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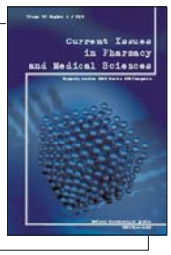

Gamma-glutamyl transferase (GGT) activity and lipid concentration in patient with *coronary artery disease* (CAD)

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ABSTRACT

A serum lipid profiles are established risk factors for atherosclerosis. High sensitivity C-reactive protein (hsCRP) level, are a powerful predictor of future myocardial infarction and cardiac death among apparently healthy individuals. The aim of this study was to investigate serum GGT activity and hsCRP level and others atherosclerosis biochemistry markers in patients with stable coronary artery disease. We studied 94 (women, n=45 and men, n=49), mean age was 64.8±9.7 years, consecutive patients with stable coronary artery disease (CAD), hospitalized in the Department of Cardiology Cardinal Wyszyński Hospital in Lublin. Patients with acute coronary syndroms (ACS) in history where 53% (n=51) of studied population (unstable angina n=3; no ST elevation myocardial infarction n=17, ST elevation myocardial infarction n=31). The patients with acute and chronic kidney disease, liver diseases, active autoimmune disease, malignancy, thyroids diseases, alcohol disease were excluded from the analysis. The patients had worse laboratory parameters than the reference group. They had increased concentration of TG, hsCRP and GGT activity, and decreased concentration of HDL-C as compared to the reference group. However, ALT activity and creatinine concentration were non-significantly increased vs. the controls. We concluded that dyslipidemia together with GGT activity and hsCRP concentration may be good markers to predict cardio-vascular events and vessels lesions in asymptomatic patients with CAD. However, these results require further studies.

Keywords: gamma-glutamyl transferase, GGT, high-sensitivity C reactive protein, (hsCRP), stable coronary artery disease (CAD)

INTRODUCTION

Coronary artery disease (CAD) is common disorder. In Europen countries, it can be estimated that 20 000–40 000 per million people suffer from CAD. CAD leads to high risk of myocardial infarction, heart failure and disabling disorder [6,7].

A serum lipid profiles are established risk factors for atherosclerosis [3]. High sensitivity serum C-reactive protein (hs-CRP) is used to identify patient with cardiovascular high risk in patients with coronary artery disease and people who have traditional risk factors e.g. smoking, hypertensive, obesity [16]. One of major arterosclerosis risk factors are reactive oxygen species and low density lipoprotein (LDL) oxidation. Major anti-oxidant is glutathione. GGT attend catabolism of glutathione [1].

Correlations between serum GGT and hsCRP levels CAD patients have not been adequately studied. The aim of this study was to investigate serum GGT activity and hsCRP level and others atherosclerosis biochemistry markers in patients with stable coronary artery disease.

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MATERIAL AND METHODS

We studied 94 (women, n=45 and men, n=49) patients with stable coronary artery disease (CAD), hospitalized in the Department of Cardiology Cardinal Wyszyński Hospital in Lublin, in April-May in 2012. Mean age was 64.8±9.7 years. Patients with acute coronary syndroms (ACS) in history accounted for 53% (n=51) of studied population (unstable angina n=3; no ST elevation myocardial infarction n=17, ST elevation myocardial infarction n=31). The studied population without ACS accounted for 47% (n=43). The studied group consisted of patients with arterial hypertension – 76% (n=74), diabetes melitus 28% (n=27), obesity 29% (n =28), overweight 44% (n=43), and 42% (n=41) patients smoked in history and 12 patients were still smoking. Acetylsalicylic acid (75-150mg/D) was received by 92% (n =89) of the patients; statins by 91% (n=88) patients. The patients with acute and chronic kidney disease, liver diseases, active inflammatory diseases,

malignancy, thyroids diseases, alcohol disease, were excluded from the analysis.

Forty-five healthy patients were the reference group (23 women and 22 men, mean age 45.89±14.50 years). They were without hypertensive, coronary artery disease symptoms, obesity. Venous blood was drawn after a 14-hour overnight fasting, and plasma was obtained by centrifugation at 3000 rpm at 4°C immediately after blood collection. Samples were either used for measurements immediately or stored frozen at -80°C. Routine laboratory parameters (the level of creatinine and ALT activity) were determined on Cobas Integra analyzer 2000, Roche. Serum GGT activity was measured by the enzymatic colorimetric test (Roche/Cobas Integra analyzer, Manheim, Germany. The total cholesterol (TC), LDL-C, HDL-C was estimated by the enzymatic-colorimetric method, (Roche tests). Triglycerides (TG) were determined using the standard enzymatic technique by Roche tests. Concentration of hsCRP was measured with immunonephelometric methods, Simens Heathcare Diagnostic Product GmbH on a Dade Behring nephelometer BNII System, Germany.

