	42.03 ± 2.36**	1.06 ± 0.07
	postprandial	32.08 ± 1.59	0.82 ± 0.04	39.60 ± 2.01**	1.00 ± 0.05	41.33 ± 2.65**	1.08 ± 0.06
Non HDL-C:	fasting	180.53 ± 7.94	4.64 ± 0.20	127.71 ± 6.17***	3.30 ± 0.16	187.10 ± 8.22	4.82 ± 0.21
	postprandial	178.56 ± 10.09	4.59 ± 0.26	134.22 ± 7.74***	3.45 ± 0.19	199.70 ± 7.31	5.16 ± 0.19
R-C:	fasting	46.53 ± 10.23	1.42 ± 0.11	20.70 ± 1.4***	0.49 ± 0.05	38.00 ± 4.92**	0.98 ± 0.13
	postprandial	138.63 ± 9.71	1.81 ± 0.17	90.01 ± 8.7***	0.85 ±0.09	149.57 ± 9.81	1.49 ± 0.25
	f-p difference	***		***		***	
Glucose:	fasting	114.83 ± 10.23	6.40 ± 0.57	92.14 ± 3.29*	5.11 ± 0.18	90.03 ± 1.81*	5.01 ± 0.10
	postprandial	121.66 ± 9.04	6.82 ± 0.50	93.01 ± 2.90**	5.17 ± 0.16	96.78 ± 4.10*	5.30 ± 0.23
LPO (nmol/ml):	fasting	3.75 ± 0.46		2.75 ± 0.37		2.10 ± 0.34*	
	postprandial	2.73 ± 0.29		3.50 ± 0.41		2.61 ± 0.28	
	f-p difference	*					
hsCRP (mg/l):	fasting	2.36 ± 0.51		1.10 ± 0.27*		1.71 ± 0.54	
	postprandial	2.28 ± 0.53		0.94 ± 0.22*		1.6 ± 0.56	
	f-p difference						

Table 2 continued: Fasting and postprandial lipids and other parameters measured before beginning of the hypolipidemic treatment

ApoA-I (g/l):			
fasting	1.44 ± 0.10	1.49 ± 0.04	1.56 ± 0.08
postprandial	1.47 ± 0.08	1.43 ± 0.07	1.52 ± 0.08
ApoB (g/l):			
fasting	1.11 ± 0.12	1.06 ± 0.04	1.28 ± 0.06
postprandial	1.09 ± 0.12	0.99 ± 0.05	1.18 ± 0.06
ApoB/ApoA-I:			
fasting	0.78 ± 0.06	0.72 ± 0.03	0.83 ± 0.05
postprandial	0.73 ± 0.07	0.71 ± 0.03	0.79 ± 0.05

Results are presented as mean ± standard error (SE). T-C: total cholesterol; TG: triglycerides; LDL-C: LDL cholesterol; HDL- (HDL2-; HDL3-) C: HDL (HDL2-; HDL3-) cholesterol; R-C: remnant cholesterol; LPO: lipid peroxides; hsCRP: high sensitivity C-reactive protein C; apoA-I (B): apolipoprotein A-I (B)

f: fasting, p: postprandial, f-p difference: the difference between the values measured in the fasting and postprandial state; * $p<0.05$; **$p<0.01$; ***$p<0.001$

*,**, *** differences statistically significant in comparison to MetSy group: * $p<0.05$; **$p<0.01$; ***$p<0.001$

a lower, in comparison to fasting values, LDL cholesterol after three hours of the fat tolerance test in men diagnosed with MetSy. Also in other studies, performed in patients with diabetes mellitus type 2, LDL cholesterol, measured by various methods, was postprandially reduced [31]. A decrease in LDL-C after a meal may occur in all people, including a healthy population (LDL-C tendency to decrease postprandially was observed also in normolipemic men in our study), and may not be in any way connected with disturbances in lipid metabolism. All the same, as LDL-C level is the most often used predictor of cardiovascular diseases, lower levels of non-fasting LDL cholesterol may cause the underestimation of cardiovascular risk, which could result in a shift of studied populations to lower-risk groups.

