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Short Communication

Intermediate and Very Low Density Lipid Particle Sizes are Important in the Clinical Manifestation of Younger Patients with Acute Coronary Syndromes

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Abstract

Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations associated with rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct - related artery.

Aim of the study was to estimate the whole lipid spectrum particles among patients in the acute phase of myocardial infarction (acute coronary syndrome in younger age - in their fourties). Lipid particle size of IDL and VLDL lipoproteins in the pathology among acute coronary syndrome younger patients have not been estimated yet.

In a group of consecutive 60 patients suffering from acute coronary syndrome serum lipid particles have been bed -side measured with FDA approved method Lipoprint Quantimetrix system. Lipid subfrections of LDL, IDL, VLDL and HDL - cholesterol have been measured with gradient polyacryamid gel electrophoresis at time of the event comparing to the controls. The subfraction - analysis allowed the examination of the cardiovascular risk beyond the common blood cholesterol testing.

The result showed, that lipid subpopulations under pathological state gives evidence of characteristic shift toward small LDL as well as small HDL par-ticles among acute coronary syndrome patients. Together with VLDL and IDL lipoproteins are counting to their impaired outcome, thus carrying the certain significant atherogenic potential they contribute to their worse outcome risk.

INTRODUCTION

The management and as a consequence, the outcome of acute coronary syndromes have improved impressively over the last decades, but they remain the most important cause of re - hospitalization, re - intervention, heart failure, and death.

The role of LDL - cholesterol particles in the pathogenesis of acute coronary syndromes is well estimated. Small -dense LDL - cholesterol particles are the most imported lipid particles contributing to the vulnerability of atherosclerotic plaque.

Early studies indicated, that cholesterol levels decrease significantly after acute coronary syndromes [1]. Most of them did not measure low density cholesterol (LDL-C) and high density cholesterol (HDL-C) directly as well as their particle sizes [2,3]. Other particles as very low density lipoproteins (VLDL) and intermediade density lipoproteins (IDL) have not been measured yet, and their characteristics among patients with acute coronary syndromes (ACS) are not known.

METHODS

60 patients with ACS (STEMI) 46 males and 14 females with the mean age of 47,2 ± 5,3 years admitted to the Heart centre for primary (primary coronary intervention) PCI were followed up. Whole lipid spectrum incl. their sizes were evaluated and compared to 30 controls. The main risk factors were smoking, diabetes mellitus, hypertension and positive familial history. Characteristics of the followed sample are in the table 1 and 2. At the time of admission to the heart centre for primary coronary intervention complete lipid analyses with FDA approved method of Lipoprint Quantimetrix system was used for estimation of the whole lipid size particles [4-6]. This enables to estimate the subfraction analysis, based on ultracentrifugation (3000 rpm/10 min) and gradient gel electrophoresis. As a results of this quantitative analysis, using polyacrylamide gel tubes, low - density cholesterol lipoprotein (LDL) subfractions were grouped into the large (LDL 1-2) middle (LDL 3-4) and small dense (LDL 5-7), the same proportion group of intermediate lipoproteins

Table 1: Characteristics of the followed sample.

	patients (n = 60)	controls (n = 30)	P
age	47,20 ± 5,30	40,52 ± 6,72	0,64
BMI	28,08 ± 5,07	27,89 ± 5,70	0,81
males/females	46/60...76,67 %	22/30...73,33 %	1,0
smoking	40/60...66,67 %	22/30... 73,33 %	0,86
diabetes mellitus	6/60...10 %	5/30...8,33 %	0,51
arterial hypertension	20/60...33,33 %		
CV family history	12/60...20 %		

Table 2: Biochemistry among patients with acute coronary syndrome.

CK (μkat/l)	33,04 ± 33,31
troponin T (μg/l)	19,61 ± 124,45
EF (%)	45 ± 10,03

(IDL) large, middle and small, VLDL lipoprotein and high density cholesterol (HDL), large (HDL 1-3), inter-mediate (HDL 4-7) and small (HDL 8-10) lipoprotein subfractions were obtained [4,5].

Statistical analysis. Values of quantitative variables with normal distribution are presented as means ± standard deviations. Values of quantitative variables without normal distribution are presented as medians ± standard errors. Normal distribution was controlled with Kolmogorov - Smirnov test. Differences of means between groups of patients and controls were compared with T-test in normal distribution and with Mann - Whittney test without normal distribution. Qualitative variables were compared with χ^2 quadrate test.

All of the patients signed the informed consent with the blood analyses and aggreed with early PCI intervention. One patient was excluded from the follow-up due to cardogenic shock, unconsciousess, and unable to sign the consent.

RESULTS

Majority of the acute coronary syndrome patients had one and two vessel disease as seen on the Table (3). Acute percutaneous coronary intervention con-sisted of stenting in whole three quarters of the followed patienrs as seen on the Table (4).

Results from the lipid evaluation brought interesting results as seen on the Table (5). As expected there have been the significant increase of the medium size LDL-C particles compared to controls. Highly atherogenic small dense LDL-C particles have been present just only among the patients with ACS. Less atherogenic large LDL-C particles (involved mainly in the LDL lipid transport) did not showed any changes.

There have been significant increase of VLDL as well as large and medium size IDL-C particles among the ACS patients, all carrying the certain added atherogenic risk potential.

Reverse finding with HDL-C levels have been seen with lower levels of large and medium size HDL-C . No differences in small size HDL-C have been present.

There have not been any other significant correlations comparing lipids to other measured variables as left ventricular ejection fraction, coronarographic findings (number of vessels involved), and troponine levels.

