Investigation of IgG anti-oxLDL antibody levels and HDL and LDL subclasses in patients with ST-segment elevation acute myocardial infarction

Abstract

Introduction
Dyslipidemia, inflammation and immunological processes play a key role in the development of atherosclerosis. This study investigates the relationship of different phenotypes of low-density lipoprotein (LDL) and high-density lipoprotein (HDL), human antibodies G classes against oxLDL (IgG anti-oxLDL antibodies) and inflammatory marker pentraxin-3 (PTX3) in patients with ST-segment elevation acute myocardial infarction (STEMI). Among STEMI patients with different Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score, we analyzed predictive abilities of these biomarkers to assess disease outcome.

Material and methods
In 69 STEMI, 21 patients with stable angina pectoris (AP) and 67 healthy controls, IgG anti-oxLDL antibodies and PTX3 were determined by ELISA. Gradient gel electrophoresis was used for lipoprotein subclasses separation.

Results
We found significantly lower HDL and LDL diameters ($p<0.001$ and $p<0.001$, respectively) and higher PTX3 concentration ($p<0.001$) in patients than in controls. Control subjects with small-sized HDL and LDL B phenotype had significantly higher IgG anti-oxLDL antibody levels ($p=0.015$), whereas STEMI patients with the same profile had higher PTX3 concentration ($p=0.005$). STEMI patients with intermediate SYNTAX score had lower levels of IgG anti-oxLDL antibodies ($p=0.008$). Multivariate logistic regression analysis showed that smaller LDL diameter was an independent predictor of intermediate SYNTAX score (OR=0.370; $p=0.019$).

Conclusions
Smaller LDL and HDL particles are associated with elevated IgG anti-oxLDL antibodies in healthy subjects, but with increased PTX3 level in STEMI patients. In addition, we found that smaller LDL size was independent predictor of higher SYNTAX score. Further studies are needed to expand our preliminary observations.

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Keywords

anti-oxLDL antibodies, STEMI, LDL size, HDL subclasses, SYNTAX score

Introduction

Atherosclerosis and its complications, acute myocardial infarction (AMI) and stroke, remain the leading cause of death worldwide for the last 15 years [1]. It is a multifactorial, systemic, chronic, progressive inflammatory disease accompanied by the accumulation of lipids, inflammatory cells and components of the extracellular matrix in the intima of the arteries. It is now well appreciated that plasma low-density lipoprotein (LDL) and high-density lipoprotein (HDL) are constituted of several subtractions that differ in size, density, apolipoprotein content, atherogenicity and oxidative properties [2]. Small dense LDL particles are particularly susceptible to oxidation, while HDL particles protect LDL against lipid peroxidation [3]. However, although HDL particles are classified as atheroprotective, modifications of their constituents can decrease their atheroprotective activity and even render them proatherogenic. [4,5]. In this respect, recent studies suggest that small-sized HDL particles possess strong antiatherogenic properties, but their functionality could be compromised and diminished in the proinflammatory, prooxidative and dyslipidemic environment [6-10].

Oxidized low-density lipoprotein (oxLDL) is thought to play an important role in the pathogenesis of atherosclerosis. Circulating oxLDL elicits autoantibodies production, resulting in the formation of oxLDL-containing immune complexes (ox-LDL-IC). Once formed, the immune complexes are predominantly internalized through the Fcγ receptors, leading to the activation of Fcγ receptor-mediated signaling pathways in macrophages and the secretion of different proinflammatory cytokines such as interleukin-1 (IL-1) and IL-6 [11,12]. Isolated human anti-oxLDL antibodies are predominantly of the IgG isotype and are directed against different epitopes within oxLDL [13]. In practice, these antibodies are considered to be markers of oxLDL, but to date, their role in the development and progression of atherosclerosis has

remained controversial. Namely, previous studies have shown that anti-oxLDL antibodies may have an atheroprotective role, at least in cardiovascular disease (CVD) free subjects [14].