Our study has also shown that postprandial LDL-C reduction was greater in men with MetSy, comparing to healthy men and men diagnosed with mixed hyperlipemia (Figure 3). This difference was not caused by different fasting levels, which were similar in all groups of men. Simultaneously, postprandial LDL-C changes, similarly to changes in TG and LPO, were dependent on postprandial non-LDL cholesterol and remnant cholesterol levels. Postprandial remnants, originating from chylomicrons and VLDLs, may reflect intestinal absorption or utilization of exogenous cholesterol.

One could suspect that the absorption of cholesterol in men with MetSy is higher in comparison to healthy men, as their postprandial remnant cholesterol is significantly greater than in controls (Table 2). However, meal-induced R-C changes in all studied groups (men with MetSy, healthy men and men with mixed hyperlipemia)

were similar. Thus, if the absorption of exogenous cholesterol was similar in all groups, the reason for the different decreases in LDL cholesterol may be a different degree of its utilization. Postprandial utilization of LDL, deriving mainly from VLDLs, is associated with the accumulation of cholesterol in peripheral tissues, including the vessel wall. A very small, but noticeable, decrease in apo B, as well as a decrease in lipid peroxides after a meal in men with metabolic syndrome may result from the utilization of low density lipoproteins. It is quite possible that a higher decrease in LDL-cholesterol is a consequence of an increased inflow of cholesterol into vessel wall. It would present a strong atherogenic mechanism in men with MetSy, not only because of an increased cholesterol inflow into vessel wall, but also because of a less efficient reverse cholesterol transport cleaning mechanism, as men with MetSy have lower HDL levels. Also, postprandial decrease in HDL-C (namely HDL$_2$-C) after a three-month hypolipidemic treatment in men with MetSy (or mixed hyperlipemia) may indicate a weakened HDL defense response.

The presence of a linear relationship between delta LDL-C (also delta LPO and delta TG) and postprandial non-LDL cholesterol (and remnant cholesterol) indicates that the mechanisms limiting (allowing) meal-induced lipid changes are associated with lipoproteins such as VLDLs, IDLs, HDLs and chylomicrones [32-34]. These mechanisms are included in residual risk existing in people with metabolic syndrome, despite normal or even low LDL-C level [35].

In this study, metabolic syndrome (similar to mixed hyperlipemia) was associated also with higher, in comparison to state of health, non-HDL-cholesterol. At present,

Table 3: Comparison between lipids and other parameters measured before and after a three month hypolipidemic treatment