DISCUSSION

At present time the common interest in medicine is to define important bio - markers with predicive value for the cardiovascular outcome of high risk patients. Among acute coronary syndromes such biomarkers are troponins, anti - coagulants, but of importance there are also serum lipoproteins [7].

Dyslipidemia belongs to the main contributing pathophysiologic factors for the acute coronary syndromes due to atherothrombosis [7,8]. Its early diagnosis and also early statin treatment is important for the early and long - term outcome of these patients [9,10].

In the daily clinical practice many physicians fail to measure serum lipids early after admission for an acute intervention in part because of their understanding that such measurements are unreable because of an early decrease in serum total cholesterol and low - density lipoprotein cholesterol soon after ACS. Although current guidelines recommend measurement of serum lipids after admission with an ACS, less than half of these patients have serum lipids measured within 24-hours of admission [10-12]. This is of importance because in hospital lipid testing and early

Table 3: Results from the coronarography.

normal coronarographic finding	5 (8,33 %)
1-vessel disease	39 (65 %)
2-vessel disease	12 (20 %)
3-vessel disease	4 (0,67 %)

Table 4: PCI interventions.

stent	51 (85 %)
CABG	1 (0,17 %)
aspiration of thrombus	2 (3,33 %)
without intervention	6 (10 %)

Table 5: Lipoprotein particles among patients with acute coronary syndrome.

	patients	controls	p
VLDL	40,00 ± 1,72	23,00 ± 1,64	‹ 0,0001
large IDL	31,03 ± 9,40	22,71 ± 5,22	‹ 0,0001
middle IDL	13,00 ± 1,23	8,00 ± 3,30	‹ 0,0001
small IDL	12,00 ± 0,91	17,00 ± 1,65	‹ 0,0001
large LDL	35,93 ± 16,42	40,23 ± 10,60	0,1905
middle LDL	21,00 ± 1,71	11,00 ± 2,34	‹ 0,05
small LDL	3,00 ± 1,79	0,00 ± 0,28	‹ 0,001
large HDL	10,00 ± 0,89	18,00 ± 1,53	‹ 0,0001
middle HDL	18,00 ± 0,79	25,00 ± 0,73	‹ 0,0001
small HDL	4,00 ± 0,43	6,00 ± 0,47	0,07

initiation of statin use in patients with an ACS is associated with decreased morbidity and mortality when administered early after admission [13,14].

LUNAR Study showed, that mean lipid levels vary relatively little in the 4 days after an ACS and can be used to guide selection of lipid lowering medication [3,12]. Most recent studies showed less pronounced changes in cholesterol levels after acute coronary syndromes [12,15]. Whole lipid profile estimation among the ACS patients is important including VLDL and IDL particles, as also carrying the certain atherogenic potential [14-16].

The role of LDL cholesterol in the process of atherosthrombosis is well known. We could demonstrate, that the most atherogenic small dense LDL particles are present during the acute phase of myocardial infarction. These are not seen among healthy controls. The relationship between the HDL family and atherosclerotic disease seems to be more complex as usually is accepted in wide clinical praxis. Their exact prognostic role for the plaque stabilization is not clearly defined, too. We could demonstrate, that the concentrations of total HDL cholesterol its size under pathological condition - ACS the significant shift from larger to smaller HDL particles is the certain feature. The explanation for this phenotype among patients can be, that the HDL cholesterol fraction has disturbed functional structure as a consequence of impaired function of small HDL particles in trapping and inactivating the constantly generated free radicals. By accumulation of these substances the whole HDL population is becoming dys - functional. As a result of this process the size of HDL particles can be crucial for the pathophysiological basis of atherogenic dyslipidemia (↑ TAG, ↓ HDL, ↑ apoB, ↑ total cholesterol/HDL, ↑ small dense LDL). Similiar findings have been reported by several authors (5.6). Thus HDL profile under ACS shows a constellation that can be considered as dysfunctional and thus countes as a residual risk contributor.

Patients with ACS are still in their high risk of early and late cardiac and all - cause mortality. Improvement of their outcome was reached with early hypolipidemic statin treatment, leading to vulnerable plaque stabilization as well as with their other pleiotrophic effects [17-19]. However among these patients still very high residual cardiovascular risk is present [20,21]. With new therapeutic treatment modalities (combination of statin with PCSK-9 inhibitors) may lower this high residual risk in the future [22-24].

It is becoming known that not just the amount of the lipid fraction but its composition is that what matters. Besides the complex structural and functional diversity of lipid size can be the lipoprotein subfraction analysis an important new biomarker for the global cardiovascular risk and treatment efficiency evaluation.

CONCLUSIONS

Current trends in cardiovascular lipidology are going to try to uncover the extended role of lipoproteins in health and as well as in disease. Novel markers for more effective estimation of atherothrombotic cardiovascular risks are needed. Among them also very low and intermediate lipoproteins are considered, too. And the concept of dysfunctional lipoproteins should have implications for the treatment of dyslipidemia among acute coronary syndrome patients. Measurement of the whole lipid spectrum at the time of the onset of acute coronary syndrome is of clinical importance for the outcome. Patients suffering from ACS of younger ages significant increase of VLDL as well as large and medium size of IDL - particle sizes were measured at time of the event comparing to the controls. Thus carrying the certain significant atherogenic potential they contribute to that of increased small dense LDL-C as well as less protective medium and small HDL-C particles. The clinical use of advanced lipoprotein subfraction capabilities brings additional benefits in blood lipid analyses and subsequent risk prediction with tailored secondary interventions.

Strength of the study

Measurement of VLDL and IDL-C size particles.

Limitations of the study

Smaller size of the followed ACS patients.

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