Beyond these, some novel biomarkers can fill an unmet need in timely recognition, early diagnosis, and ACS risk stratification. Asymmetric dimethylarginine can play an important role in the events leading to stenosis, galectin-3 can predict poor outcomes and mortality in patients with heart failure, pentraxin 3 (PTX 3) is an early marker of primary local activation of innate immunity and heart-type fatty acid-binding protein is a marker with certain potential in ACS prognosis [15-17]. For this study, we will confine attention to PTX3, since its high blood concentration can be induced by inflammatory cytokines and modified LDL [18]. PTX3 overexpression in endothelial cells is also caused by HDL, specifically HDL 3 particles [19]. Its overexpression promotes oxLDL uptake, inhibits cholesterol efflux and expression of the ABCA1 cholesterol transporter and nuclear transcription factors, peroxisome proliferator-activated receptor-γ and liver X receptor α in macrophages [20].

One of the common consequences of coronary artery disease (CAD) is acute coronary syndrome (ACS), represented as a spectrum of events ranging from unstable angina pectoris (AP) to AMI, which can occur without (NSTEMI) or with ST-segment elevation (STEMI). To gain further insight into the relationship between investigated biomarkers concerning the extent of myocardial ischemia, we analysed plasma lipoprotein subclasses, serum levels of human antibodies G classes against oxLDL (IgG anti-oxLDL antibodies) and PTX3 concentration among STEMI, stable AP patients and healthy subjects. Besides, we tried to evaluate ability of the investigated parameters to predict disease outcomes estimated by the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score [21]. To our knowledge, there are no published studies related to this topic.

Material and Methods

Subjects

The study was designed as a pilot one and it included a total of 157 subjects. 21 AP and 69 STEMI patients were treated at two clinics in Belgrade: at the Clinical Hospital Centre "Bezanijska kosa" and at the Clinical Hospital Centre "Zemun". Information about health conditions and treatment of studied patients were obtained from their medical records. From the patients, blood samples were collected immediately after their admission to the emergency units. The control group consisted of 67 healthy volunteers, employees of the Faculty of Pharmacy in Belgrade and persons who checked-in for a regular medical exam in a general hospital "Medigroup" in Belgrade. The criteria for exclusion during the formation of the control group were: CVD, recent clinical infection and trauma, presence of any systemic, inflammatory, or metabolic diseases, liver or kidney diseases. The control group underwent a detailed cardiology exam that excluded the presence of coronary disease. Blood samples from control subjects were collected in a regular medical check-up appointment after overnight fasting.

All subjects' demographic data, including age, body weight, height, smoking status, alcohol consumption, and data on therapy and family history of CVD, were collected by interviewing respondents. For more detailed analysis, the following criteria were established: 1) hypertension (HT) was defined by a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg, or the use of any antihypertensive medication [22]; 2) body mass index (BMI) for each individual was calculated using standard procedures as a ratio of body weight (in kg) divided by the square of the height (in m) of the examinees. We divided patients in groups according to SYNTAX score which combines information on extent, anatomy and lesion characteristics of CAD. The SYNTAX score ≤ 22 (low SYNTAX score) is indicator of

lower disease severity with a less complicated lesion and lower probability for all-cause mortality, stroke, AMI, or repeat revascularization. SYNTAX score > 22 (intermediate SYNTAX score), indicates higher disease severity and a higher likelihood of complications [21]. Since only three patients had SYNTAX score higher than 32, these patients were not included in the study. Further, all patients and volunteers were informed about the aims of the study and gave written consent before enrolment. The study was planned and executed according to the ethical guidelines of the Helsinki Declaration [23]. The ethical committees of Clinical Hospital Centres "Zemun" and "Bezanijska kosa" as well as of Faculty of Pharmacy, University of Belgrade and General hospital "Medigroup" (for control subjects) approved our study protocol.

Methods

Determination of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and glucose were performed on Dimension® Xpand Plus biochemical analyser (Siemens, Munich, Germany) by routine enzymatic methods. The concentration of low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula [24] using determined TC, TG and HDL-C levels as follows: LDL-C = TC – HDL-C – TG/2.2 (in mmol/L). High-sensitivity C-reactive protein (hsCRP) was determined using a latex-enhanced immunoturbidimetric method (Tina-quant CRP Roche, Indianapolis, USA). PTX3 was measured by enzyme-linked immunosorbent assay (ELISA) (Human Pentraxin3 DuoSet ELISA R&D Systems, Minneapolis, USA). IgG anti-oxLDL antibodies in serum were measured using a commercially available ELISA kit (OLAB IgG Anti Oxidized Low Density Lipoprotein, Biomedica Medizinprodukte GmbH & Co KG, A-1210 Wien, Austria) according to manufacturer's specifications.