		Group			
		MetS (12 men)		Control II (10 men)	
		mg/dl	mmol/l	mg/dl	mmol/l
T-C:					
	fasting before the treatment	219.91 ± 8.67	5.67 ± 0.22	240.60 ± 7.24	5.52 ± 0.19
	fasting after the treatment	197.00 ± 11.78*	5.08 ± 0.31*	192.20 ± 10.37***	4.95 ± 0.26***
	postprandial before the treatment	218.50 ± 11.03	5.62 ± 0.28	249.30 ± 6.69	6.42 ± 0.17
	postprandial after the treatment	196.54 ± 11.92*	5.06 ± 0.31*	189.10 ± 9.91***	4.88 ± 0.26***
TG:					
	fasting before the treatment	275.41 ± 21.93	3.11 ± 0.25	188.70 ± 24.23	2.1 ± 0.27
	fasting after the treatment	176.09 ± 24.65***	1.99 ± 0.28***	118.80 ± 15.48*	1.33 ± 0.17*
	postprandial before the treatment	350.83 ± 30.25	3.97 ± 0.34	292.20 ± 49.35	3.3 ± 0.55
	postprandial after the treatment	201.72 ± 27.95***	2.28 ± 0.32***	159.90 ± 26.32**	1.80 ± 0.29**
LDL-C:					
	fasting before the treatment	134.10 ± 12.31	3.46 ± 0.32	149.30 ± 7.11	3.84 ± 0.18
	fasting after the treatment	116.81 ± 12.33	3.00 ± 0.31	107.60 ± 10.76**	2.79 ± 0.28**
	postprandial before the treatment	108.60 ± 8.60	2.79 ± 0.22	141.50 ± 9.63	3.64 ± 0.25
	postprandial after the treatment	113.90 ± 12.70	2.94 ± 0.33	104.30 ± 9.45*	2.68 ± 0.24*
Non-LDL-C :					
	fasting before the treatment	94.33 ± 5.01	2.43 ± 0.13	91.40 ± 3.10	2.35 ± 0.08
	fasting after the treatment	80.18 ± 3.19 ***	2.10 ± 0.08***	84.60 ± 6.75*	2.1 ± 0.17*
	postprandial before the treatment	110.10 ± 6.22	2.84 ± 0.16	107.80 ± 8.82	2.79 ± 0.23
	postprandial after the treatment	82.63 ± 4.74***	2.10 ± 0.12***	84.80 ± 3.74*	2.1 ± 0.09*
HDL-C:					
	fasting before the treatment	39.38 ± 1.84	1.00 ± 0.05	53.50 ± 3.28	1.37 ± 0.09
	fasting after the treatment	45.09 ± 3.44	1.16 ± 0.09	54.00 ± 4.24 .	1.39 ± 0.11
	postprandial before the treatment	39.93 ± 2.55	1.03 ± 0.07	49.60 ± 2.70	1.29 ± 0.07
	postprandial after the treatment	42.45 ± 3.70	1.08 ± 0.09	52.90 ± 4.60	1.37 ± 0.12
HDL_2-C:					
	fasting before the treatment	7.35 ± 1.18	0.19 ± 0.03	12.52 ± 2.76	0.32 ± 0.07
	fasting after the treatment	10.82 ± 1.89	0.28 ± 0.05	12.82 ± 1.79	0.33 ± 0.05
	postprandial before the treatment	7.28 ± 1.46	0.18 ± 0.04	8.51 ± 1.10	0.22 ± 0.03
	postprandial after the treatment	7.37 ± 1.28	0.19 ± 0.03	9.44 ± 2.11	0.24 ± 0.05
HDL_3-C:					
	fasting before the treatment	32.00 ± 1.75	0.82 ± 0.05	42.03 ± 2.36	1.06 ± 0.07
	fasting after the treatment	34.26 ± 2.33	0.88 ± 0.06	41.04 ± 3.41	1.06 ± 0.09
	postprandial before the treatment	32.08 ± 1.59	0.82 ± 0.04	41.33 ± 2.65	1.08 ± 0.06
	postprandial after the treatment	35.18 ± 2.82	0.90 ± 0.07	43.36 ± 2.95	1.11 ± 0.07
Non-HDL-C :					
	fasting before the treatment	180.53 ± 7.94	4.64 ± 0.20	187.10 ± 8.22	4.82 ± 0.21
	fasting after the treatment	151.90 ± 10.39**	3.92 ± 0.27**	131.66 ± 17.23***	3.40 ± 0.44***
	postprandial before the treatment	178.56 ± 10.09	4.59 ± 0.26	199.70 ± 7.31	5.16 ± 0.19
	postprandial after the treatment	154.09 ± 10.93*	3.97 ± 0.28*	129.36 ± 17.07***	3.33 ± 0.44***

Table 3 continued: Comparison between lipids and other parameters measured before and after a three month hypolipidemic treatment

R-C:				
fasting before the treatment	46.53 ± 10.23	1.42 ± 0.11	38.00 ± 4.92	0.98 ± 0.13
fasting after the treatment	35.09 ± 4.94	0.91 ± 0.12	30.58 ± 8.88	0.81 ± 0.13
postprandial before the treatment	138.63 ± 9.71	1.81 ± 0.17	149.57 ± 9.81	1.49 ± 0.25
postprandial after the treatment	40.27 ± 5.66***	1.03 ± 0.15***	31.90 ± 5.18***	0.83 ± 0.14***
Glucose:				
fasting before the treatment	114.83 ± 10.23	6.40 ± 0.57	90.03 ± 1.81	5.01 ± 0.10
fasting after the treatment	105.63 ± 7.58	5.89 ± 0.42	93.00 ± 2.84	5.17 ± 0.16
postprandial before the treatment	121.66 ± 9.04	6.82 ± 0.50	96.78 ± 4.10	5.30 ± 0.23
postprandial after the treatment	109.90 ± 7.38	6.11 ± 0.41	99.40 ± 5.01	5.50 ± 0.28
LPO (mmol/ml):				
fasting before the treatment	3.75 ± 0.46		2.10 ± 0.34	
fasting after the treatment	2.35 ± 0.34		2.09 ± 0.32	
postprandial before the treatment	2.73 ± 0.29		2.61 ± 0.28	
postprandial after the treatment	2.33 ± 0.43		2.30 ± 0.46	
hsCRP (mg/l):				
fasting before the treatment	2.36 ± 0.51		1.71 ± 0.54	
fasting after the treatment	2.59 ± 0.71		0.61 ± 0.14	
postprandial before the treatment	2.28 ± 0.53		1.6 ± 0.56	
postprandial after the treatment	2.47 ± 0.66		0.71 ± 0.24	
ApoA-I (g/l):				
fasting before the treatment	1.44 ± 0.10		1.56 ± 0.08	
fasting after the treatment	1.45 ± 0.07		1.54 ± 0.11	
postprandial before the treatment	1.47 ± 0.08		1.52 ± 0.08	
postprandial after the treatment	1.49 ± 0.07		1.53 ± 0.08	
ApoB (g/l):				
fasting before the treatment	1.11 ± 0.12		1.28 ± 0.06	
fasting after the treatment	1.12 ± 0.06		0.93 ± 0.05***	
postprandial before the treatment	1.09 ± 0.12		1.18 ± 0.06	
postprandial after the treatment	1.13 ± 0.06		0.97 ± 0.06*	
ApoB/ApoA-I:				
fasting before the treatment	0.78 ± 0.06		0.83 ± 0.05	
fasting after the treatment	0.78 ± 0.05		0.61 ± 0.06*	
postprandial before the treatment	0.73 ± 0.07		0.79 ± 0.05	
postprandial after the treatment	0.77 ± 0.05		0.66 ± 0.06	