Statistical analysis was performed using the Student-T test for comparison of patients and the reference group. The data are expressed as mean ± standard deviation (SD). The relation between concentration of hsCRP and GGT activity were examined by Spearman's correlation analysis. The statistical significance of all variables was established at $p<0.05$. Statistical analysis was performed using the STATISTICA program (StatSoft, Krakow, Poland).

RESULTS

Lipids and hsCRP level and ALT and GGT activity of patients with CAD are presented in Table1. The patients had worse laboratory parameters than the reference group. They had increased concentration of TG, hsCRP and GGT activity, and decreased concentration of HDL-C as compared to the reference group. However, ALT activity and creatinine concentration were non-significantly increased vs. the controls. The concentration of hsCRP was significantly positively correlated with GGT ($R= 0.285$, $p= 0.006$).

DISCUSSION

Markers of systemic inflammation, such as C-reactive protein (CRP) and interleukin 6 (IL-6), are consistently and independently associated with increased cardiovascular disease (CVD) risk in the general population [13,18]. High sensitivity C-reactive protein (hsCRP) level, are a powerful predictor of future myocardial infarction and cardiac death among apparently healthy individuals [12,13].

Table 1. Lipid and hsCRP concentrations, and ALT and GGT activity in patients and the reference group

	Patients n=94	Reference group n=45
TG mg/dl	152±72***	89±25
TC mg/dl	165±42	179.50±27.03
LDL-C g/dl	94±42	97.92±22.42
HDL-C mg/dl	48±14*	57±8
GGT IU	24±15*	12±9
ALT IU	24±17	17±11
hsCRP mg/L	0.42±0.34***	0.02±0.01
Creatinine mg/dl	0.99±0.39	0.80±0.37

* $p<0.05$; *** $p<0.001$ vs. reference group

Many studies showed that high serum concentrations of hsCRP were associated with stenotic coronary vessels. However, these studies were controversial [8-11]. Taniguchi et al. reported correlations between concentration of hsCRP and the stenotic coronary vessels in patients [17]. However Azar et al. reported no correlations between hsCRP level and the extent score in 98 patients with the stenotic vessels [2].

Our study showed that CAD patients had dyslipidemia and increased hsCRP and moderately increased GGT activity. Moreover, the same patients who had high serum concentration of hsCRP had significantly higher serum GGT activity. These findings strongly suggested a role of GGT in pathophysiology of atherosclerosis. However, the specific role of serum GGT in relation to early atherosclerosis remains unclear, and the relationship between GGT and arterial stiffness has not been fully investigated [15]. Authors showed significant association between serum activity of GGT and serum level of hsCRP in arterosclerosis. These results suggest that GGT is associated with increased CRP levels in males and females, and that GGT is related to arterial stiffness in males [15].

Authors suggest that probably GGT can promote prooxidant effects because GGT retains enzymatic activity, as shown by previous histochemical studies [8, 14]. Patients divided in classes according to their serum GGT levels, mean plaque GGT concentrations were significantly correlated with increasing serum GGT values [8]. The identification of molecular GGT-containing complexes in serum specifically related with enzyme forms accumulating in plaques could provide a means for a better evaluation of risk in atherosclerotic patients, through a stratification based on the serum levels of specific GGT forms [8].

Breitling and al. suggest that moderate positive association of higher serum level of GGT with CVD events and all-cause mortality. They also report correlations between high serum level hsCRP and high serum concentration GGT and other biochemical and clinical parameters. Breitling and al. suggest that GGT activity values might be a useful prognostic marker in secondary

CVD prevention and the availability of this marker in routine clinical practice would allow a broad use for risk stratification [4]. The association of GGT activity and cardiovascular mortality in these patients may be related to left ventricular function, clinical instability, and increased inflammatory activity rather than the extent of CAD [5].

Similarly, Aksakal and al. indicate that baseline serum GGT activity was independently associated with the complexity of the coronary lesions and all cause mortality rate throughout the long-term follow-up, however, baseline serum GGT activity was not associated with the incidence of any revascularization [1].

In our study significant positive correlations between serum GGT activity and hsCRP in patients with CAD showed that moderately increased serum GGT activity like hsCRP can be good marker of progressive CAD. Patients with CAD and higher serum GGT activity require special medical care. Both parameters together may by strongly predictor of CAD events or vessels lesions but further research of GGT activity in progressive CAD are required.

CONCLUSION

We suggest that dyslipidemia together with GGT activity and hsCRP concentration may be good markers to predict ACS or other CAD events and vessels lesions in asymptomatic patients with CAD. However, these results require further studies.

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