Polyacrylamide gradient (3–31%) gel electrophoresis was used to separate LDL and HDL subfractions. Electrophoretic separation was performed in a vertical *Hoefer SE 600 Ruby system* (Amersham Pharmacia Biotech, Vienna, Austria). Calibration of gels was performed using high molecular weight protein standards (Amersham Pharmacia Biotech, Vienna, Austria), human plasma and carboxylated polystyrene microspheres (Duke Scientific Corporation, Palo Alto, CA, USA). Gels were analysed using the Image Scanner (Amersham Pharmacia Biotech, Vienna, Austria) with Image Quant Software (version 5.2; Molecular Dynamics). The migration distance for each absorbance peak was determined and the particle size corresponding to the major peak in the LDL and HDL regions was referred to as LDL and HDL diameter, respectively. Additionally, relative proportions of four LDL subfractions (LDL I, LDL II, LDL III and LDL IV) and two main HDL subfractions (HDL 2 and HDL 3) were determined. LDL phenotype B was defined if the dominant LDL particle diameter was ≤ 25.5 nm. Similarly, the dominant HDL particle diameter ≤ 8.8 nm was the criterion for defining a small-sized HDL phenotype.

Statistical analyses

The normality of distributions of the examined variables was tested by Kolmogorov-Smirnov or Shapiro Wilk test, depending on sample size. Data are shown as mean ± standard deviation (SD) for normally distributed variables, as median (interquartile range (IQR)) for non-normally distributed variables and as relative or absolute frequencies for categorical variables. Normally distributed variables were compared by ANOVA (with Tukey's *post hoc* test for subgroup differences) and by Student's t-test for independent populations. For comparison of asymmetrically distributed variables, Kruskal Wallis and Mann-Whitney U exact test (with Bonferroni correction) were performed. The Chi-square test was used for the examination of group differences for categorical variables. Analysis of variables associated to the SYNTAX

scores was evaluated based on the univariate and multivariate logistic regression. Multivariate logistic regression analysis was used to investigate the association of LDL and HDL diameter, PTX3 and IgG anti-oxLDL antibodies with intermediate SYNTAX scores, unadjusted and adjusted for other interfering variables such as hsCRP, glucose and age. The statistical analyses were performed with PASW® Statistic v. 25 (Chicago, Illinois, USA) software. A two-tailed p-value <0.05 was considered to indicate statistical significance.

Results

Demographic characteristics and biochemical parameters of all study groups (AP, STEMI and controls) are presented in Table I. As expected, a higher frequency of HT was present in both patients groups than in the control group, while the prevalence of smokers was the highest among STEMI patients. The patients had significantly lower HDL-C level but higher frequency of LDL B phenotype, small-sized HDL phenotype and higher concentrations of hsCRP and PTX3 than controls. Both HDL and LDL particle diameters were significantly smaller in patients than in controls. We detected a significant difference in the relative proportions of LDL II and LDL IV subfractions between AP and STEMI patients. AP patients had lower TG, TC and LDL-C levels than STEMI patients. However, there was no significant difference when IgG anti-oxLDL antibody levels were compared.

Table I

We further examined the differences in examined parameters in the control and STEMI group with and without the simultaneous presence of small-sized HDL and LDL B phenotypes. The data presented in Table II show that control subjects with both small-sized HDL and LDL B phenotypes had increased concentrations of IgG anti-oxLDL antibodies and TG, and reduced

HDL-C levels. In contrast, no significant difference in the IgG anti-oxLDL antibody concentrations was found between corresponding groups of STEMI patients (Table III). Nevertheless, increased PTX3 was evident in STEMI patients with small-sized HDL and LDL B phenotypes.