Results are presented as mean ± standard error (SE). T-C: total cholesterol; TG: triglycerides; LDL-C: LDL cholesterol; HDL- (HDL2-; HDL3-) C: HDL (HDL2-; HDL3-) cholesterol; R-C: remnant cholesterol; LPO: lipid peroxides; hsCRP: high sensitivity C-reactive protein C; apoA-I (B): apolipoprotein A-I (B)

*,**,*** difference statistically significant in comparison to values measured before the treatment: *p<0.05; ** p<0.01; ***p<0.001 using paired t tests for dependent samples

Table 4: Fasting and postprandial lipids and other measured parameters measured after a three month hypolipidemic treatment

		Group MetS (12 men)		Control II (10 men)	
		mg/dl	mmol/l	mg/dl	mmol/l
T-C:					
	fasting	197.00 ± 11.78	5.08 ± 0.31	192.20 ± 10.37	4.95 ± 0.26
	postprandial	196.54 ± 11.92	5.06 ± 0.31	189.10 ± 9.91	4.88 ± 0.26
TG:					
	fasting	176.09 ± 24.65	1.99 ± 0.28	118.80 ± 15.48	1.33 ± 0.17
	postprandial	201.72 ± 27.95	2.28 ± 0.32	159.90 ± 26.32	1.80 ± 0.29
	f-p difference			**	
LDL-C:					
	fasting	116.81 ± 12.33	3.00 ± 0.31	107.60 ± 10.76	2.79 ± 0.28
	postprandial	113.90 ± 12.70	2.94 ± 0.33	104.30 ± 9.45	2.68 ± 0.24
Non-LDL-C :					
	fasting	80.18 ± 3.19	2.10 ± 0.08	84.60 ± 6.75	2.1 ± 0.17
	postprandial	82.63 ± 4.74	2.10 ± 0.12	84.80 ± 3.74	2.1 ± 0.09
HDL-C:					
	fasting	45.09 ± 3.44	1.16 ± 0.09	54.00 ± 4.24	1.39 ± 0.11
	postprandial	42.45 ± 3.70	1.08 ± 0.09	52.90 ± 4.60	1.37 ± 0.12
	f-p difference	***			
HDL_2-C:					
	fasting	10.82 ± 1.89	0.28 ± 0.05	12.82 ± 1.79	0.33 ± 0.05
	postprandial	7.37 ± 1.28	0.19 ± 0.03	9.44 ± 2.11	0.24 ± 0.05
	f-p difference	*		*	
HDL_3-C:					
	fasting	34.26 ± 2.33	0.88 ± 0.06	41.04 ± 3.41	1.06 ± 0.09
	postprandial	35.18 ± 2.82	0.90 ± 0.07	43.36 ± 2.95	1.11 ± 0.07
	f-p difference			**	
Non-HDL-C :					
	fasting	151.90 ± 10.39	3.92 ± 0.27	131.66 ± 17.23	3.40 ± 0.44
	postprandial	154.09 ± 10.93	3.97 ± 0.28	129.36 ± 17.07	3.33 ± 0.44
R-C:					
	fasting	35.09 ± 4.94	0.91 ± 0.12	30.58 ± 8.88	0.81 ± 0.13
	postprandial	40.27 ± 5.66	1.03 ± 0.15	31.90 ± 5.18	0.83 ± 0.14
Glucose:					
	fasting	105.63 ± 7.58	5.89 ± 0.42	93.00 ± 2.84	5.17 ± 0.16
	postprandial	109.90 ± 7.38	6.11 ± 0.41	99.40 ± 5.01	5.50 ± 0.28
LPO (mmol/ml):					
	fasting	2.35 ± 0.34		2.09 ± 0.32	
	postprandial	2.33 ± 0.43		2.30 ± 0.46	
hsCRP (mg/l):					
	fasting	2.59 ± 0.71		0.61 ± 0.14*	
	postprandial	2.47 ± 0.66		0.71 ± 0.24*	
	f-p difference	*			