Table II and Table III

Next, we analysed examined parameters based on disease severity determined by SYNTAX score in patients with STEMI (Table IV). As expected, lower LDL diameter was found in patients with intermediate SYNTAX scores compared to those with low SYNTAX scores. However, we found higher IgG anti-oxLDL antibody levels in the group with low SYNTAX score.

Table IV

Patients with smaller LDL diameters were more likely to have higher SYNTAX scores than patients with larger LDLs. To eliminate other confounding effect of other variables, adjustment was performed for IgG anti-oxLDL antibodies, hsCRP, glucose and PTX3 levels, HDL diameters, and age as single independent predictors. Smaller LDL diameter remained an independent predictor of intermediate SINTAX score (Figure 1). Moreover, after inclusion of all above-mentioned confounders in the same model, smaller LDL size remained independently associated with intermediate SYNTAX score. None of other examined parameters were predictive for intermediate SINTAX score [IgG anti-oxLDL antibody levels OR=0.986 (0.972-1.001), HDL diameter OR=0.593 (0.253-1.380) and high PTX3 concentration OR=1.233 (0.758-2.004)].

Figure I

Discussion

To the best of our knowledge, this is the first study that evaluates the association of the small-sized HDL and LDL B phenotypes with IgG anti-oxLDL antibody levels. In the real-world condition, we examined the concept that these antibodies might have different roles in STEMI patients and healthy individuals.

Analysis of lipoprotein subclasses distribution showed that LDL and HDL particles were more shifted toward smaller diameters in both patients groups as compared to healthy control subjects. These findings agreed with other studies [6,7] and were in line with the hypothesis that small LDL and HDL diameters are atherosclerosis risk factors and contributors of its development [25]. Although control subjects had higher LDL-C levels, they had a similar distribution of LDL subclasses as AP patients, which could be attributed to the effect of statin therapy in AP group [26]. Small-sized HDL phenotype was increased in STEMI and AP patients, suggesting that these particles have diminished protective role in lipid efflux processes from the plaque, oxidative modification of LDL, inflammatory processes promoted by modified LDL and plaque progression [9,10]. It is already known that atherogenic lipoprotein phenotype (higher TG and decreased HDL-C concentrations and increased levels of small, dense LDL) are common in patients with high cardiovascular risk [27] so the finding of higher frequency of LDL B phenotype in our patients groups was expected.

Once formed, oxidized LDL particles can stimulate the inflammatory response and promote adhesion molecules and chemokines expression on endothelial cells surface [28]. In accordance, we found that the levels of inflammatory markers (hsCRP, PTX3) were significantly higher in both patient groups than in controls. Moreover, Nebuloni and co-workers [29] confirmed the presence of PTX in atherosclerotic plaques and myocardial tissues of AIM

patients. In Inoue et al. study [30], PTX3 levels in the plasma of patients with unstable AP were elevated as compared to control subjects. It is unknown whether this increase is a consequence of the proatherogenic effect of PTX3, or it represents the immunoinflammatory response of the damaged cells. Additionally, oxLDL can trigger T and B lymphocyte cells' response specific to apoB-derived epitopes [11,31]. This study, however, did not show a difference in oxLDL antibody levels between patients and the control group. Similarly, McDowell et al. [32] and Rossi et al. [33] did not find a significant difference in serum IgG titers to oxLDL between patients with CAD and healthy subjects. On the other hand, our data are not consistent with those of Laczik et al. [28] and Mokhtar et al. [34], who described higher serum IgG anti-oxLDL antibody levels in patients with ACS versus healthy controls. Inconsistencies in study results are related to individual variations in the immune response, isotype, and avidity of the used autoantibodies [35].

Our study provided an intriguing finding that control subjects with a higher proportion of small HDL and LDL particles had elevated IgG anti-oxLDL antibody levels. This finding suggests that oxidative modifications of LDL and the consequent increased production of IgG anti-oxLDL antibodies occur more readily in healthy individuals with an unfavorable lipid profile. In physiological conditions, IgG anti-oxLDL antibodies might be responsible for clearance and neutralization of oxLDL [36]. The same analysis in STEMI patients revealed no differences in IgG anti-oxLDL antibody levels. A probable mechanism of this phenomenon could be explained by the subsequent formation of insoluble immune complexes, oxLDL-IC, which are deposited in the tissues [11,12]. However, oxLDL-IC express a more substantial proinflammatory effect on macrophages than either IgG anti-oxLDL antibodies or oxLDL alone. Even more, oxLDL-IC induce inflammasome activation and IL-1β production, as demonstrated

by the *in vitro* study on mice [37]. In future studies, in addition to IgG anti-oxLDL antibodies, it would be useful to determine the oxLDL-IC level in circulation, atherosclerotic plaque and endothelial cells. Our study results support the concept of IgG anti-oxLDL antibodies dualistic role, i.e., a possibility that these antibodies have a protective role in healthy individuals and a proatherogenic role in advanced atherosclerosis, such is our STEMI group. Nevertheless, among STEMI patients exhibiting both small-sized HDL and LDL B phenotypes, elevated levels of PTX3 were found. This finding supports the fact that small-sized HDL might stimulate PTX3 expressions, which is similar to the study of Norata et al. [19]. The results mentioned above are in line with the study of Liu et al. [20], who demonstrated that PTX3 affects lipid accumulation in human macrophages, by increasing oxLDL uptake and inhibiting cholesterol efflux.

Another interesting finding of this study was that STEMI patients with intermediate SYNTAX scores had decreased LDL diameters and reduced IgG anti-oxLDL antibody levels. A finding of lower IgG anti-oxLDL antibody levels in STEMI patients with intermediate SYNTAX scores could be attributed to reduction of free antibodies due to intense oxLDL-IC formation and their deposition in atherosclerotic tissue [31]. Major limitations of the standard SYNTAX score are the absence of clinical and laboratory parameters and individualized approach in risk stratification. Therefore, some guidelines recommend addition of clinical variables, particularly those which can impact prognosis [38]. Our data showed that STEMI patients with smaller LDL size had a higher probability of severe CAD and worse outcomes following coronary revascularization. Observed association was independent of patients' age, glycemia, HDL size, immune response and inflammatory status. Identification of patients with intermediate SYNTAX score and smaller LDL size may improve risk stratification, therapeutic approach and

patients monitoring after hospital discharge. IgG anti-oxLDL antibodies and PTX3 concentrations were not significant predictors of intermediate SYNTAX scores.

Also, we should mention some limitations of the current study. Firstly, this study was performed on a relatively small number of patients. Future studies with a greater sample size are needed to expand our observations. Secondly, in STEMI patients the blood was sampled after admission to the emergency room at any time of the day. In contrast, samples from control subjects were taken according to the recommended blood sampling protocol, i.e. after overnight fasting. It should be noted that lipid concentrations are temporarily reduced in patients with AMI. Also, it should not be neglected that IgG anti-oxLDL antibody levels are mainly influenced by an individual's immune response. Finally, the patients received hypolipidemic medications, which could affect the interpretation of obtained data.

Conclusion

The results of our study showed no difference in IgG anti-oxLDL antibody levels between STEMI, AP and control group. However, the subjects with small-sized HDL and LDL B phenotypes in the control group had elevated IgG anti-oxLDL antibodies, while those in STEMI group had increased levels of PTX3. STEMI patients with intermediate SYNTAX scores had smaller LDL diameters and reduced IgG anti-oxLDL antibody levels. In addition, smaller LDL size was independent predictor of higher SYNTAX score. Our current study could serve as a ground for future studies to explore whether addition of blood biomarkers to SYNTAX score could improve its ability to predict disease outcomes.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

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Figure 1. Crude and adjusted OR ratios for intermediate SYNTAX scores predicted by LDL diameter

All independent variables included in the analysis were continuous; dependent variable (SYNTAX scores were dichotomous – low SYNTAX scores were coded 0 and intermediate SYNTAX scores were coded 1).

LDL, low-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; PTX3, pentraxin 3.