Table 4 continued: Fasting and postprandial lipids and other measured parameters measured after a three month hypolipidemic treatment

ApoA-I (g/l):		
fasting	1.45 ± 0.07	1.54 ± 0.11
postprandial	1.49 ± 0.07	1.53 ± 0.08
f-p difference	*	
ApoB (g/l):		
fasting	1.12 ± 0.06	0.93 ± 0.05*
postprandial	1.13 ± 0.06	0.97 ± 0.06
ApoB/ApoA-I:		
fasting	0.78 ± 0.05	0.61 ± 0.06*
postprandial	0.77 ± 0.05	0.66 ± 0.06

Results are presented as mean ± standard error (SE). T-C: total cholesterol; TG: triglycerides; LDL-C: LDL cholesterol; HDL- (HDL2-; HDL3-) C: HDL (HDL2-; HDL3-) cholesterol; R-C: remnant cholesterol; LPO: lipid peroxides; hsCRP: high sensitivity C-reactive protein C; apoA-I (B): apolipoprotein A-I (B)

*, difference statistically significant in comparison to group of men with mixed hyperlipidemia: p<0.05

f: fasting, p: postprandial, f-p difference: the difference between the values measured in the fasting and postprandial state; * p<0.05; **p<0.01; ***p<0.001

* difference statistically significant in comparison to MetSy group: * p<0.05

the non-HDL-C was established as a secondary treatment target, whereas a non-HDL-C reporting as a factor improving non-HDL-C goal attainment [36].

Increased pro-oxidative and pro-inflammatory activities are further risk factors. At a fasting state, men diagnosed with metabolic syndrome, in comparison to normolipemic men, displayed elevated high sensititivity C-reactive protein and slightly increased lipid peroxides. The slightly increased fasting hsCRP level was observed also in men diagnosed with mixed hyperlipemia (Table 1). A pro-oxidative and inflammatory state is commonly present in persons with metabolic syndrome [14,16,37]. Multiple mechanisms can lead to elevation of LPO and/or CRP, e.g. obesity, resistance to insulin and hypertriglyceridemia [38]. However, in our study, like in other studies [39], lower LDL-C after a meal were accompanied by a decrease in LPO. The relation between LDL and LPO seems to be strict after a meal, as an exogenous oxidized cholesterol esters are directly incorporated into lipoproteins and transferred via the LDL into endothelial cells [40].

Of course, this study has some limitations. Only men who regularly ate fat-rich foods agreed to take part in the study (hence the small number of volunteers). We measured lipid levels before and 3 hours after the standardized high-fat (approximately 50% fat) meal, although in other studies, the maximal postprandial lipid changes were observed 4 to 6 hours after a meal. It depended on the composition of fats and also on the method of measurement. However, modified β quantification test, as recommended by NCEP, demands the observation after 3hours [31]. An advantage of this study is the fact that the studied group consisted only of men with newly diagnosed MetSy, who had not been treated before.

5 Conclusion

The present study shows postprandial decreases in LDL cholesterol in men diagnosed with metabolic syndrome. This decrease may cause underestimation of cardiovascular risk. On the other hand, in men with MetSy, postprandial decrease in LDL cholesterol was not observed after three months of hypolipidemic treatment. Simultaneously, the apoB/apoA-I ratio remained the same, which suggests that in those patients, the reduction in risk of cardiovascular event was only partial.

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