Table I. Demographic characteristics and laboratory parameters in control subjects, AP and

STEMI patients

Variable	Control group	AP	STEMI	*p*-value
N	67	21	69	
Age, years	55.45±9.49	60.57±10.43[*]	60.80±11.78[*]	0.010
Prevalence of males, %	73	71	80	0.591
BMI, kg/m^2	26.35(24.38-29.46)	28.09 (25.61-31.35)[#]	25.39 (23.40-27.76)	0.009
Smokers, %	19.4	23.8	58[**]	<0.001
HT, %	38.8	66.7[*]	61.8[*]	0.011
Statin therapy, %	/	38.1[*]	1.4	0.002
Glucose, mmol/L	5.5 (5.0-5.9)	5.8 (4.8-7.4)	6.7 (5.9-8.7)[**]	<0.001
hsCRP, mg/L	0.7 (0.3-1.9)	2.7 (1.9-4.9)[**]	3.7 (2.1-7.2)[**]	<0.001
PTX3, ng/mL	1.0 (0.7-1.2)	1.8 (1.6-2.2)[**]	2.4 (1.5-5.4)[**]	<0.001
TC, mmol/L	5.70±1.09	4.56±1.14[*#]	5.53±1.30	0.001
TG, mmol/L	1.37 (0.97-1.72)	0.94 (0.71-1.93)[#]	1.68 (1.20-2.32)[*]	0.003
HDL-C, mmol/L	1.26 (0.96-1.54)	1.01 (0.77-1.15)[*]	0.96 (0.80-1.18)[**]	<0.001
LDL-C, mmol/L	3.65±1.06	2.92±1.07[*#]	3.67±1.12	0.019
IgG anti-oxLDL, mU/mL	90.5 (50.3-275.7)	69.0 (23.5-268.2)	103.0 (53.6-230.6)	0.427
HDL diameter, nm	10.08 (8.68-10.50)	8.54 (8.35-8.90)[**]	8.63 (8.37-9.49)[**]	<0.001
HDL 2, %	60.43±9.08	58.05±5.52	58.46±7.53	0.285
HDL 3, %	39.46±8.99	41.95±5.52	41.32±7.32	0.288
Small-sized HDL phenotype, %	26.9	75[**]	62.1[**]	<0.001
LDL diameter, nm	26.80 (25.65-27.26)	25.99 (24.26-26.77)[*]	24.84 (23.59-26.03)[**]	<0.001
LDL I, %	19.7 (17.0-25.5)	20.7 (17.6-25.5)	19.3 (17.4-23.3)	0.547
LDL II, %	26.4 (22.9-28.8)	28.5 (25.1-31.7)[#]	25.2 (22.6-27.9)	0.030
LDL III, %	22.2 (18.8-24.6)	22.8 (18.2-24.9)	21.6 (20.0-24.3)	0.957

LDL IV, %	29.2 (23.7-33.3)	27.4 (20.3-32.6) [#]	30.8 (26.8-35.3)	0.035
LDL B phenotype, %	22	40[**]	62[**]	<0.001

*p<0.017 vs control group; ** p<0.001 vs control group; # p<0.017 vs STEMI

Continuous variables were compared by ANOVA (with Tuckey post hoc test) and Student's t-test or by Kruskal Wallis and Mann Whitney U test (with Bonferroni correction). Categorical variables were compared using the χ^2 test.

Table II. Laboratory parameters in the control group concerning the presence of small-sized HDL and LDL B phenotypes

Variable	Small-sized HDL and LDL B phenotype		p-value
	Without	With	
N	42	25	
Age, years	57.86±7.89	51.40±10.69	0.006
BMI, kg/m2	25.82 (23.88-29.55)	27.22 (24.92-29.31)	0.269
Glucose, mmol/L	5.5 (5.0-6.0)	5.5 (4.9-6.0)	0.662
hsCRP, mg/L	0.5 (0.2-1.7)	1.0 (0.4-3.2)	0.065
PTX3, ng/mL	1.0 (0.7-1.2)	1.0 (0.8-1.1)	0.850
TC, mmol/L	5.65±1.10	5.80±1.09	0.601
TG, mmol/L	1.20 (0.89-1.56)	1.61 (1.28-2.22)	0.001
HDL-C, mmol/L	1.41 (1.09-1.66)	1.15 (0.90-1.36)	0.014
LDL-C, mmol/L	3.65±1.09	3.66±1.04	0.972
IgG anti-oxLDL, mU/mL	74.7 (47.7-157.7)	269.3 (57.7-380.7)	0.015

Table III. Laboratory parameters in STEMI patients concerning the presence of small-sized

HDL and LDL B phenotypes

| Variable | Small-sized HDL and LDL B phenotype | | p-value |
	Without	With	
N	15	54	
Age, y	62.42±11.60	60.89±11.91	0.688
BMI, kg/m2	25.06 (22.03-28.65)	25.39 (23.44-27.69)	0.742
Glucose, mmol/L	6.4 (5.0-9.0)	6.8 (6.0-8.4)	0.274
hsCRP, mg/L	5.5 (1.7-8.1)	3.2 (1.9-4.4)	0.191
PTX3, ng/mL	1.4 (1.3-2.3)	2.4 (1.7-5.7)	0.004
TC, mmol/L	5.72±0.92	5.52±1.39	0.637
TG, mmol/L	1.60 (1.21-2.32)	1.69 (1.21-2.31)	0.940
HDL-C, mmol/L	1.09 (0.78-1.43)	0.93 (0.80-1.14)	0.266
LDL-C, mmol/L	3.76±0.72	3.68±1.20	0.810
IgG anti-oxLDL, mU/mL	161.0 (65.7-233.2)	88.7 (43.7-179.5)	0.366

Table IV. Laboratory parameters in STEMI patients with low and intermediate SYNTAX scores

Variable	Low SYNTAX score	Intermediate SYNTAX score	p-value
N	58	11	
Age, years	60.62±12.35	62.55±9.50	0.626
BMI, kg/m2	25.06 (23.37-28.47)	25.39 (23.84-26.83)	0.886
Glucose, mmol/L	6.6 (5.9-8.6)	7.2 (5.6-9.5)	0.652
hsCRP, mg/L	3.4 (1.8-5.1)	2.8 (2.0-4.0)	0.572
PTX3, ng/mL	2.4 (1.5-6.2)	1.8 (1.4-3.4)	0.284
TC, mmol/L	5.62±1.33	4.90±0.97	0.094
TG, mmol/L	1.65 (1.17-2.19)	1.69 (1.11-2.33)	0.763
HDL-C, mmol/L	0.98 (0.81-1.21)	0.90 (0.78-1.04)	0.392
LDL-C, mmol/L	3.76±1.14	3.05±0.89	0.055
HDL diameter, nm	8.64 (8.36-9.60)	8.57 (8.38-8.73)	0.304
HDL 2, %	57.2 (53.0-62.4)	59.5 (50.2-64.2)	0.992
HDL 3, %	42.8 (37.6-47.0)	40.5 (35.8-43.9)	0.576
LDL diameter, nm	25.06 (23.65-26.36)	23.94 (23.09-24.90)	0.038
LDL I, %	19.2 (17.2-23.8)	20.1 (17.5-21.7)	0.865
LDL II, %	25.3 (22.6-27.9)	24.6 (21.8-28.1)	0.670
LDL III, %	21.5 (20.1-24.2)	22.2 (19.1-25.2)	0.886
LDL IV, %	30.8 (26.7-34.5)	34.1 (28.4-37.3)	0.497
IgG-anti-oxLDL, mU/mL	123.3 (60.7-262.1)	41.3 (25.5-92.5)	0.008

Normally distributed variables were compared using Student's t-test and presented as mean ± SD. Skewed

variables were compared by the Kruskal Wallis test and presented as median (interquartile range).

Figure: LDL diameter as predictor of intermediate SYNTAX score

Y-axis: OR (95% CI), ranging from 0.0 to 1.2

Category	Upper CI	OR	Lower CI
LDL diametar	0.929	0.614	0.406
LDL diameter adjusted for IgG anti-oxLDL antibody	0.969	0.617	0.393
LDL diameter adjusted for hsCRP	0.937	0.619	0.408
LDL diameter adjusted for glucose	0.919	0.568	0.351
LDL diameter adjusted for HDL diametar	0.940	0.616	0.404
LDL diameter adjusted for PTX3	0.859	0.470	0.257
LDL diameter adjusted for age	0.925	0.611	0.404
LDL diameter adjusted for all confounders	0.848	0.370	0.161